IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
THE DEPARTMENT OF HEALTH, EASTERN CAPE PROVINCE	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, EASTERN CAPE PROVINCE	Fourth Respondent
THE DEPARTMENT OF HEALTH, FREE STATE PROVINCE	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, FREE STATE PROVINCE	Sixth Respondent
THE DEPARTMENT OF HEALTH, GAUTENG PROVINCE	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, GAUTENG PROVINCE	Eighth Respondent
THE DEPARTMENT OF HEALTH, KWAZULU-NATAL PROVINCE	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, KWAZULU NATAL	Tenth Respondent
THE DEPARTMENT OF HEALTH, LIMPOPO PROVINCE	Eleventh Respondent

MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, LIMPOPO PROVINCE	Twelfth Respondent
THE DEPARTMENT OF HEALTH, MPUMALANGA PROVINCE	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, MPUMALANGA PROVINCE	Fourteenth Respondent
THE DEPARTMENT OF HEALTH, NORTHERN CAPE PROVINCE	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, NORTHERN CAPE	Sixteenth Respondent
THE DEPARTMENT OF HEALTH, NORTH-WEST PROVINCE	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, NORTH-WEST PROVINCE	Eighteenth Respondent
THE DEPARTMENT OF HEALTH, WESTERN CAPE PROVINCE	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, WESTERN CAPE PROVINCE	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

NOTICE OF MOTION

TAKE NOTICE THAT the abovenamed applicant hereby calls upon the twenty-second respondent to show cause, if any, why an order should not be granted in the following terms:

THAT:

1. The twenty-second respondent's decision, taken on or about 25 January 2022, and purportedly taken under section 15 of the Medicines and Related Substances Act 101 of 1965, to register Pfizer's "COMIRNATY" vaccine, is unlawful, reviewed and set aside.

2. The twenty-second respondent's decision, taken on or about 15 November 2022, to register Pfizer's "Ready To Use (RTU) adult vaccine", is unlawful, reviewed and set aside.

3. The twenty-second respondent's decision, dated on or about 15 November 2022, to register Pfizer's "Dilute To Use (DTU) paediatric vaccine", is unlawful, reviewed and set aside.

4. Insofar as may be necessary:

    4.1. the applicant's failure to institute a review application, in respect of one or more of the decision referred to in paragraphs 1, 2 and 3 above, is hereby condoned, and the time periods prescribed in the Promotion of Administrative Justice Act 3 of 2000 ("**PAJA**") for the institution of review proceedings are hereby extended to the date of institution of this application;

4.2. the applicant is exempted from any obligation to exhaust internal remedies, in respect of one or more of the decision referred to in paragraphs 1, 2 and 3 above.

5. Insofar as any respondent opposes the relief sought in this application, the applicant is awarded costs of this application to be paid by such respondent, jointly and severally with any other respondent so opposing.

6. The applicant is granted such further and/or alternative relief as may be just in the circumstances.

TAKE NOTICE FURTHER that the affidavit of **DR HERMAN JACOBUS EDELING** attached hereto (and all attendant annexures and confirmatory affidavits) shall be used in support of the relief sought.

TAKE NOTICE FURTHER that in terms of Rule 53(1)(b) of the Uniform Rules of Court, the twenty-second respondent is required, within fifteen (15) days of receipt of this notice of motion, to dispatch to the Registrar:

a) All records, including internal memoranda, Pfizer's documentation as it pertains to the COMIRNATY, DTU and RTU vaccines, Pfizer's trial data as it pertains to the COMIRNATY, DTU and RTU vaccines, correspondence with Pfizer as it pertains to the COMIRNATY, DTU and RTU vaccines, directives, policy documents, records of deliberations, minutes of meetings and any other documents relating to the aforementioned impugned decisions.

b) Such full written reasons for the impugned decision(s) as the twenty-second respondent can give in relation thereto.

TAKE FURTHER NOTICE that the applicant may within ten (10) days of receipt of the record from the Registrar, by delivery of notice of motion and accompanying affidavit amend, add to or vary the terms of its notice of motion and supplement its founding affidavit, in terms of Rule 53(4) of the Rules of Court.

TAKE NOTICE FURTHER THAT should any of the respondents desire to oppose the granting of the relief sought, such party shall:

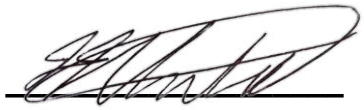
1. within 15 days after receipt of the amended notice of motion and supplementary founding affidavit (if any), deliver notice to the applicants that such party intends to so oppose the application;

2. in such notice of intention to oppose the application, appoint an address within referred to in Rule 6(5)(b) at which such party will accept notice and service of all process in these proceedings; and

3. within 30 days after the expiry of the period afforded to the applicant in terms of Rule 53(4) deliver any affidavit such party may desire in answer to the allegations made by the applicant.

TAKE FURTHER NOTICE that if no intention to oppose is given, the application will be set down for hearing at a date and time to be arranged with the Registrar of the above Court.

SIGNED AND DATED AT PRETORIA ON THIS THE 23RD DAY OF MARCH 2023



HURTER SPIES INC.
APPLICANT'S ATTORNEYS
LOFTUS PARK
2ND FLOOR, BUILDING A
416 KIRKNESS STREET
ARCADIA
PRETORIA, 0007
TEL: 012 941 9239
E-MAIL: eloff@hurterspies.co.za
johann@hurterspies.co.za
REF: D ELOFF/MAT5408

TO: **THE REGISTRAR OF THE HIGH COURT**
PRETORIA

AND TO: **THE FIRST RESPONDENT**
THE MINISTER OF HEALTH
CIVITAS BUILDING, FLOOR 20
CORNER STRUBEN AND THABO SEHUME STREETS
PRETORIA
C/O THE STATE ATTORNEY, PRETORIA
316 THABO SEHUME STREET
PRETORIA

AND TO: **THE SECOND RESPONDENT**
DEPARTMENT OF HEALTH
1112 VOORTREKKER RD
PRETORIA
C/O THE STATE ATTORNEY, PRETORIA
316 THABO SEHUME STREET
PRETORIA.

AND TO**:** **THE THIRD RESPONDENT**
EASTERN CAPE DEPARTMENT OF HEALTH
DUKUMBANA BUILDING
INDEPENDENCE AVENUE
BHISHO

AND TO: **THE FOURTH RESPONDENT**
THE MEC: EASTERN CAPE DEPARTMENT OF HEALTH
DUKUMBANA BUILDING
INDEPENDENCE AVENUE
BHISHO

AND TO: **THE FIFTH RESPONDENT**
FREE STATE DEPARTMENT OF HEALTH
CNR. CHARLES & HARVEY RD
CITY CENTRE
BLOEMFONTEIN

AND TO: **THE SIXTH RESPONDENT**
THE MEC: FREE STATE DEPARTMENT OF HEALTH
CNR. CHARLES & HARVEY RD
CITY CENTRE
BLOEMFONTEIN

AND TO: **THE SEVENTH RESPONDENT**
GAUTENG DEPARTMENT OF HEALTH
45 COMMISSIONER ST
JOHANNESBURG, 2000

AND TO: **THE EIGHTH RESPONDENT**
THE MEC: GAUTHENG DEPARTMENT OF HEALTH
45 COMMISSIONER ST
JOHANNESBURG, 2000

AND TO: **THE NINTH RESPONDENT**
KWAZULU-NATAL DEPARTMENT OF HEALTH
NATALIA BUILDING, 11TH FLOOR
330 LANGALIBALELE STREET
PIETERMARITZBURG

AND TO: **THE TENTH RESPONDENT**
THE MEC: KWAZULU NATAL DEPARTMENT OF HEALTH
NATALIA BUILDING, 11TH FLOOR
330 LANGALIBALELE STREET
PIETERMARITZBURG

AND TO: **THE ELEVENTH RESPONDENT**
LIMPOPO DEPARTMENT OF HEALTH
18 COLLEGE STREET
HOSPITAL PARK
POLOKWANE

AND TO: **THE TWELFTH RESPONDENT**
THE MEC: LIMPOPO DEPARTMENT OF HEALTH
46 HANS VAN RENSBURG STREET
POLOKWANE

AND TO: **THE THIRTEENTH RESPONDENT**
MPUMALANGA DEPARTMENT OF HEALTH
OFFICE 14
JASPIS STREET
AEORAND
MIDDELBURG

AND TO: **THE FOURTEENTH RESPONDENT**
THE MEC: MPUMALANGA DEPARTMENT OF HEALTH
GOVERNMENT BOULEVARD
BUILDING 3, RIVERSIDE PARK
EXTENSION 2, NELSPRUIT

AND TO: **THE FIFTEENTH RESPONDENT**
THE NORTHERN CAPE DEPARTMENT OF HEALTH
JAMES EXUM BUILDING
DU TOIT SPAN ROAD
KIMBERLEY

AND TO: **THE SIXTEENTH RESPONDENT**
THE MEC: NORTHERN CAPE DEPARTMENT OF HEALTH
JAMES EXUM BUILDING
DU TOIT SPAN ROAD
KIMBERLEY

AND TO: **THE SEVENTEENTH RESPONDENT**
NORTH WEST DEPARTMENT OF HEALTH
CNR 1ST STREET & SEKAME STREET
MAHIKENG

AND TO: **THE EIGHTEENTH RESPONDENT**
THE MEC: NORTH WEST DEPARTMENT OF HEALTH
CNR 1ST STREET & SEKAME STREET
MAHIKENG

AND TO: **THE NINETEENTH RESPONDENT**
WESTERN CAPE DEPARTMENT OF HEALTH
4 DORP STREET
CAPE TOWN

AND TO: **THE TWENTIETH RESPONDENT**
THE MEC: WESTERN CAPE DEPARTMENT OF HEALT
4 DORP STREET
PROVINCIAL ADMINISTRATION BUILDING, 21ST FLOOR
CAPE TOWN

AND TO: **THE TWENTY FIRST RESPONDENT**
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA
UNION BUILDINGS
GOVERNMENT AVENUE
PRETORIA

AND TO: **THE TWENTY SECOND RESPONDENT**
SAHPRA
BUILDING A
LOFTUS PARK
402 KIRKNESS STREET
ARCADIA, PRETORIA

AND TO: **THE TWENTY THIRD RESPONDENT**
PFIZER
85 BUTE ROAD
SANDOWN
SANDTON

IN THE HIGH COURT OF SOUTH AFRICA
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MEMBER OF THE EXECUTIVE COUNCIL: DEPARTMENT OF HEALTH, NORTH-WEST PROVINCE	Eighteenth Respondent
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THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

FOUNDING AFFIDAVIT

I, the undersigned

HERMAN JACOBUS EDELING

do hereby make oath and state that:-

1. I am an adult male specialist neurosurgeon, medico-legal practitioner, and mediator. I have been engaged in private practice for 40 years.

2. This application has been duly authorised by the Board of the applicant. Pursuant to section 38 of the Constitution, 1996, the applicant brings this case in its own interest, in the interests of its members, and in the public interest. As these papers make clear, the public are being adversely effected by what the applicant (and its members) believes to be a defective exercise of administrative power, and their rights are being infringed. A resolution of the Board of the applicant confirming the authorisation of this application is annexed as "**HE1**", and a confirmatory affidavit of Dr Paolo Brogneri, one of the Directors of the applicant, is annexed as "**HE2**".

3. The facts in this affidavit are, to the best of my knowledge, both true and correct, and, unless the contrary appears from the context of this document, they fall within my personal knowledge. Where I make legal submissions, I do so on the advice of the legal team in this case, and I accept their advice as correct.

4. In this matter, my testimony is predominantly that of a factual nature. To the extent that I opine as an expert, I do so based on my qualifications which are detailed in my *curriculum vitae* annexed as "**HE3**", and my established expertise in medical ethics, general medical science, evidence-based medicine and rational interpretation of clinical studies, scientific and medical articles, and scientific and medical data.

5. In the aforementioned areas of expertise, I have provided evidence to South African Courts in two hundred and thirty-five (235) cases.

6. The opinions I express in this document are based on conclusions I have drawn from a careful consideration of available facts. Where I reference peer-reviewed journal articles, I ask the Court to accept them on the basis that I have satisfied myself of the correctness of the views and conclusions expressed in those articles, given that I have carefully scrutinised and assessed them by applying my aforementioned skillset.

SUMMARY OF THE CASE AND NECESSITY FOR A JUDICIAL CASE MANAGEMENT

7. I am advised that the applicant's legal representatives will, in due course, seek to have this application assigned to judicial case management. In this section, I set out – broadly – the significance of this matter.

8. The SARS CoV-2 (severe acute respiratory syndrome coronavirus 2) virus, which is a strain of coronavirus that causes Covid-19 (coronavirus disease 2019) was first identified in an outbreak in the Chinese city of Wuhan in December 2019. From that point on, it spread rapidly throughout the world causing illness, death and global panic.

9. Following what was trumpeted as a necessary, herculean, and collaborative scientific effort, numerous vaccines flooded the market in the hopes of providing a panacea to the Covid-19 pandemic. Those vaccines were all developed and trialed

under severely truncated time periods. These vaccines were developed and trialed in a matter of months.

10. Vaccines normally take between ten to fifteen years from trial to market.

11. Amongst these vaccines was the Pfizer BioNTech BNT162b2 mRNA Covid-19 Vaccine, branded in South Africa as "Comirnaty" ("Comirnaty"). According to a press release by SAHPRA, the Comirnaty vaccine is authorised for use in South Africa by SAHPRA in adults and children aged 12 years and older". Comirnaty was (and continues to be) marketed as "safe" and "effective".

12. Comirnaty has now been supplemented by the authorisation of the adult "Ready to Use" vaccine ("RTU vaccine"), and the paediatric "Dilute to Use" vaccine ("DTU vaccine") – both based on the same mRNA technology.

13. South Africa did not conduct its own independent trials of Comirnaty, the RTU vaccine or the DTU vaccine. My understanding is that SAHPRA relied solely on datasets provided by the very party contractually responsible for *commercializing* these vaccines – Pfizer. There is a fundamental conflict of interest at play, cloaking the registration of these vaccines in irrationality.

14. Prior to the release of Comirnaty, mRNA had never been successfully tested – let alone used – in combatting infectious diseases such as Covid-19. It had been tested as a possible intervention against cancers, and, to a limited and unsuccessful extent, as a potential intervention against HIV-1. It had not previously been tested in any human trials against SARS-CoV-2, the causative agent of Covid-19, or against any other coronaviruses.

15. In this case, I set out – in this affidavit - clear evidence showing that Pfizer's vaccine trial for Comirnaty was a whitewash – mired by what appears to be substantial data manipulation, data inaccuracies, and inaccurate outcomes. It is difficult to avoid the conclusion that this misled global regulators, like the twenty-second respondent ("**SAHPRA**") into granting authorization for Comirnaty, to the detriment of public health.

16. Global real-world data, in the form of official data from Governments around the World, as well as vaccine adverse event monitoring systems, and scientists and doctors on the ground are sounding the alarm about serious adverse events (including blood clotting disorders, cardiac disorders, neurological disorders, autoimmune disorders, pregnancy and fertility issues and aggressive cancers) arising out of the inadequately tested Comirnaty vaccine.

17. Battling the tide of information suppression and "cancellation" of unpopular opinions, medical and scientific experts around the world are now succeeding in publishing these adverse events, as well as the mechanisms causing them, in established peer-reviewed journals.

18. This application is a call on Pfizer to explain its conduct for public scrutiny. It is also a call on the South African regulators and Government to hold Pfizer to account and to act in the best interests of the South African public. As a last resort, the applicant humbly requests this Court to come to the aid of bodies like the applicant, in the interests of the health of the South African public.

19. I will, in this affidavit, demonstrate that the Comirnaty vaccine is not (and should never have been branded as) "safe" and/or "effective".

THE STRUCTURE OF THESE PAPERS

20. These papers are structured a follows:

20.1. First, I set out the parties to the litigation.

20.2. Second, I deal with the admission of the hearsay evidence contained in these papers.

20.3. Third, I apprise the Court of the various experts whose testimony stands in support of this case.

20.4. Fourth, I deal with the Vaccine Adverse Events Reporting System ("VAERS") and the alarming safety signals that it is showing regarding adverse events associated with Pfizer's vaccines. VAERS was created in the United States in 1990 by the Food and Drug Administration (FDA) and Centres for Disease Control and Prevention (CDC) to receive reports of Adverse Events ("AEs") that may be associated with any vaccine that goes to market. It is widely known as one of the world's foremost adverse events reporting systems. In relation to Pfizer's vaccines, it is already showing drastic increases (of hundreds or thousands of percentage points) in adverse events such as cancers, deaths, disability, fertility issues, and adverse events in children compared to all other vaccines over a decade long period. I put this section upfront in order to apprise the Court of the gravity of the problem that the remainder of the papers tackle.

20.5. Fifth, I detail the collaboration between Pfizer and BioNTech that led to the development and mass marketing of Pfizer's vaccines. In this section, I apprise the court of the reasons that Pfizer's intentions and motivations, as they pertain to the conduct of the clinical trial in question, fall to be treated with substantial skepticism.

20.6. Sixth, via information provided by an mRNA expert, I explain the mRNA technology in the Comirnaty vaccine, and the mechanisms through which it operates in the human body. This section details the potential harms and unknowns associated with the vaccine. With reference to peer-reviewed articles (contained in the relevant supporting affidavit) the section demonstrates links between the mRNA technology and conditions such as autoimmune diseases, aggressive deadly cancers, severe inflammatory conditions, prion diseases (contagious untreatable diseases resulting in the gradual decline of brain function leading to personality changes and death), myocarditis, blot clotting, impaired fertility, miscarriages and spontaneous abortions.

20.7. Seventh, I detail the Pfizer trial. I set out the trial protocol and explain what was trialed and what was not trialed, and compare this to the stated outcomes and the government narrative. I detail Pfizer's 2-month trial data and their 6-month trial data, and highlight data anomalies and factual inaccuracies. In particular, I detail evidence in the trial data that shows lack of effectiveness at preventing disease or death, as well as subsequent surveillance data that shows lack of effectiveness at preventing disease or death. I also detail evidence of severe adverse

events as per post-authorization pharmacovigilance, and explain how Pfizer has torpedoed the collection of any adequate long-term safety data in their "randomized controlled trial".

20.8. Eighth, I set out reports from two local medical practitioners to demonstrate to the Court that the adverse events that are signaled by the data canvassed elsewhere in the papers, are manifesting on the ground locally. I can attest to the fact that many medical practitioners are scared to speak up about what they diagnose or suspect as vaccine injuries. In the preparation of these papers, we approached twenty-two doctors from around the country who confirmed vaccine injuries seen in their practices. Only two of those doctors were willing to provide evidence on affidavit due to fear of reprisal. They explained that they had seen what had happened to those doctors (such as Dr Susan Vosloo) who had warned against the Pfizer injections: they had been sidelined, attacked viciously in the press, and harassed by their professional bodies, and explained further that they were not willing to subject themselves to that onslaught for the sake of this case. They had not even reported the adverse events to SAHPRA because of the same fear, and because SAHPRA's pharmacovigilance reporting system is so complicated and time consuming as to be prohibitive. Over and above this, it has been difficult terrain for doctors to navigate because the State's official narrative has been that these vaccines are "*safe and effective*", and any information to the contrary has been heavily suppressed. This means that no official guidance has been forthcoming

to doctors in terms of how to diagnose and treat vaccine injuries. I ask the Court to bear this in mind when dealing with this leg of the evidence.

THE PARTIES TO THE LITIGATION

21. The applicant is the Freedom Alliance of South Africa ("FASA"), a registered non-profit company domiciled and headquartered at 49 Victoria Rd Camps Bay Cape Town South Africa, 8005. As detailed more fully in Dr Brogneri's affidavit, FASA is an organisation principally committed the promotion and protection of human rights, and its core objectives include the promotion of equal rights, the expansion of freedoms, access to information without censorship and one-sided narratives, and equality and protection for all independent men and women of South Africa.

22. The first respondent is the Minister of Health, the member of the national executive responsible for the national Department of Health and National Health Policy as well as the administration of Public Health ("the Minister"). The Minister's principal place of administration is at Civitas Building, Floor 20, corner Struben and Thabo Sehume Streets, Pretoria and in the care of the State Attorney, Pretoria, at 316 Thabo Sehume Street, Pretoria. The incumbent Minister is Dr Joe Phaala.

23. The second respondent is the Department of Health. It is the executive department of the national government that is assigned to oversee healthcare in South Africa. Of relevance to this case, and pursuant to GN 1502 in Government Gazette 45487 of 15 November 2021, it is the authorised seller of all vaccines, including the Comirnaty vaccine, the Pfizer Ready To Use Adult vaccine and Pfizer's Dilute To Use Paediatric vaccine. The second respondent's place of business is 1112

Voortrekker Rd, Pretoria care of the State Attorney, Pretoria, at 316 Thabo Sehume Street, Pretoria.

24. The third respondent is the Eastern Cape Department of Health. It is the executive department responsible for healthcare in the Eastern Cape. Its place of business is in Bisho, Eastern Cape.

25. The fourth respondent is the Member of the Executive Council of the Eastern Cape Department of Health cited in her capacity as the head of the Department of Health in the Eastern Cape, and having the responsibilities as set out in section 25 of the National Health Act 61 of 2003. Her place of business is in Bisho, Eastern Cape.

26. The fifth respondent is the Free State Department of Health. It is the executive department responsible for healthcare in the Free State. Its place of business is at Cnr. Charles & Harvey Rd, City Centre, Bloemfontein.

27. The sixth respondent is Member of the Executive Council of the Free State Department of Health cited in his capacity as the head of the Department of Health in the Free State, and having the responsibilities as set out in section 25 of the National Health Act 61 of 2003. His place of business is at Cnr. Charles & Harvey Rd, City Centre, Bloemfontein.

28. The seventh respondent is the Gauteng Department of Health. It is the executive department responsible for healthcare in Gauteng. Its place of business is 45 Commissioner St, Johannesburg, 2000.

29. The eighth respondent is the Member of the Executive Council of the Gauteng Department of Health cited in her capacity as the head of the Department of Health in Gauteng, and having the responsibilities as set out in section 25 of the National Health Act 61 of 2003. Her place of business is 45 Commissioner St, Johannesburg, 2000.

30. The ninth respondent is the KwaZulu Natal Department of Health. It is the executive department responsible for healthcare in KwaZulu Natal. Its place of business is Magwaza Maphalala St, Dalbridge, Durban.

31. The tenth respondent is the Member of the Executive Council of the KwaZulu Natal Department of Health cited in his capacity as the head of the Department of Health in Gauteng, and having the responsibilities as set out in section 25 of the National Health Act 61 of 2003. His place of business is Magwaza Maphalala St, Dalbridge, Durban.

32. The eleventh respondent is the Limpopo Department of Health. It is the executive department responsible for healthcare in Limpopo. Its place of business is College Ave, Hospital Park, Polokwane.

33. The twelfth respondent is the Member of the Executive Council of Limpopo cited in her capacity as the head of the Department of Health in Limpopo, and having the responsibilities as set out in section 25 of the National Health Act 61 of 2003. Her place of business is 46 Hans van Rensburg Street, Polokwane.

34. The thirteenth respondent is Mpumalanga Department of Health. It is the executive department responsible for healthcare in Mpumalanga. Its place of business is office 14, Jaspis St, Aeorand, Middelburg.

35. The fourteenth respondent is the Member of the Executive Council of Mpumalanga cited in her capacity as the head of the Department of Health in Mpumalanga, and having the responsibilities as set out in section 25 of the National Health Act 61 of 2003. Her place of business is 7 Government Boulevard, Building 3, Riverside Park, Extension 2, Nelspruit.

36. The fifteenth respondent is the Northern Cape Department of Health. It is the executive department responsible for healthcare in the Northern Cape. Its place of business is at James Exum Building Du Toit Span Road Kimberley.

37. The sixteenth respondent is the Member of the Executive Council of the Northern Cape cited in his capacity as the head of the Department of Health in the Northern Cape , and having the responsibilities as set out in section 25 of the National Health Act 61 of 2003. His place of business is James Exum Building Du Toit Span Road Kimberley.

38. The seventeenth respondent is the North West Department of Health. It is the executive department responsible for healthcare in the North West. Its place of business is Cnr 1st Street & Sekame Street, Mahikeng.

39. The eighteenth respondent is the Member of the Executive Council of the North West cited in his capacity as the head of the Department of Health in the North West, and having the responsibilities as set out in section 25 of the National Health Act 61 of 2003. His place of business is Cnr 1st Street & Sekame Street, Mahikeng.

40. The nineteenth respondent is the Western Cape Department of Health. It is the executive department responsible for healthcare in the Western Cape. Its place of business is 4 Dorp Street, Cape Town.

41. The twentieth respondent is the Member of the Executive Council of the Western Cape cited in her capacity as the head of the Department of Health in the Western Cape, and having the responsibilities as set out in section 25 of the National Health Act 61 of 2003. Her place of business is 4 Dorp Street, Provincial Administration Building, 21st Floor, Cape Town.

42. The twenty first respondent is President of the Republic of South Africa, cited in his capacity as head of state and head of the national executive with his principal place of administrative business at the Union Buildings, Government Avenue, Pretoria.

43. The twenty second respondent is the South African Health Products Regulatory Authority ("SAHPRA"), established as an organ of state under section 2 of the Medicines and Related Substances Act 1010 of 1965. It has its principal place of business at Building A, Loftus Park, 402 Kirkness St, Arcadia, Pretoria.

44. The twenty third respondent is Pfizer, a company registered and incorporated in terms of the company laws of South Africa. It is the manufacturer of the vaccines sought to be interdicted in this application. Its registered place of business is 85 Bute Rd, Sandown, Sandton.

ADMISSION OF HEARSAY EVIDENCE

45. These papers contain hearsay evidence. The applicant humbly requests that the Court admit that evidence in the interests of justice under section 3(c) of the Law of Evidence Amendment Act 45 of 1988 ("ELAA").

45.1. **First**, reference is made to peer-reviewed journal articles without direct evidence from the authors of those articles. This evidence demonstrates that the vaccines are ineffective and unsafe. There is no prejudice to any of the respondents in admitting this evidence. They, no doubt, will adduce peer-reviewed articles to bolster their argument, and the applicant will not object to the introduction of that evidence. The reasons why the authors of the articles have not given direct evidence in this application follow. The relevance to the case is beyond question, and there are safeguards around its reliability and credibility because the articles are sourced from peer-reviewed journals. The peer-review process helps to ensure the accuracy, reliability, and credibility of scientific papers by subjecting them to rigorous scrutiny by experts in the same field. The peer-review process is sufficient to secure the probative value of the articles annexed. The process involves a number of steps:

45.1.1. Submission: The author(s) submit their paper to a journal for consideration.

45.1.2. Editorial evaluation: The editor of the journal evaluates the paper to see if it meets the minimum requirements for publication. If it does not meet the requirements, it may be rejected at this stage without being sent for peer review.

45.1.3. Selection of reviewers: If the paper passes the initial evaluation, the editor will select two or more experts in the same field as the paper to review it.

45.1.4. Peer review: The reviewers read the paper and evaluate its quality, relevance, and originality. They may suggest changes or improvements, or they may recommend that the paper be rejected if they find major flaws or if it does not meet the journal's standards.

45.1.5. Decision: Based on the feedback from the reviewers, the editor makes a decision on whether to accept or reject the paper. The author(s) are informed of the decision and, if necessary, are given the opportunity to revise the paper and resubmit it for further consideration.

45.2. **Second**, comprehensive reference is made to read-world data sets without the direct evidence of the statisticians responsible for producing or compiling that data. One such set of data, for example, is data released by the UK government. In assessing whether it is in the interests of justice to admit this category of evidence, it is important to understand why it has been necessary to rely on the data published from other governments. The primary reason for this is that our own government has not been publishing the relevant vaccine-related statistics. On 10 August 2021, I wrote to the Honourable President requesting the publication of relevant vaccine-related statistics. I attach that email (which I sent five times) and the four responses I received collectively as "**HE5**". Specifically, I asked for the following:

> *"Track and publish daily statistics on the numbers (and proportions) of vaccinated individuals who (a) have any serious health issue; (b) have been admitted to hospital for any reason; and (c) who have died for any reason; as well as (d) the number (and proportion) of hospitalized individuals who have been vaccinated."*

> *Direct the authorities to immediately ensure full transparency in the collection of data and the reporting of adverse events, as well as numbers of all deaths, the causes thereof and contextual information, such that simple, easy to understand reports become openly available on the official SA Coronavirus website on a daily and annualized basis."*

45.3. The Presidency responded to me promising that they would make contact. This did not happen. Despite pleas for the relevant vaccine-related data, none was forthcoming.

45.3.1. On 7 September 2021, having not heard back from the Presidency, I wrote to the Minister of Health and echoing the pleas made to the President. In that letter, annexed as "**HE6**", I made it clear that my requests for data were supported by 3510 other concerned citizens. I received no reply.

45.3.2. In the context of the South African Government having chosen to not make vaccine-related data publicly available, it would be unjust to prevent the applicants from relying on data from other countries who have published such data. Those data sets are simply the best we have.

45.3.3. In the context of the absence of South African data, the international data is highly probative and should be admitted.

45.3.4. The respondents are free to counter it with local datasets should they choose a level of transparency before this Court that they were not inclined to afford to the South African people.

45.4. **Third**, Pfizer's 2-month and 6-month reports containing the data supporting the safety and efficacy profiles of the relevant vaccines are also referenced. Pfizer is a party in this application.

DELAY AND THE EXHAUSTION OF INTERNAL REMEDIES

46. The Comirnaty vaccine was registered in January 2022. In February 2022, an organisation called "Free the Children Save the Nation" ("FCSN") instituted an appeal process under the Medicines and Related Substances Act against the registration of the Comirnaty vaccine.

47. FCSN's grounds of appeal were similar to the grounds on which the applicant relies in this application – irrationality. To date, a year later, an appeal panel still has not been constituted under the Act, due to delays occasioned primarily at the hands of the Minister of Health and SAHPRA, who have still not nominated members for the appeal panel.

48. The applicant was aware of the FCSN's internal appeal, and decided that the most responsible course of action was to allow that process to unfold.

49. However, the severe, unwarranted, and inexplicable delays in the finalization of that appeal left the applicant with no option, but to approach this Court.

50. A further reason the applicant has decided to approach this Court is that the vaccination campaign is now being heavily targeted at children. The safety and efficacy concerns raised by the evidence in this case merited a direct approach to this Court. This is because it is unlikely that the internal appeal process will definitely resolve the issues arising from the impugned decisions. On the contrary, findings of our courts are binding on all.

51. The issue of delay does not arise in the context of the RTU and DTU products. Those products were authorised on 15 November 2022.

52. Given the scope of these papers, and the length of time required to prepare them, there is also no unreasonable delay that could possibly bar the applicant from a review.

53. With the internal appeal (referred to above) having ground to a halt, consultations for this case commenced in late November 2022. The process of assembling the relevant evidence and expert testimony commenced in late December 2022, and commencement of the drafting of these papers began in earnest in or around January 2022.

54. The process of reading all the relevant documentation, (and then detailing, and simplifying) what is extremely complex medical and data-based evidence, demanded months of dedicated work.

55. Over and above that, consultations had to be set up with expert witnesses overseas. Those consultations involved complex medical and scientific evidence and occurred over weeks.

56. What therefore emerges from the above is that the interests of justice permit the:

56.1. Condonation of any late institution of the review application, in respect of one or more of the impugned decisions, and the extension of the period prescribed for the institution of a review application to the date in which this application is actually instituted; and

56.2. Exemption of the applicant from any obligation(s) to exhaust internal remedies, in respect of the decisions impugned in this application.

EXPERT TESTIMONY SUPPORTING THE APPLICANT'S CASE

57. This affidavit is supported by evidence from domestic and international independent experts. Prior to including their evidence in these papers, I have consulted with all of these experts, I have taken the effort to:

57.1. verify the accuracy of the information that appears in this document; and

57.2. prior to finalization of the document, I circulated a draft of this document to the relevant experts in order to ensure that they were satisfied with the accuracy of its contents.

58. In circumstances where I have made use of the evidence of other independent expert witnesses, their confirmatory affidavits together with their *curriculum vitaes* are annexed, and their qualifications, their expertise, and the bases for their independent conclusions and opinions are available for the scrutiny of the Court. The expert affidavits attached to these papers are as follows:

58.1. **Dr Jessica Rose:** Dr Jessica Rose is an expert computational biologist, whose affidavit and *curriculum vitae* are annexed as "**HE8**". A computational biologist is a highly trained expert specializing in developing and/or analysing data to obtain useful results and models.

This includes a knowledge of the data itself, and understanding where it comes from and how it is to be used. Dr Rose pursued a Bachelor of Science in Applied Mathematics at Memorial University of Newfoundland, and a Master of Science in Medicine in Immunology at the same institution. She continued with her studies in Israel, having been invited to pursue a PhD in Computational Biology (Viral Kinetic studies on Cytomegalovirus (CMV) and Hepatitis B Virus (HBV)) at Bar Ilan University. Since its completion, she has successfully completed two Post-Doctoral degrees in Molecular Biology, with a focus on Rickettsiology at the Hebrew University of Jerusalem, and Biochemistry, with a focus on Anisotropic Network modeling of ATP-Cassette-Binding Transporter molecule mechanisms at the Technion Institute of Technology. Since completion of the second Post Doctoral degree in December 2019, and the declaration of the global 'pandemic', she has applied her mathematical, computational and modelling expertise to analyzing the Vaccine Adverse Event Reporting System (VAERS) data from the United States. VAERS is a pharmacovigilance tool launched by the U.S. Government in 1990 to provide safety signals not detected in pre-market testing in the context of pharmaceuticals and biologicals such as the COVID-injectable products. She has published her findings twice in the journal "Science, Public Health Policy and the Law" and has another publication co-authored with Dr. Peter McCullough. The first publication is a general analysis, the second is a critical appraisal of VAERS pharmacovigilance and the third is an analysis of myocarditis adverse events reported to VAERS in the context of the Moderna, Pfizer

and Janssen COVID19 injectable products. Her evidence shows alarming increases in adverse events associated Pfizer's vaccines compared to all other vaccines over the course of a decade.

58.2. **Dr Anthony Kyriakopoulos**: Dr Kyriakopoulos is a medical microbiologist and mRNA expert. His supporting affidavit and his *curriculum vitae* are annexed collectively as "**HE9**". His CV shows that he has been researching the molecular genetics of aging and cancer for more than 20 years. During that research he has used mRNA technology extensively in producing two Ph.D. theses and sustaining postdoctoral positions for other colleagues. He graduated from the Faculty of Medicine of the University of London UK, and received a Postgraduate Diploma in Medical Microbiology from The London School of Hygiene and Tropical Medicine London, UK, and a Master's Degree from the Faculty of Medicine, Medical School, University of London UK. In Greece, he completed medical training in Medical - Molecular Microbiology and obtained a Doctorate in Medicine, from the Medical School of the University of Athens. This has been recognised after official panel examination as a Doctorate of Philosophy in Medical Microbiology from The Institute of Biomedical Sciences in the United Kingdom (UK). Currently he is the President of the Hellenic Society of Turin and Fellow of the Institute of Biomedical Sciences UK. He explains that in his expert opinion, the mRNA technology was used prematurely as a weapon against infectious diseases, and that it is causing severe health harms. With reference to peer-reviewed papers, he sets out links

between the mRNA technology and conditions such as autoimmune diseases, aggressive deadly cancers, severe inflammatory conditions, prion diseases (contagious untreatable diseases resulting in the gradual decline of brain function leading to personality changes and death), myocarditis, blood clotting, impaired fertility, miscarriages and spontaneous abortions.

58.3. **Professor Norman Fenton**, whose affidavit and *curriculum vitae* are annexed as "**HE10**" is Professor Emeritus of Risk at Queen Mary University of London (retired as Full Professor December 2022). He is also a Director of Agena Ltd, a company that specialises in artificial intelligence and Bayesian probabilistic reasoning. He is a mathematician by training with a current focus on quantifying risk and uncertainty using causal, probabilistic models that combine data and knowledge (Bayesian networks). He has published 7 books and over 400 peer reviewed articles, and his works cover multiple domains including law and forensics and health. He has been an expert witness in major criminal and civil cases throughout his career. He holds a PhD (1981) in Mathematics, Sheffield University; an MSc (1979) in Mathematics, Sheffield University; a BSc (Class I) in Mathematics, University of London (LSE) 1978; a CEng Chartered Engineer, Member of the IET (since 1987); and a CMath Chartered Mathematician. He is a Fellow of the IMA (AFIMA 1988, FIMA 1998); a FBCS Fellow of the BCS (British Computer Society) since 2005; and a FHEA Fellow of the Higher Education Academy, since June 2019. He completed Expert Witness

Training with Bond Solon under the auspices of Cardiff University Law Dept (2007-2008). He gives evidence confirming my interpretation of the Pfizer data and my interpretation of real world data (including data from the UK). He confirms my assessment of the Pfizer trial data.

58.4. **Dr James Thorp**: Dr Thorp, whose supporting affidavit and curriculum vitae are annexed collectively as "**HE11**" is a Obstetrician-Gynaecologist (OBGYN) practising in the sub-speciality of Maternal Foetal Medicine in the United States. He has been a practising Medical Doctor (M.D.) for forty-three (43) years. He obtained his undergraduate degree (B.A.) in 1975 from Western Michigan University, which is in Kalamazoo, Michigan, majoring in Chemistry, with Biology minor and Math minor, and his Doctor of Medicine in 1979 from Wayne State University School of Medicine, which is in Detroit, Michigan. He has called for a world-wide ban and moratorium on the use of any Covid-19 mRNA vaccines, including the Pfizer vaccine products, in pregnancy until long-term safety data are irrefutable. He agrees with my analysis of Pfizer's protocol and data showing that the Comirnaty vaccine's safety was not tested in pregnant or breastfeeding women. The fact that, despite this, the relevant Government and regulatory authority recommended the product to pregnant or breastfeeding women, or for that matter, to any woman who wants to have children, violates the long-standing golden rule of pregnancy: never ever use an investigational drug, a new substance, a new vaccine, in pregnancy even if there is a potential benefit. To the best of his knowledge and experience, he testifies that there is an increased

risk of the following complications related to the COVID-19 "vaccines": menstrual irregularities, miscarriage, fetal deaths (also known as stillbirths), fetal growth abnormalities, abnormal fetal vascular abnormalities, fetal malformations, fetal arrhythmias and fetal cardiac arrests.

58.5. **Dr Aseem Malhotra**:, whose affidavit and curriculum vitae are annexed as "**HE12**" is an NHS Trained Consultant Cardiologist, and visiting Professor of Evidence Based Medicine. He is twice vaccinated, and stood in public support of the Covid-19 vaccines until the circumstances surrounding the death of his double-vaccinated Father led him to investigate the safety and efficacy of the Comirnaty vaccine. Relying on his assessment of the Pfizer data (which accords with my own), and global data sources, his evidence focuses on his conclusion that Comirnaty is not as safe and effective as we have been told, as well as the rationale supporting his conclusion. Dr Malhotra also testifies to the corruption of the medical fraternity, academia, the mainstream media and health policy makers that led to the perpetuation of the distorted narrative around the Pfizer vaccines.

58.6. **Dr Stephen Schmidt**: Dr Schmidt, whose curriculum vitae and supporting affidavit are annexed collectively as "**HE13**", is a specialist physician and gastroenterologist, and an expert drug trialist. He has been involved in drug trials for over thirty (30) years and has completed trails for the following manufacturing companies: Pfizer, Astra Zeneca,

Janssen Cilag, Novavax, Gilead, Johnson and Johnson, Glaxo Smith, Adcock-Ingram, and the US Defence Force. He holds an MBChB and MMed(Int) from the University of Stellenbosch. From 1990 to 2022 he was part of, or was the responsible principal investigator in, fifty-seven clinical drug trials. His experience as a training trialist and eventual Principal Investigator taught him every skill needed to conduct clinical trials, including the complete administrative management of the trial site, logistics, pharmacy control, dispensing and drug accountability, blood and tissue sampling and shipping, writing of- and updating 72 standard operative procedures detailing every action at the trial site, assessing and understanding novel drug protocols, continuous training of staff and refresher courses in Good Clinical Practice every 2 years, attending international trial commencement meetings, receiving clinical trial monitors and auditors, assessing and management of adverse events of any type, acting as first responder to safety signals observed at the site. He acted as national investigator in several studies and was audited by sponsors' auditors, CRO auditors, the Medical Control Council, SAHPRA and the FDA. Neither of his trial sites ever received a negative audit report. His conduct as a Principal Investigator was based on the ethical principles of national and international institutions . He conducted his trial work in South Africa following the strict ethical guidelines of SA-GCP (South African Good Clinical Practice), the DOH research guidelines and the Constitution of South Africa. He is perfectly placed, therefore, as an expert to comment on Pfizer's trial procedures, and irregularities therein.

THE WORLD'S MOST COMPREHENSIVE AND RELIABLE ADVERSE EVENTS REPORTING SYSTEM SHOWS THAT THE PFIZER COMIRNATY VACCINE CAUSES FAR MORE SERIOUS ADVERSE EVENTS THAN ALL PREVIOUS VACCINES

59. The Vaccine Adverse Events Reporting System ("VAERS") was created in the United States in 1990 by the Food and Drug Administration (FDA) and Centres for Disease Control and Prevention (CDC) to receive reports of Adverse Events ("AE") that may be associated with any vaccine that goes to market. It is widely known as one of the World's foremost adverse events reporting systems.

60. VAERS was created because vaccines can cause adverse events, including death, that may not have been detected in clinical trials. Many times, serious adverse effects of vaccines only emerge once they have been released onto the market.

61. The main goal of VAERS is to act as an early warning system for such events. The reports onto the system are filed primarily by medical practitioners (approximately 70%) who have, as a result of their medical expertise and in their best judgments, concluded that the relevant adverse effect was related to vaccine.

62. The remaining reports stem primarily from family members. In analysing the below data, I ask the Court to bear in mind that false reporting to VAERS would constitute making a false and misleading statement to the US Government which is, in turn, a federal crime. Therefore, the data has a high probability of accuracy.

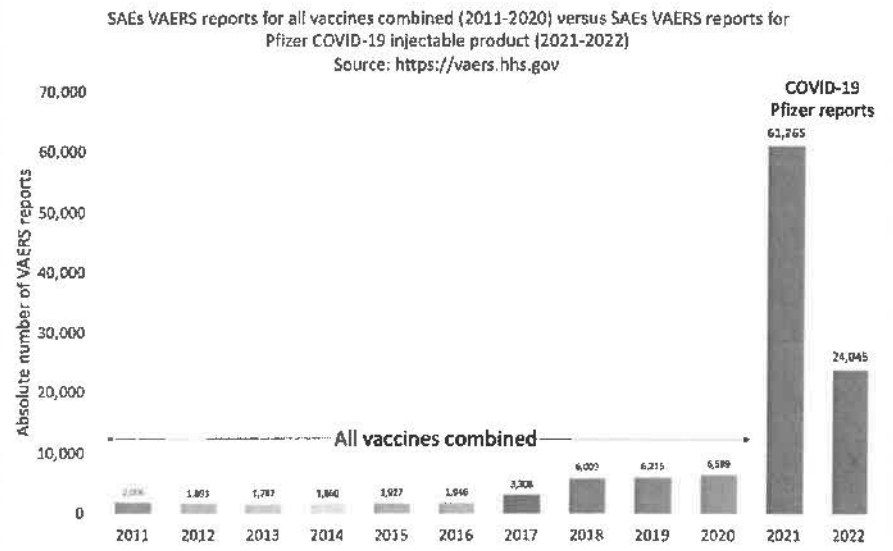
63. False reporting is simply not incentivised in any way. If anything, the risk is of under-reporting, not over-reporting. In any event, the data once filed is vetted by data analysts hired specifically for that purpose. Only those reports that are fully vetted make it onto the system which is where Dr Rose accesses it and analyses it.

64. Despite the fact that the National Childhood Vaccine Injury Act of 1986 (NCVIA) requires health care providers and vaccine manufacturers to report to the Department of Health and Human Services specific AEs following the administration of vaccines outlined in the Act, underreporting is a known imperfection of the VAERS system.

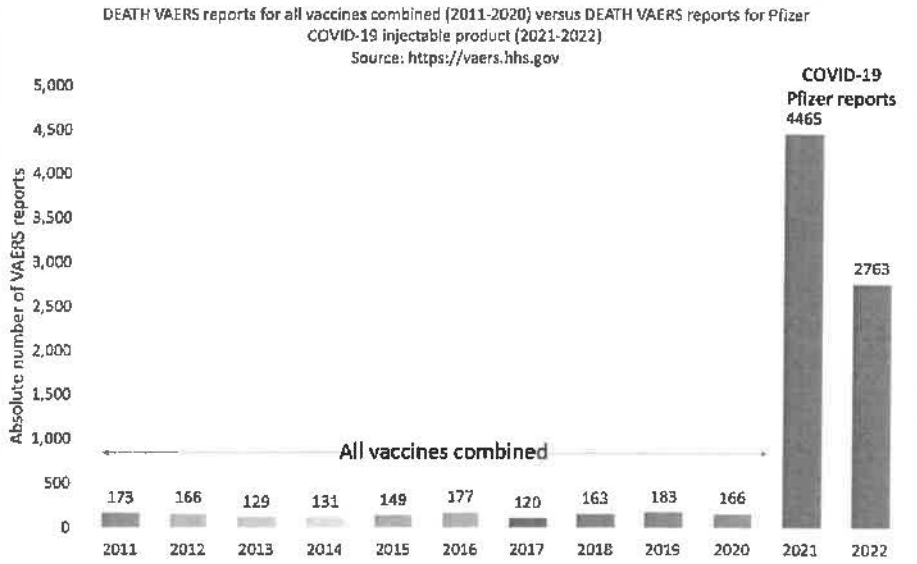
65. There is no consensus on the exact rate of under-reporting, but there is a consensus on the fact that under-reporting exists.

66. Dr. Rose (whose CV and affidavit are annexed above) has been studying VAERS data on Covid-19 vaccines for 2 years and has found alarming results. The Covid-19 Pfizer vaccine reports show higher rates of adverse events than all other vaccines combined over the past decade in every metric analysed. For example:

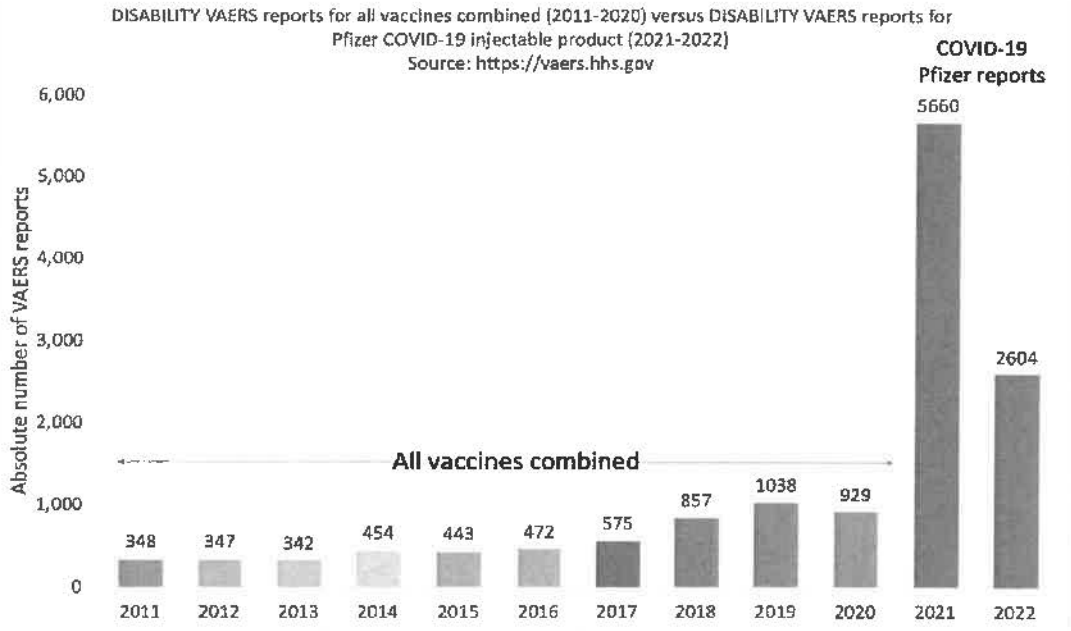
66.1. The severe adverse event reports for Pfizer's Covid-19 vaccine in 2021 and 2022 are 1,727% higher than all other vaccines combined from 2011 to 2020. This data is still being updated for 2022.



66.2. Death reports for the Pfizer Covid-19 in 2021 and 2022 are 2,768% higher than all other vaccines combined from 2011 to 2020. This data is still being updated for 2022. According to the precautionary principle, when a death is linked to a biological or pharmaceutical product, it should be removed from distribution. The precautionary principle is a risk management approach that states that, when an action or policy has the potential to harm human health or the environment, in the absence of scientific consensus, the burden of proof falls on those advocating for the action or policy. This principle calls for cautious action to be taken to prevent harm, even if the cause-and-effect relationships are not fully established scientifically. In the context of the vaccine report, it suggests that if a death is associated with a vaccine, the vaccine should be removed from distribution as a precautionary measure.

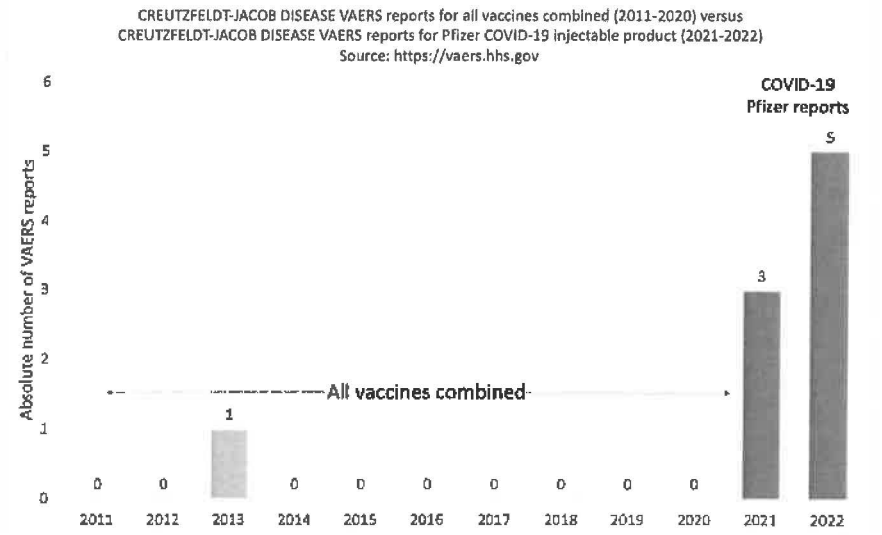


66.3. Reports of disability after receiving the Pfizer Covid-19 vaccine in 2021 and 2022 are 875% higher than all other vaccines combined from 2011 to 2020. The data is still being updated for 2022. Disability can include serious conditions such as a loss of walking ability or tremors from neurological damage, and they often persist.

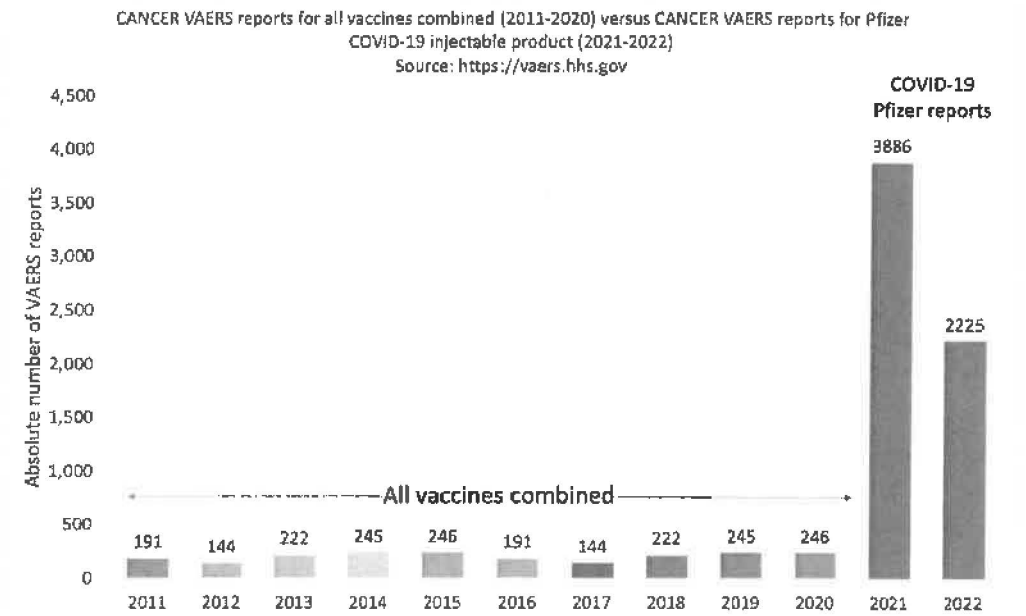


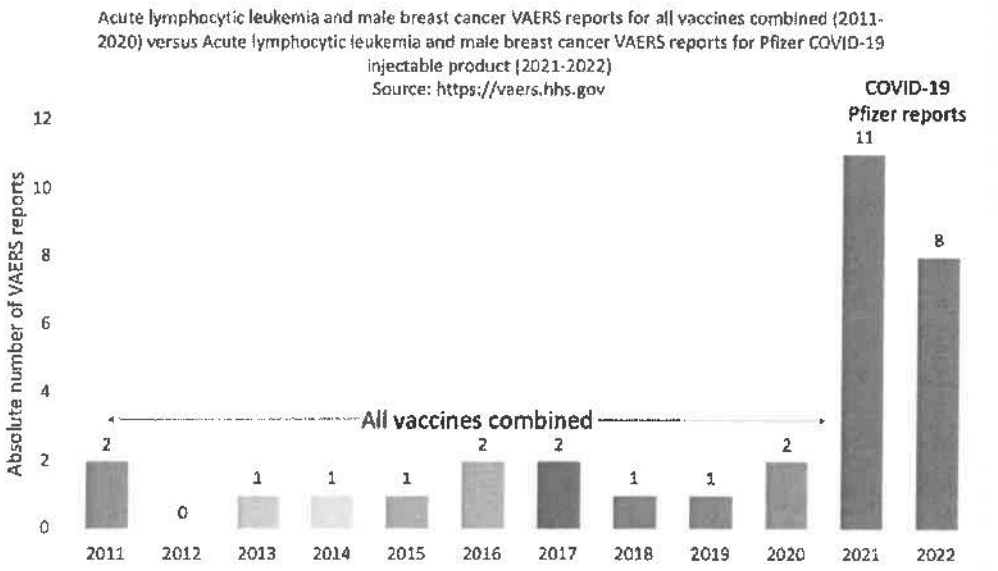
66.4. VAERS reports of Creutzfeldt-Jakob Disease ("CJD"), a serious brain disease, have skyrocketed 2,900% for the Pfizer COVID-19 vaccine compared to all vaccines combined from 2011-2020. CJD is a rare, degenerative, and fatal brain disorder that affects about one in every one million people worldwide.

66.5. This is extremely concerning as the number of reports far exceeds the background reporting rate for CJD is the U.S. The National Institutes of Health (NIH) website states that the average number of reports of CJD, per year, per million individuals in the United States is 1. Thus, if we consider that about 270,000,000 people have been injected at least once with one of the COVID-19 injectable products, then we would expect 270 people in the U.S. to report CJD as a background number of cases. The combined number of reports of CJD in the VAERS domestic data set is 16. Thus if we consider an underreporting factor of 31, (as estimated by Dr Rose and co-investigators), then we are already at 226 individuals above background. That's more than 2.1 times more cases already originating only from VAERS domestic data. These findings are cause for alarm and further investigation is needed.

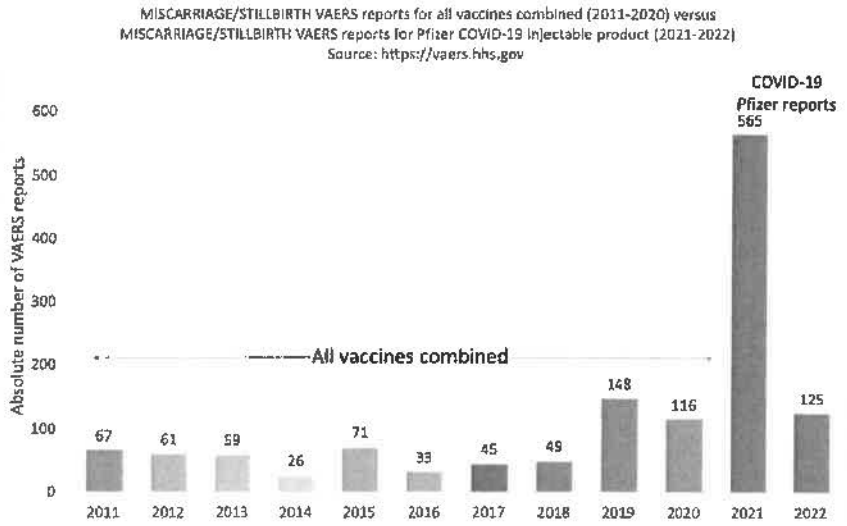


66.6. VAERS reports show a 1,754% increase in cancer cases related to the Pfizer vaccine compared to all vaccines combined from 2011-2020. Rare cancers such as Acute Lymphocytic Leukaemia and male breast cancers are also being reported in older individuals. Data is still being updated for 2022.

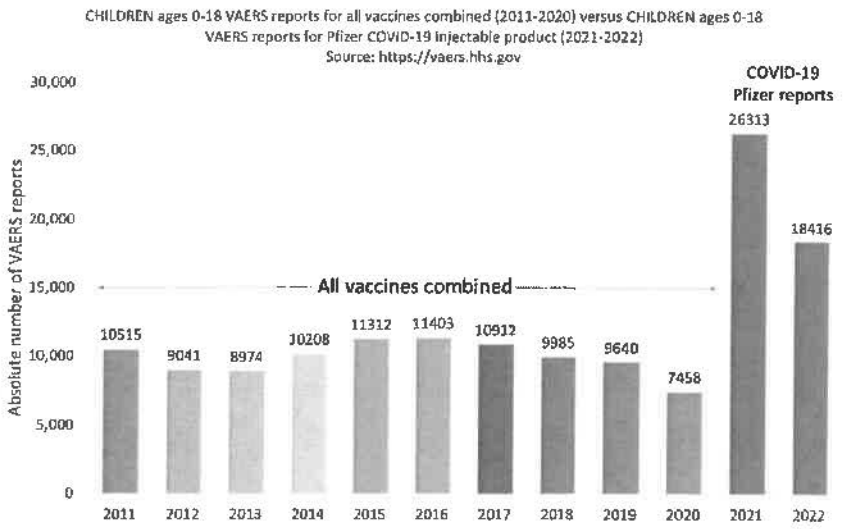




66.7. VAERS reports show a 737% increase in serious pregnancy-related issues (spontaneous abortion, miscarriages, stillbirths) when comparing the mean number of reports for all vaccines from 2011-2020 to a single product (Pfizer) in 2021 and 2022. Reports are still being updated for 2022.



66.8. VAERS reports show 165% increase in adverse events in children after receiving Pfizer vaccine in 2021 compared to all vaccines combined from 2011-2020. This may continue to rise as children have not been vaccinated for as long as adults. This data is based on reports since the CDC Emergency Use Authorization of the vaccine in children.



67. Dr Rose's analysis of VAERS is weighty in its own terms. However, as the learned Judge will realise upon a further perusal of the papers, her findings tie up with (i) the dangers associated with mRNA vaccine technologies as set out by Dr Kyriakopoulos, and, more disturbingly with Pfizer's own listed adverse events of special interest ("AESI") expounded upon later in these papers. An AESI refers to a specific type of adverse event or side effect potentially associated with a medical product or treatment that is closely monitored by regulatory agencies and medical communities due to its potential severity or uniqueness. AESIs are typically selected based on current scientific knowledge and understanding of the medical product or treatment, and they may be considered high-priority or red flag events that warrant prompt investigation and reporting. Examples of AESIs include serious

adverse events such as death, life-threatening conditions, hospitalization, or disability, as well as events that are unexpected or may indicate a safety risk associated with a medical product or treatment.

68. Pfizer's list of Adverse Events of Special interest (which is detailed later in this affidavit) include all the issues catalogued and referenced above by Dr Rose.

THE PFIZER BIONTECH COLLABORATION, AND WHY PFIZER'S INTENTIONS, CLINICAL TRIALS, AND DATA SHOULD BE HANDLED WITH CAUTION.

69. Against the backdrop of the Covid-19 pandemic, and on or around March 17 2020, a collaboration agreement was entered into between Pfizer (an American multinational pharmaceutical and biotechnology corporation) and BioNTech (a German biotechnology company that develops and manufactures active immunotherapies for patient-specific approaches to the treatment of diseases) ("the agreement"). That agreement is annexed in full as "**HE14**".

70. The preamble to the agreement explains the reason for the collaboration between these two companies: Pfizer and BioNTech wished to engage in "*expedited*" collaborative research and development to identify and develop vaccine candidates to aid in combatting the Covid-19 pandemic. They wished to "*seek expedited regulatory approval for [the vaccines], and launch [the vaccines worldwide, excepting China] as quickly as reasonably possible*."

71. BioNTech was the owner or controller of the necessary patents, patent applications, technology, know-how, scientific and technical information and other

proprietary rights and information relating to the identification, research and development of the necessary vaccines. As for Pfizer, the agreement makes plain that its contribution was its "*expertise in development and commercialization of pharmaceutical and biopharmaceutical products*".

72. It is important for the Court to note the singularly commercial tone of the agreement, and to bear the associated consequences in mind when considering the remaining data presented in these papers.

73. The agreement was to produce vaccines as quickly as possible, and to use Pfizer's commercialization expertise to market it throughout the world with haste.

74. There is no indication anywhere in the agreement that this haste in development, commercialization and distribution was to be subject to rigorous safety checks of the vaccine. There is a rationale for this, and the purely commercial, profit-driven nature of the agreement is unsurprising. Pfizer is, after all, an ordinary commercial entity like any other.

75. It is perhaps for this reason that the pharmaceutical industry is amongst the most highly fined industries in the word (for unethical and unlawful conduct): Between 2009 and 2014, the industry in the United States alone received fines totalling $13bn for criminal behaviour that included hiding data on harms and adverse events associated with its products, and manipulation of clinical trial data results. As proof of this, I annex as "**HE15**" a peer-reviewed journal article titled "*Restoring the pharmaceutical industry's reputation*".

76. The aforementioned fact is of contextual import because it adds credence and credibility to the applicant's allegations in this case. In particular, the applicant contends that Pfizer's data on the Covid-19 vaccines is inaccurate.

77. Given that the pharmaceutical manufacturers have no duties of their own to produce safe medical products, the only safety checks and balances come from global regulatory authorities (in the case of South Africa, SAHPRA). Those regulatory authorities require safety and efficacy data before they will approve new medicines (such as the vaccines in question in these papers). That is the only reason that companies like Pfizer conduct clinical safety and efficacy trials.

78. When it came to the marketing of Comirnaty, the authorities (including SAHPRA), in apparent collaboration with Pfizer, encouraged the public to "*trust the science*". Trust is, however, based on transparency.

79. I have reason to believe that the behaviour of Pfizer has been anything but transparent. Pfizer has successfully negotiated deals with several major governments, globally (including the South African Government) that (i) force governments to keep the agreements confidential, and that (ii) indemnify them (Pfizer) against any financial liability in the event of vaccine-related harm.

    79.1. I ask the Court to note that India, the world's largest democracy, refused to conclude the agreement, and to grant Pfizer indemnity for any harms that may be caused by its vaccines. It did not trust Pfizer's data and sought to conduct its own domestic trials on the product. Rather than undertake a local safety and immunogenicity study, Pfizer walked away from the Indian market.

79.2. If Pfizer was confident in the integrity of its trial data, and the safety and efficacy of its product, why would it have shied away from India's request to conduct its own product trials?

79.3. The fact that Pfizer abandoned the Indian market, together with the fact of the confidentiality and indemnity bonds it has forced other Governments to sign, creates serious suspicion about the integrity of Pfizer's intentions, trial work, and subsequent data. I annex as "**HE16**" and "**HE17**" respectively two articles from Reuters verifying these facts.

80. These facts are, however, not the only reasons to exercise caution when assessing the integrity of Pfizer's claims pertaining to its Covid-19 vaccines.

80.1. Dr Aseem Malhotra, whose affidavit and *curriculum vitae* are annexed above, is a British cardiologist and science writer. He is a Fellow of the Royal College of Physicians (FRCP) and a member of the British Medical Association. He is also a Fellow of the Royal Society for Public Health (FRSPH) and a Fellow of the Faculty of Public Health (FFPH). Dr Malhotra has also been an honorary consultant cardiologist at Croydon University Hospital, London. In his published, peer-reviewed article (annexed as "**HE18**") titled "*Curing the pandemic of misinformation on COVID-19 mRNA vaccines through real evidence-based medicine - Part 2*" which I request the Court to accept as his expert opinion, he explains the following:

80.1.1. There is a long-documented history (both through studies and lawsuits) of the strategies in which drug companies hide, ignore or misrepresent evidence about new drugs. Distortion of medical literature and misrepresentation of data by companies keen to expand the marketplace for their product, may result in overprescribing with predictable consequences of millions of patients suffering from avoidable adverse reactions.

80.1.2. In an international survey of respondents from higher education institutions, 14% admitted to knowing a colleague who fabricated, falsified and modified data, and 34% of scientists report questionable research practices that included selective reporting of clinical outcomes in published research and concealing conflicts of interest. This information comes from an official UK parliament enquiry and can be accessed at the web address in the attached footnote[1].

80.1.3. Pfizer has yet to share all the raw data from its pivotal clinical trials for its vaccines. The raw data from clinical trials comprises thousands of pages that have yet to be released for independent scrutiny. This information is sourced from an article published in the British Medical Journal titled "*We must have raw data, now*". The article is annexed as "**HE19**".

[1] https://researchbriefings.files.parliament.uk/documents/POSTPN-0544/POST-PN-0544.pdf.

80.1.4. This lack of transparency is important because what it means is that global approval of the vaccines has not been granted based complete data sets from Pfizer.

80.1.5. A major risk factor for failure to protect the public from the harms of data manipulation is the lack of independence of the global regulators. For example, the FDA's Centre for Drug Evaluation Research (CDER) receives 65% of its funding from the pharmaceutical industry (mainly in the form of user fees). For example, as part of the approval process for its COVID-19 vaccine, Pfizer made a wire transfer to the FDA of $2 875 842 in May 2021. FDA approval for Pfizer's COVID-19 injection duly followed in August 2021 despite recent evidence emerging that the original randomized control trial data suggested a greater risk of serious adverse events from the vaccine than from hospitalisation because of COVID-19.

81. One of the many questions that arise in these papers is this: could Pfizer manipulate data, or present misleading data, or sabotage the conduct of its trials in order to mislead regulatory authorities to secure regulatory approval to protect their own financial vested interests? Unfortunately, the evidence presented in these papers suggests as much.

82. Because of the seriousness of the accusations levelled against Pfizer, and the seriousness of the consequences thereof, Pfizer's domestic offices have of course been cited in these papers.

83. Furthermore, a copy of these papers has also been couriered to the Pfizer head office in New York in the United States.

84. I will return to Pfizer's trials and the data that emanated from those trials later in these papers. For now, though, I want to take the Court through an explanation of the type of vaccine that was developed as a result of this collaborative agreement, namely an mRNA (messenger ribonucleic acid) vaccine, and the facts and concerns associated with this technology.

PFIZER'S COMIRNATY VACCINE'S mRNA TECHNOLOGIES – THE FACTS, AND THE DANGERS

85. The information below is a summary of Dr Anthony M Kyriakopoulos' evidence (contained in his affidavit already annexed above). He is an expert in mRNA technology. It is his expert opinion that the mRNA technology was used (prematurely) as a weapon against infectious diseases, and especially against the SARS-CoV-2 pandemic.

86. The product was rushed to market with grossly inadequate evaluation of either safety or effectiveness. The public was told that this product was "safe" even

though mRNA technology had never before been successfully tested for efficacy and safety in tackling infectious diseases.

87. The result is that an unsafe, inadequately tested product is being administered to the global population.

88. Peer reviewed papers in recent months are showing links between the mRNA technology and conditions such as autoimmune diseases, aggressive deadly cancers, severe inflammatory conditions, prion diseases (contagious untreatable diseases resulting in the gradual decline of brain function leading to personality changes and death), myocarditis, blot clotting, impaired fertility, miscarriages and spontaneous abortions. In the paragraphs that follow, I set out a summary of Dr Kyriakopoulos' reasoning.

88.1. The Pfizer vaccines are synthetic mRNA "gene vaccines". mRNA stands for "messenger RNA". It is a molecule that acts as a blueprint for making proteins.

88.2. Proteins perform many essential functions in the body. mRNA is made by copying a section of DNA, which is the genetic material that contains the instructions for making all the proteins in the body. This process is called transcription.

88.3. The mRNA molecule then leaves the cell's nucleus and travels to the ribosome, which is the cellular structure responsible for making proteins.

88.4. At the ribosome, the mRNA serves as a template for making the relevant protein. Another type of RNA called transfer RNA brings the building blocks of proteins (amino acids) to the ribosome, and the ribosome links these amino acids together in the sequence specified by the mRNA to create a chain of amino acids, which folds into a functioning protein.

88.5. In this way, the cellular mRNA acts as a go-between, transmitting the instructions stored in DNA to the ribosome to produce proteins.

88.6. Pfizer's mRNA "gene vaccines" make use of the above process providing instructions (in the form of synthetic viral mRNA) for the ribosomes to make a synthesized version of the virus SARS-CoV-2's spike protein.

88.7. The theory is that once the SARS-CoV-2 spike protein is produced from the synthetic viral mRNAs in "gene vaccines", the immune system will recognize it as foreign, and mount an immune response, ultimately enabling it to kill the virus by attacking the spike protein of the virus.

88.8. In this way, the Pfizer "gene vaccines" are unlike traditional vaccines. Traditional vaccines contain attenuated (inactivated or weakened) viruses or pieces of viruses, in order to trigger immune responses, whereas Pfizer's novel mRNA "gene vaccines" use the body's protein synthesis production as a mechanism to produce a viral protein in order to trigger an immune response.

88.9. The mRNA in the vaccine is encased in a lipid nanoparticle, which helps it enter cells and be translated into the viral spike protein. After this, the immune system creates antibodies against the spike protein. That is in turn supposed to provide protection against COVID-19 if the person is exposed to the virus in the future.

88.10. In summary, mRNA "vaccines" are supposed to work by using the synthetic mRNA to instruct or "hijack" the cells in the human organism to make a version of the virus's spike protein, thus meant to trigger an immune response that can provide protection against COVID-19.

88.11. Moreover, the mRNAs in the "gene vaccines" are equipped with robust synthetic caps that protect the viral mRNA from breakdown, thereby leading to endurance of the mRNA inside the cell for an unnatural and unwanted duration. This can lead, as Dr. Kyriakopoulos has published in peer-reviewed journals, to cancer, autoimmunity and aging defects.

88.12. Dr. Kyriakopoulos accepts in his affidavit that mRNA technology was, and still is, a promising therapeutical intervention against cancer and genetic disorders. But, he points out that it is crucial to understand that prior to Covid-19, mRNAs had never been successfully trialed as a weapon against infectious diseases such as Covid-19.

88.13. Due to the lack of adequate testing of this technology's efficacy and safety in targeting infectious diseases, the reality is that much remains unknown, and what is known creates serious doubt as to its

effectiveness at preventing disease or death, and more importantly, its safety.

88.14. Even when the mRNA technology has been used (prior to the Covid-19 pandemic) for cancer treatment, there were severe detected side effects in related clinical trials, prompting more safety related clinical research prior to use. For example, Bell's palsy, a form of acute facial paralysis, was also indicated as a serious side-effect of mRNA technology.

88.15. Unsurprisingly, it has also been widely reported as a serious side effect due to the Pfizer "gene vaccines" against covid-19.

88.16. Marketing these vaccines as "safe" and "effective" under the circumstances, was (and still remains), in Dr Kyriakopoulos' expert opinion, a gross misrepresentation that has jeopardized public health and has caused severe disease and death.

88.17. In the following paragraphs I detail some of the real risks associated with the mRNA technology to buttress the view that these viral "gene vaccines" have, to date, not been found to be "safe". The reality is that there are still too many unknowns about how this technology operates in the human body, particularly in the context of expressing a highly toxic spike protein, to qualify this "gene vaccine" as "safe".

88.18. While the science is complex, the immune response to these injections can be described in relatively simple terms, and it is quite distinct from

the immune response to a natural infection with SARS-CoV-2 in many ways.

88.19. The mRNA gene "vaccine" is injected into the deltoid muscle. The injection contains a large number of mRNA molecules coding for a modified form of the Covid-19 virus' spike protein ("the spike protein"), normally produced by the virus. These mRNA molecules are packaged into lipid nanoparticles ("LNP"). These LNPs serve several roles: to protect the mRNA from breakdown, to facilitate its uptake into the cell and to facilitate its release into the cell's cytoplasm. The LNPs also act as adjuvants to further provoke an immune response, and to promote rapid synthesis of the spike protein within the cell, according to the mRNA code.

88.20. Essentially, these nanoparticles also hijack human host cell machinery to get it to synthesize the spike protein, and present it on the surface of the cells, provoking an immune cellular response.

88.21. It is important to understand the differences between the spike protein in the Covid-19 virus, and the spike protein in the Pfizer "vaccines". The virus (and attendant spike protein) enters cells mainly via a specific type of receptor called the ACE2 receptor.

88.22. Those receptors are present only in certain cell types, which means that the virus and attendant spike protein can only enter certain cells, and not others.

88.23. The vaccine is different. The LNP enables the mRNA molecules to enter all cells throughout the human body, where spike protein will then be synthesized. The net effect is that the vaccine results in a greater biodistribution (distribution throughout the human body) of the spike protein than does the virus.

88.24. Notably, the injected nanoparticles are rapidly taken up by immune cells that would not normally be infected by the virus because they have no ACE2 receptors. What could logically result theoretically is an autoimmune response, in which the immune system attacks and removes its own immune cells, because they are displaying a toxic foreign protein on their surface.

88.25. Before the advent of the use of mRNA "gene vaccines" against COVID-19, Dr Kyriakopoulos had contributed to prognose and analyze the causation of autoimmunity by the mRNAs in "gene vaccines".

88.26. Later publications proved his initial medical prognosis and reinforced that mRNAs in "gene vaccines" cause elevation of autoimmune antibodies, which in turn increase the risk of severe autoimmune diseases.

88.27. Enhancing the toxicity even more, the mRNA sequence coding for the spike protein itself is also very different from the sequence present in the RNA of the original SARS CoV-2 virus.

88.28. Most notably, it has been "humanized" by inserting special sequences on both ends that disguise its viral origins. This results in a stealth entry mechanism, that does not provoke the normal immediate response to viral mRNA, which normally serves as an early warning system.

88.29. The developers felt this was necessary because otherwise the mRNA would be destroyed before it ever got a chance to make the spike protein. This "humanization" causes the mRNA to be extremely resistant to breakdown. While most mRNA molecules only survive for a few hours after they are produced, the mRNA in these injections has been shown to still be present in the draining lymph nodes two months after vaccination.

88.30. Following injection of the nanoparticles into the deltoid muscle, the muscle cells rapidly take up the particles and begin producing spike protein at a high rate, which is then displayed on their surface shortly thereafter.

88.31. Circulating immune cells respond to the alarm signals released by the muscle cells by swarming into the arm muscle. They too cannot stop themselves from taking up the nanoparticles and also synthesizing spike protein. They rapidly begin migrating into the lymph system, congregating initially in the lymph nodes under the arm, to begin the process of informing antibody-producing immune cells of the imminent danger.

88.32. Swollen lymph nodes under the arms are normally a signal for breast cancer, but this phenomenon is now often observed following vaccination with the Pfizer vaccines, showing clearly that much of the action is taking place in these lymph nodes.

88.33. The limited animal tracer studies that have been done on the biodistribution of mRNA vaccine nanoparticles injected into muscle have shown that, while the bulk of the product remains localized to the injection site, a substantial amount of the mRNA ends up in the draining lymph nodes, and detectable amounts also show up in multiple organs throughout the body.

88.34. Among organs, the highest concentration is consistently found in the spleen, with the liver and ovaries not far behind, and detectable, although low levels have been found in mouse brains.

88.35. In immunology, the term antigen refers to a foreign molecule (usually a protein) whose presence in the body provokes an immune response, and antibodies are the proteins that are produced by the immune cells (through interactions between B-cells and T-cells) in response to the foreign antigen.

88.36. With subsequent exposures to that same antigen, the antibodies bind to the antigen and interfere with its uptake by cells, thus thwarting an infection with a virus such as SARS-CoV-2.

88.37. Research has shown that immune cells in the spleen release exosomes (small lipid particles) containing the antigen into the external space, and the antibody-producing cells (B-cells and T-cells) take up those exosomes as a central and essential activity during antibody induction.

88.38. In *vitro* experiments with the "gene vaccine" mRNA nanoparticles coding for the spike protein have shown that exposed cells release exosomes containing the spike protein, along with certain microRNAs that alter protein expression in recipient cells.

88.39. Furthermore, this same study showed that microglia (immune cells in the brain) can take up those exosomes and react by inducing an inflammatory response (inflammation in the brain, which can lead to neurological damage).

88.40. In the same experiment, two specific microRNAs were found: miR-148a and miR-590. These microRNAs can weaken the body's response to a signal called the type-1 interferon response, which helps the immune system fight cancer and infections. When immune cells absorb exosomes with these microRNAs, their ability to respond to type-1 interferons is reduced.

88.41. A predicted result is increased risk to cancer and infection by any pathogen. Indeed, there is a strong signal in the Vaccine Adverse Event Reporting System (VAERS), maintained by the United States CDC, for

conditions such as Bell's palsy and shingles in association with the COVID vaccines.

88.42. Many medical practitioners have reported alarming increases in cancer among their patient's following vaccination. Particularly noteworthy is cancer that was in remission resurfacing in an aggressive form. The VAERS database also shows significantly more reports linking cancer to the COVID vaccines than to all other vaccines, particularly breast cancer. This is what Dr Kyriakopoulos predicted in his recent publication even before the cancer reports emerged.

88.43. A likely pathway by which exosomes released by immune cells in the spleen could be taken up by microglia in the brain is via major nerves in the trunk.

88.44. Exosomes are known to be able to migrate along nerve fibers as a transport system to reach distant places. The released exosomes would travel along the splanchnic nerve to a nerve center called a ganglion, whence they can continue along the vagus nerve to reach not only the brain, but also the heart, lungs, liver and gut.

88.45. VAERS contains a huge repository of vaccine adverse events related to the Pfizer vaccines. These events far outnumber events reported for other vaccines over the same time period, and many of the symptoms are typical symptoms of inflammation in the vagus nerve and other

nerves, particularly in the face, such as the auditory nerve, the optic nerve, the trigeminal nerve and the facial nerve.

88.46. The exosomes can also reach, via these nerve conduits, major centers in the brain stem controlling basic life functions such as heart rhythm and heart rate, blood pressure, consciousness, and breathing. Disturbances in these centers, leading to an intense inflammatory response and subsequent nerve damage, can have life-threatening consequences.

88.47. A recent peer reviewed paper published by the late Professor Luc Montagnier (Nobel prize winner for his work on the HIV virus) and colleagues discussed 26 cases, mostly in Europe, of severe Creutzfeldt Jakob Disease (CJD, essentially human MADCOW disease) associated with COVID-19 vaccination.

88.48. In all cases involving the Pfizer "gene vaccine", symptoms first appeared within one month of the second "vaccine". Progression towards paralysis was very rapid, and many of these patients died within three months of the onset of symptoms. All except one of the original 26 are now dead. This is very alarming, as CJD is very rare, with only 1 out of a million people previously diagnosed with it.

88.49. This rare, but severe adverse reaction to the mRNA vaccine is likely due to the fact that the spike protein has prion-like properties.

88.50. A prion is a type of protein that can cause certain diseases in the brain and nervous system. Unlike most pathogens, such as viruses and

bacteria, prions are not composed of DNA or RNA, and they do not replicate by dividing or making copies of themselves. Instead, they cause disease by changing the shape of normal proteins in the body into abnormal, infectious forms.

88.51. Prion diseases are a group of neurological disorders that are caused by prions. They are characterized by a gradual decline in brain function, leading to memory loss, personality changes, and eventually death. Some well-known prion diseases include Creutzfeldt-Jakob disease, Kuru, and variant Creutzfeldt-Jakob disease (vCJD), which is associated with consumption of infected beef in the United Kingdom. Prion diseases are rare, but they are of great concern because they can spread from person to person, and there is currently no cure or effective treatment for these diseases.

88.52. CJD is a prion disease, caused by misfolding of the prion protein, a protein which normally has multiple important roles in neurons but which turns rogue when it misfolds into a toxic structure that precipitates out as a plaque. Dr Kyriakopoulos surmises that the spike protein, given its prion-like properties, acts as a seed to crystallize the prion protein into its misfolded form.

88.53. There are several papers in the literature that have identified certain sequences within the spike protein that are characteristic of prion-like proteins. This property, combined with its ability to reach the brain via exosomes released from immune cells in the spleen, can likely explain

many of the neurological symptoms that people are experiencing in response to these vaccines. Of course, the spike protein produced by the virus could cause similar problems, but an important distinction is that the virus is mostly confined to the lungs in patients with a healthy immune response, whereas the vaccine immediately breaches both the lung- and vascular barriers such as the blood-brain barrier.

88.54. Furthermore, the association of mRNA-spike protein injections with multiple deadly cancers was highlighted in Dr Kyriakopoulos' recent publication.

88.55. The potential molecular reasons for severe autoimmunity due to increased levels of p53 have been recently published in a paper where Dr Kyriakopoulos was first author. That paper unravels the complex reasons why the p53 levels are elevated due to the spike protein.

88.56. The elevated levels of p53 will cause prion and prion related disease since they boost the production of prion proteins within the organism. In many ways, p53 is a protein that is critical for preventing the development of cancer. It acts as a tumor suppressor by regulating the cell cycle and promoting cell death (apoptosis) in cells that are damaged or have the potential to become cancerous. P53 also plays a role in the immune system by regulating the function of immune cells and promoting the activation of the type-1 interferon response, which helps the immune system fight infections and cancer.

88.57. However, increased levels of p53 have been linked to autoimmunity, which is when the immune system mistakenly attacks and damages the body's own tissues. This can occur because p53 can disrupt the normal balance of immune cells, causing them to become overactive and attack the body's own tissues. In addition, high levels of p53 can suppress the type-2 interferon response, which normally helps to control and limit the immune response, leading to further immune system overactivity and autoimmunity.

88.58. Thus, the delicate balance between p53 and other immune regulatory proteins is important for maintaining a healthy immune response and avoiding autoimmunity. This homeostatic balance unfortunately is disrupted in the gene mRNA vaccinated sufferers that develop autoimmune diseases like multiple sclerosis and polyneuropathies.

88.59. A much more common adverse reaction to the vaccine is myocarditis (inflammation in the heart), which is especially affecting young male athletes, but also affects the rest of population, and unfortunately it can result in sudden death.

88.60. Because young people rarely suffer from severe disease when they are exposed to COVID-19, any risk from the vaccine quickly offsets any putative benefits for them. The mechanism leading to this in many ways parallels the mechanism causing neurological symptoms. Exosomes containing the spike protein can easily breach the vascular barrier in the heart via nerve fiber pathways.

88.61. The spike protein has been shown to cause an inflammatory response in the heart, likely related in part to its ability to bind to ACE2 receptors, which are prevalent in heart muscle cells.

88.62. Athletes in particular are known to have significantly more ACE2 receptors in their hearts than those who don't exercise vigorously. Mechanistically, inflammation causes the release of inflammatory cytokines. These cytokines trigger the release of reactive oxygen species (ROS), which damage the heart muscle cells.

88.63. The subsequent infiltration of fibroblasts leads to the production of scar tissue replacing certain portions of the heart muscle, thereby weakening heart function and predisposing to arrhythmias.

88.64. The presence of preexisting myocarditis due to the vaccine can be very dangerous in the context of an adrenalin rush, because the inflamed heart is less able to react appropriately to the excess load induced by the adrenalin response. This can lead to arrhythmias and cardiac arrest, which is often fatal, particularly if emergency assistance to restart the heart is not immediately available.

88.65. There are now several peer-reviewed case studies and epidemiological studies linking fatal myocarditis to the "gene vaccines", and also showing that the risk is much greater from the "gene vaccines" than it is from the disease itself.

88.66. The COVID "gene vaccines" may have serious side effects on platelets, causing severe blood clotting problems. Most of the reports in VAERS show a strong link between the COVID "gene vaccines" and blood clots, including a dangerous condition where a blood clot moves to the lungs (pulmonary embolism). This may be because the "gene vaccine" triggers the body to produce antibodies that attack platelets, leading to clumping and formation of clots. This could happen because the antibodies target the spike protein in the virus, which is similar to proteins found in platelets.

88.67. There may also be a risk of other autoimmune diseases because the spike protein is similar to other proteins in the body that are associated with autoimmune diseases.

88.68. Further, the expression of the spike protein post "gene vaccination" in the testes and ovaries could result in an autoimmune attack against these tissues, leading to impaired fertility. There is a strong signal in VAERS for miscarriages and disrupted menstrual cycles associated with these "gene vaccines".

88.69. One major class of antibodies are the immunoglobulin G (IgG) antibodies. Within that class, researchers have identified three major subclasses categorized as IgG1, IgG2 and IgG4. IgG2 is especially important as it is known to be very effective in stopping the virus from infecting cells. IgG4, on the other hand, is recognized as an anti-

inflammatory antibody that binds to the antigen but does not prevent infection.

88.70. Furthermore, it interferes with the binding of the productive antibodies like IgG2. In studies it has been observed that IgG4 made up only 0.04% of the total IgG pool following the second vaccine, but the percentage of IgG4 after the booster shot rose to nearly 20% on average. This was a complete surprise to the researchers, and it suggests that the vaccines are leading the immune system towards a state of anergy (absence of the normal immune response) possibly due to immune exhaustion.

88.71. Disturbingly, high levels of IgG4 are linked to many autoimmune diseases. On top of this a recent publication describing a rare case of IgG4 related nephritis relapse post the mRNA "gene vaccination" presents a forthcoming great worldwide risk for kidney failure patients receiving the "gene vaccination".

88.72. In a series of autopsy studies in 25 individuals who died unexpectedly from myocarditis, the major prevailing histopathological finding was death due to arrhythmia and heart failure. The cause of these deaths was clarified by the authors of this clinical investigation as a severe complication following the mRNA-spike protein expressing injections.

88.73. In relevance to the mRNA-spike protein expressing injection-produced myocarditis study, it has been found that in all (16 out of 16) patients who received the mRNA and developed myocarditis, the full-length spike

protein persisted in a concentration of 33.9 ± 22.4 pg/mL in their plasma post their second mRNA injection.

88.74. In a recent sudden death incident in a 22-year-old Korean patient who suffered from myocarditis 5 days after the first mRNA-spike protein shot, and died 7 days later, the main histopathological finding from the autopsy performed was extensive band necrosis in the atria and ventricles of the heart. As the authors conclude, "the primary cause of death was determined to be myocarditis, causally-associated with the BNT162b2 vaccine".

89. In summary, Dr Kyriakopoulos states that his expert opinion is that that the mRNA genetic biologics, mistakenly called "vaccines," are producing severe illnesses in a vast section of the population, and, most importantly, cancer, autoimmunity, neurodegeneration and death. They are neither safe nor effective, and therefore it does not make sense to continue to encourage the general population to get repeated boosters.

90. It is his further opinion that the mRNA technology should be reconsidered and, in many ways, can be described as a complete failure in the fight against COVID-19. He recommends that authorities should acknowledge this fact and stop the manufacture and sales of this harmful biologic agent.

91. I now return to the Pfizer trials. In the following section, I take the Court through the conduct of the Covid-19 vaccine trials, the data that emanated therefrom, and the concerns around both the trial conduct and the data.

THE PFIZER TRIALS: THEIR DESIGN, CONDUCT, AND DATA

92. On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act, the Secretary of the Department of Health and Human Services in the United States (HHS), determined that there was a public health emergency that had a significant potential to affect national security, or the health and security of United States citizens living abroad, and that involved the virus that caused the Coronavirus Disease 2019 (Covid-19).

93. On the basis of such determination, the Secretary of HHS, on March 27 2020, declared that circumstances existed justifying the authorization of *emergency use* of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act.

94. It was under this Act that Pfizer and BioNTech, who were collaborating in vaccine development, would ultimately seek Emergency Use Authorisation (EUA) in the US for their mRNA vaccines, followed later by boosters, and further Covid-related vaccine products.

95. Pfizer's press release dated 18 November 2020, and annexed as "**HE20**" explains that the clinical trial for the Pfizer BioNTech BNT162b2 mRNA Covid-19 Vaccine

(the Comirnaty vaccine), began in April 2020 and ended on November 18, 2020 (a period of six months).

96. The vaccine's initial 2-month safety and efficacy data was collected during this time period. At the data cut-off date of October 9 2020, a total of 37,706 participants had a median of at least 2 months of safety data available after the second dose, and they contributed to the main safety data set.

The two-month trial data

97. It was on the basis of Pfizer's 2-month data that the Comirnaty vaccine was given Emergency Use Authorization by the FDA in the US on December 11 2020.

98. Pfizer published its 2-month safety data two weeks later, on 31 December 2020, in the New England Journal of Medicine in an article annexed as "**HE21**", and titled "*Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine*".

99. At face value, in the 2-month report, the efficacy findings (as set out by the authors) looked compelling, and the safety findings looked reasonable. The following emerges from the safety and efficacy claims in the 2-month report:

99.1. In terms of safety, the vaccine was considered to have a mild-to-moderate safety profile, with the most common adverse events being pain at the injection site, fatigue and headache.

99.2. The majority of local and systemic reactions were reported by younger participants, but the frequency of severe systemic events was regarded as low and the frequency of serious adverse events was also regarded as low.

99.3. The majority of documented adverse events were mild to moderate and resolved within 1-2 days. No significant safety concerns were identified during the trial, and the vaccine was granted Emergency Use Authorization by the FDA on December 11, 2020.

99.4. In terms of efficacy, the study observed 36,523 participants who had not previously had Covid-19. 8 Cases of Covid-19, with onset at least 7 days after the second dose, were observed among vaccine recipients; and 162 among placebo recipients. This corresponded to a vaccine efficacy calculation, or relative risk reduction (RRR), of 95.0%.

100. The problem is that the published summary of safety and efficacy profiles does not bear scrutiny. The authors did not publish any calculation of absolute risk reduction (ARR), as required in terms of an FDA publication "Communicating Risks and Benefits: An Evidence-Based User's Guide". On page 60 of this Guide, in paragraph 2, the FDA advises "*Provide absolute risks, not just relative risks. Patients are unduly influenced when risk information is presented using a relative risk approach; this can result in suboptimal decisions. Thus, an absolute risk format should be used.*"

101. The authors also did not publish any information about "effectiveness" as opposed to "efficacy". Thorough, independent analysis of the information in the 2-month report raises concerns.

102. A serious issue of concern relates to the conveniently and selectively chosen study population itself, and the blanket vaccine efficacy and safety claims made in the published summary of the trial data.

103. In trials that test for efficacy, it is only possible to make efficacy claims for the population demographics and other circumstances that applied in the trial. For example if you're trialing medicine X, and you test it in adults in the trial, you cannot then claim efficacy or safety for children. The reasons are self-evident. I attach as "**HE22**" the affidavit of Dr Stephen Schmidt, whose expertise is in the conduct of clinical trials.

104. The 2-month report claims that the vaccine has a general 95% efficacy and a "favourable" safety profile. But these claims are misleading. The reason is that the vaccine was not trialed on all the target population demographics. The vaccine was only trialed in healthy individuals over age 16, and those with stable disease. This fact appears from page 49 of the trial protocol (annexed as "**HE23**") which states as follows:

> *"Type of Participant and Disease Characteristics:*
>
> *[...]*
>
> *3. Healthy participants who are determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study.*

Note: Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, can be included. [...]"

105. That means that the efficacy finding of 95% and the alleged "favourable" safety profile only held true for the population demographic on which the vaccine was tested (being healthy individuals over the age of 16). That is what Pfizer should have said in its report - but instead it presented the efficacy finding as being effective, generally, in the population.

106. The problem is that vulnerable portions of the population (individuals over 75 years of age and pregnant/lactating women, for example) were either entirely excluded, or substantially excluded, from the trial.

107. That, in turn, means, that the efficacy and safety findings could not, and should not, have been considered to apply to them – but they were.

108. The result was that Comirnaty, once approved, was marketed and administered to some of the most vulnerable people in society even though there was no efficacy or safety data for those people. Four examples will suffice (though many more can be found):

108.1. First, adolescents below the age of 16 years were excluded from the initial trial. Adolescents between 12 and 15 years of age were only included after the 2-month data had been collected. Notwithstanding this exclusion, the Pfizer 2-month data made a blanket claim of 95% efficacy and a favourable safety profile, which leads one to believe that the

vaccine's safety and efficacy on adolescents is supported by Pfizer's data – but it wasn't.

108.2. Second, and perhaps most alarmingly, pregnant women and women who were breastfeeding, were excluded from the trial. This appears from the protocol at page 42, where the following is stated:

> *"5.2. Exclusion Criteria*
>
> *[...]*
>
> *11. Women who are pregnant or breastfeeding."*

108.3. Notwithstanding this exclusion, the Pfizer 2-month data makes a blanket claim of 95% efficacy and a favourable safety profile, which leads one to believe that the vaccine's safety and efficacy on pregnant women is supported by Pfizer's data – but, again, it was not.

108.4. In fact, Pfizer and BioNTech acknowledge in official documentation that the effect of the vaccine on pregnant woman and unborn babies is wholly unknown.

108.5. I have been provided with an official informed consent for Pfizer's trial (presently underway) of study vaccines to fight the parent SARS-CoV2 virus, the alpha strain, the delta strain and the omicron strain. The informed consent document is annexed as "**HE24**". In clause 1.8.2 of that document, the following is stated:

"It is not yet known whether the use of the study vaccines (which includes the Comirnaty product) in a parent could be harmful to an unborn baby or an infant."

108.6. It is important to note that an informed consent document contains a lay explanation of the totality of all available trial safety data of the drug in the question (Comirnaty). The implication, therefore, of the above statement is that there is no viable trial safety data on the effect of Comirnaty on pregnancy and unborn babies.

108.7. Third, this Court may take judicial notice of the fact that 85% of the people most at risk from Covid-19 were those over the age of 75 years[2], and it was to that age group that the vaccine was most aggressively marketed. The trial should therefore have had proportional numbers of trial participants who were aged over 75 years. But that wasn't the case.

108.8. Instead, those of age 75 and above only represented 4.3% of trial subjects. That figure comes from the fact sheet for healthcare providers administering Covid-19 Pfizer vaccines (annexed as "**HE25**"), where the following is stated:

"Clinical studies of Pfizer-BioNTech COVID-19 Vaccine include participants 65 years of age and older who received the primary series and their data contributes to the overall assessment of safety and efficacy [...] Of the total number of Pfizer-BioNTech COVID-19 Vaccine recipients [...] 4.3% (n=860) were 75 years of age and older.

[2] Source: https://wonder.cdc.gov/bridged-race-v2019.html.

108.9. Notwithstanding this substantial exclusion, the Pfizer 2-month data makes a blanket claim of 95% efficacy and a favourable safety profile, which leads one to believe that the vaccine's safety and efficacy on the aged population over 75 years is supported by Pfizer's data – but, again, it wasn't.

108.10. Fourth, the vaccine was also not tested in those who were sick with underlying health conditions, despite the fact that those individuals were most at risk from Covid-19. That demographic was completely excluded (a full list of exclusion appears on pages 42 and 43 of the protocol).

108.10.1. Their exclusion from the trial is astounding given that 95% of people who have died from Covid-19 have had at least 1 co-morbidity.

108.10.2. In fact, the average is four co-morbidities[3].

108.10.3. Again, the vaccine was not tested for safety or efficacy in these demographics, but was nevertheless marketed aggressively to them, and duly administered.

109. A further serious issue of concern is that the 95% efficacy appears to be overstated. The reasons follow:

[3] Source: https://www.cdc.gov/nchs/nvss/vsrr/covid_weekly/index.html.

109.1. Firstly, the 2-month report explains that, in the trial, the vaccine group of trial participants were compared to a group of trial participants that received a saline placebo:

> ***"Trial Procedures***
>
> *With the use of an interactive Web-based system, participants in the trial were randomly assigned in a 1:1 ratio to receive 30 µg of BNT162b2 (0.3 ml volume per dose) or saline placebo. Participants received two injections, 21 days apart, of either BNT162b2 or placebo, delivered in the deltoid muscle."*

109.2. This is a flaw in the trial design. Again, Dr Schmidt can attest to this. In order to obtain a true efficacy profile, the trial should have compared the vaccine intervention to, at the very least, other interventions against Covid-19 and/or natural immunity.

109.3. Not only is that the only way to design a trial to test true efficacy – but it is also necessary for the maintenance of equipoise. But, as set out in the Pfizer trial protocol, patients who had been treated with medicines intended to prevent infection, and those with previous exposure to Covid-19 (and who therefore had natural immunity) were excluded. As evidence of this, see page 41 of the trial protocol which reads as follows:

> ***"5.2. Exclusion Criteria***
>
> *Participants are excluded from the study if any of the following criteria apply:*

[...]

4. Receipt of medications intended to prevent COVID-19.

5. Previous clinical (based on COVID-19 symptoms/signs alone, if a SARS-CoV-2 NAAT result was not available) or microbiological (based on COVID-19 symptoms/signs and a positive SARS-CoV-2 NAAT result) diagnosis of COVID-19.

109.4. Secondly, the protocol sets out that the primary end point (a primary end point is the main outcome or measure that the trial is designed to evaluate) was preventing the occurrence of confirmed Covid-19 cases 7 days post dose 2 of the vaccine. In lay terms, what that means is that they gave the trial subjects injections on day 1 of the trial, then again 21 days later, and only screened for Covid-19 seven days after the second dose.

109.5. So, the trial participants were only screened for Covid-19 four weeks after receiving their first injection. That is a serious problem for efficacy because what it means is that any trial subjects who presented with Covid-19 in the four-week period following their first injection were not included in the trial data. Why not?

109.6. It is a known fact that vaccines cause temporary immune suppression for a few weeks following the injection, making subjects more vulnerable to illness and disease (including Covid-19) during that period.

109.7. Not including those who presented with Covid during the relevant four-week time frame had the effect of artificially inflating the efficacy figures.

109.8. Next, an examination of the end points as defined in the protocol makes plain that, whereas the study was designed to test whether the vaccine protects recipients from contracting Covid-19; it was not designed to test whether the vaccine:

109.8.1. protects others from transmission of Covid-19,

109.8.2. protects recipients from hospitalization for Covid-19, or

109.8.3. protects recipients from death by Covid-19.

109.9. The above omissions are significant because, as will be demonstrated later in these papers:

109.9.1. the South Africa Government claimed repeatedly that the Comirnaty vaccine protected against transmission and hospitalization. These were inaccuracies given that these aspects had not been tested in the Pfizer trial; and

109.9.2. scrutiny of the trial data finds that Comirnaty was **not effective** at preventing disease or death in the vaccinated study group:

109.9.2.1. 300% more participants in the vaccinated study group suffered health problems by 1 month than in the unvaccinated placebo study group;

109.9.2.2. 75% more participants in the vaccinated study group suffered severe health problems by 1 month than in the unvaccinated placebo study group;

109.9.2.3.10% more participants in the vaccinated study group suffered serious health problems by 6 months than in the unvaccinated placebo study group; and

109.9.2.4.20 vaccinated participants died by 6 months, as opposed to 14 unvaccinated placebo participants.

110. As stated above, the EUA for Comirnaty (based on the two-month data discussed above) was given in the US in December 2020, and the rollout in the United Stated commenced in the second half of December 2020.

111. Immediately following the rollout, post-authorization research was commissioned by Pfizer to assess how the vaccine performed in the general population and, specifically, to monitor any safety concerns or adverse events that may have not presented in the two-month data.

112. The post-authorization surveillance data highlighted some significant safety signals (as early as they were), and it is to that which I now turn.

Data from post-authorization surveillance conducted for two and a half months after December 2020 EUA and rollout to the public.

113. The early post-authorization surveillance considered data from the date of the rollout in US (mid-December 2020) to 28 February 2021.

114. The purported reason for collecting the data was so that the FDA could track the real-world performance of the Pfizer BioNTech BNT162b2 mRNA Covid-19 Vaccine (Pfizer's "COMIRNATY" vaccine), including its adverse events, and use that data to reach conclusions and make rational decisions about whether to continue with the vaccine rollout.

115. Instead of making this data public, the FDA subjected it to confidentiality clauses, and did not disclose it.

116. Transparency advocate groups in the United States sued the FDA to gain access to the data upon which Comirnaty was granted its EUA. They won the case, but the FDA wanted the Federal Judge to allow the agency fifty-five years to release the data. That was not allowed by the Judge - but it begs this question: Why would the FDA – who is responsible for oversight of products like Comirnaty – go to these lengths to keep the data away from the public. What were they trying to hide?

117. The lawyer acting on behalf of the plaintiff in the case aptly summarized the situation as follows:

"[T]he government also sought to delay full release of the data it relied upon to license this product until almost every American alive today is dead. That form of governance is destructive to liberty and antithetical to the openness required in a democratic society."

118. The post-authorization surveillance data, now released in part under Court order, appears in a document titled "*Cumulative Analysis of Post-Authorization Adverse Event Reports of PF-07302048 (BNT162B2) [i.e. Comirnaty] received through 28-Feb-2021*".

119. The document was drafted by a company called Worldwide Safety, and is annexed as "**HE26**". It provides an integrated analysis of the cumulative post-authorization safety data including US and foreign post-authorization adverse event reports received through 28 February 2021.

120. The report shows concerning safety signals. It commences by noting that there were a large number of adverse events reported. It notes inter alia that:

"Due to the large numbers of spontaneous adverse event reports received for the product, the [marketing authorization holder] has prioritized the processing of serious cases, in order to meet expedited regulatory reporting timelines and ensure these reports are available for signal detection and evaluation activity."

121. It proceeds to set out information about the adverse events reported. The relevant section appears in paragraph 3.1 of the document, on page 6, titled "*Safety Database*".

122. Although the document does not say how many doses of Comirnaty had been administered (that information has been redacted) by the time the data was collected, the following is recorded in the document:

> *"Cumulatively, through 28 February 2021, there was a total of 42,086 case reports (25,379 medically confirmed and 16,707 non-medically confirmed) containing 158,893 events Most cases (34,762) were received from United States (13,739), United Kingdom (13,404) Italy (2,578), Germany (1913), France (1506), Portugal (866) and Spain (756); the remaining 7,324 were distributed among 56 other countries."*

123. Table 1 of the same document is titled "*General Overview: Selected Characteristics of All Cases Received During the Reporting Interval*". The relevant portion of the table showing the case outcomes of the 42,086 reports is reproduced below for ease of reference:

Case outcome:	Recovered/Recovering	19582
	Recovered with sequelae	520
	Not recovered at the time of report	11361
	Fatal	1223
	Unknown	9400

124. It is not known how many individuals were vaccinated (this information has been redacted) so it is impossible to assess what percentage of vaccinated individuals suffered various adverse events – but what is clear is that significant numbers of adverse events were being reported globally.

125. In this respect, it is important to note that the data collection was passive: vaccinated individuals were not actively contacted and followed up with. As the reporting was voluntary, there is a strong likelihood of a significant under-reporting factor.

126. Of the 42,086 case reports of adverse events following the vaccines, 1223 people were dead within 2½ months of the roll-out, 11361 were not recovered at the time of the reports, and 9400 had unknown outcomes, any number of which may have died or suffered other serious adverse outcomes. Those figures are not insignificant by any measure.

127. The death figure, as well as the unrecovered and unknown figures, are particularly alarming. Historically the FDA, or drug manufacturers themselves, have pulled drugs off the market in circumstances where fewer serious adverse effects had been reported, or where as few as 4 deaths (let alone 1223 as in this case) had been associated with the medicine in question. This raises the question why Pfizer's Comirnaty vaccines are still being marketed as "*safe and effective*" despite such alarming safety signals.

128. Examples of previous drug withdrawals, and the comparatively low numbers of adverse event reports that resulted in those withdrawals follow below:

128.1. In August 2001, drug maker Bayer pulled its popular cholesterol-lowering medication off the market. According to the Food and Drug Administration, Bayer Pharmaceuticals voluntarily withdrew Baycol, known generically as Cerivastatin, as a result of the 31 patients deaths associated with the drug over the last four years. In support of this, I annex as "**HE27**" an article in the BMJ titled "*Bayer decides to withdraw cholesterol lowering drug*".

128.2. A drug called Brombenac was retracted in 1998. This pain killer was effective in relieving pain, but it caused 4 deaths, 8 liver transplants, and 12 cases of severe liver damage in the year it was on the market.

128.3. A drug called Bextra was withdrawn in 2005 for lack of effectiveness and because it caused adverse heart effects including death, heart attacks, and strokes, as well as an increased risk for serious skin reactions, such as epidermal necrolysis, erythema multiforme, and Stevens-Johnson syndrome.

128.4. Vioxx, a drug for arthritis, infamously heightened the risks for heart attack and stroke, and was tied to nearly 28,000 heart attacks in the US population between 1999 and 2003. Researchers reported that the drug resulted in an estimated four heart attacks per 1,000 patients who took it. Its manufacturer, Merck, voluntarily pulled it from the market in 2004. In total, this drug was given to more than 20 million people.

128.5. Accutane, a drug for acne, was recalled in 2009 due to its increased risk of birth defects, miscarriage, and premature deaths among pregnant women who used it, as well as suicidal ideation and inflammatory bowel disease.

128.6. Seldane, an antihistamine was recalled in 1998 due to fatal heart problems.

128.7. Rezulin, an antidiabetic and anti-inflammatory drug was pulled from the market in 2000 because it was associated with 90 cases of liver failure and at least 63 deaths. It also resulted in 35,000 lawsuits against its maker, Parke-Davis/Warner Lambert (now Pfizer).

128.8. Raptiva, a drug used to treat psoriasis, was recalled from the market when it was found to cause progressive multifocal leukoencephalopathy—a rare and lethal disease that results in inflammation and damage of the white matter of the brain.

129. The severe events reported in the Comirnaty 2½ month post-authorization data included:

> *"General disorders and administration site conditions (51,335 AEs), Nervous system disorders (25,957), Musculoskeletal and connective tissue disorders (17,283), Gastrointestinal disorders (14,096), Skin and subcutaneous tissue disorders (8,476), Respiratory, thoracic and mediastinal disorders (8,848), Infections and infestations (4,610) [...]."*

130. Of further and particular concern, given that the Comirnaty vaccine had not been tested on pregnant women, were the adverse events reported in pregnant women in the 2½ month post-authorization data.

131. Two hundred and seventy four cases of adverse events were reported in pregnant women, with issues that included spontaneous abortions (23 of them), outcome pending (5 of them), premature birth with neonatal death, and normal outcome (1 each), and no outcome was provided for 238 pregnancies.

132. What that means, statistically, is startling. If no outcome was provided for 238 pregnancies, that means they only collected data for 32 pregnancies. Of those 32 pregnancies that had data, 31 of them had either an abortion or foetal death. That equates to 97% of pregnant women in the available data set having an abortion or foetal death.

133. These concerns notwithstanding, the report claimed that a review of the available data confirmed a favorable benefit/risk balance for Pfizer's "COMIRNATY" vaccine, but that further pharmacovigilance was required and would be conducted.

134. That conclusion appears to be a whitewash – especially considering the absence of any effectiveness data, as well as the death statistics, the pregnancy statistics, and the likely under-reporting factor I highlighted above, which do not appear to have been considered in the report.

135. To re-cap, at the time of the publishing of the two-month trial data in December 2020, no further data was available, and the next available data that was gathered and analysed was presented in the 2½ month post-authorisation paper detailed above.

136. In total, that's four and a half months of data. Already at that stage, serious concerns were apparent, or should have been apparent to anyone who looked, and these should have raised red flags for regulators including SAHPRA.

137. The picture of Pfizer's inaccurate data, and concerns about adverse side effects truly begins to rear its head in the six-month data. It is to that data that I will turn shortly, but before I do, there is one crucial piece of information requiring ventilation. That information appears in the section immediately following.

The unblinding, the cross-over and destruction of any long-term efficacy and safety datasets resulting in an invalidated trial

138. In any phase three clinical randomised controlled trial (RCT), which is what the Pfizer trial purported to be, there must be an inoculated group of trial subjects and an equivalent placebo group. Those groups must subsist until the end of the trial. It is the long-term comparison of the efficacy and safety profiles between the vaccinated trial arm and the placebo trial arm which allows for a proper assessment as to whether or not the product (in this case, Comirnaty) has acceptable efficacy and safety profiles.

139. Without this data it is impossible to assess long term efficacy or safety. Again, Dr Schmidt can attest to this.

140. Usually, vaccine trials are run for a period of ten to fifteen years. This time, because of the exigencies of the situation, the trial period was severely truncated to three years, due to terminate sometime in 2023. The vaccine arm and placebo arm should have been maintained until the culmination of the trial in order to secure decent efficacy and safety data sets.

141. But Pfizer crippled the comparative data collection process, thereby invalidating their trial. Below, I describe how they did this:

141.1. After only 2 months, the trial groups were unblinded. "Unblinding" is a term used in the context of clinical trials to refer to the process of revealing the group assignment of a participant in a study – in other words, telling trial subjects whether they were part of the vaccine arm, or the placebo arm of the study.

141.2. Following the unblinding, those in the placebo group were offered the vaccine. This information appears in Pfizer's 6-month report (published in the New England Medical Journal under the title "*Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months*") and annexed as "**HE28**". At pg. 1762, the following appears:

> *"Starting in December 2020, after BNT162b2 became available under emergency or conditional use authorizations, participants 16 years of age or older who became eligible for Covid-19 vaccination according to national or local recommendations were given the option to learn their trial assignment. Those who had been randomly assigned to receive placebo were offered BNT162b2. After unblinding of the group assignments, participants were followed in an open-label trial period."*

142. 88.8% of the trial subjects in the placebo group elected to take the vaccine and crossed over. This appears from an official FDA document titled "BLA Clinical Review Memorandum"[4].

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4 https://www.fda.gov/media/152256/download.

143. On page 37 of that document, the following is stated:

> *"During the open-label follow-up period, most participants originally randomized to the placebo group for Doses 1 and 2 of study vaccine received BNT162b2 as Doses 3 and 4 (88.8% and 72.4%, respectively) of study vaccine."*

144. An 88.8% crossover is a calamity. It effectively annihilates any prosect of collecting reliable long-term efficacy and safety data about the vaccines.

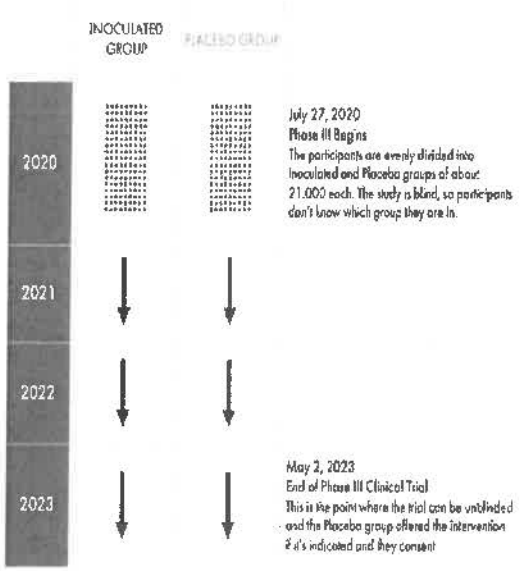
145. The applicant calls on Pfizer to explain how comparative efficacy and safety data is going to be collected under these circumstances.

146. The applicant also calls on SAHPRA to explain how it concluded that they vaccine was safe given that long-term safety data collection processes had been destroyed.

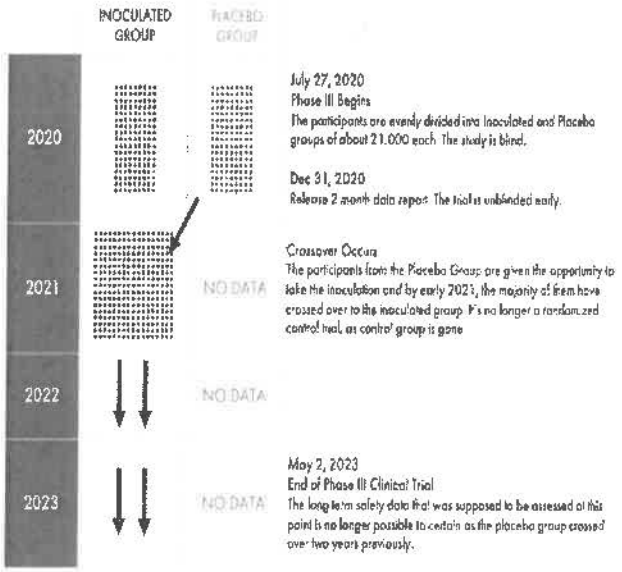
147. In the event that no such answer is forthcoming, the applicant will ask this Court to conclude that no long-term efficacy or safety data for these vaccines will be available at any juncture.

148. For the convenience of the Court, I highlight below in graphic format (with thanks to Deanna McLeod, and the Canadian Covid Care Alliance) how the trial was supposed to be conducted for the purposes of the collection of long-term efficacy and safety data versus what actually happened:

WHAT WAS SUPPOSED TO HAPPEN



WHAT ACCTUALLY HAPPENED



Pfizer's 6-month trial data

149. I turn now to deal with the six-month trial data. Before I canvass the data, it is important to note that in my opinion, and in the opinion of Dr Schmidt, the 6-month report should never have been published.

150. Any data it cites, and any and all conclusions it purports to draw are invalidated by the 2-month cross-over detailed above.

151. However, for the purposes of analysis only, I will work with the data and conclusions as presented by Pfizer.

152. The six-month trial data has already been annexed above. It was published in the New England Journal of Medicine on 4 November 2021. It must; however, be read together with its supplementary appendix, which is annexed as "**HE29**".

153. The conclusions that the authors draw from the Pfizer six-month data is that the vaccine had a "*favorable*" safety profile, and a 91.3% efficacy profile (down from 95% in the 2-month data).

154. However, an evaluation of the raw data presented paints a concerning safety picture and torpedoes the efficacy claim. Not only that, but it unmasks clear inaccurate data which must be viewed with the utmost seriousness.

155. I begin with the safety issues raised in the six-month report.

156. On page 11 of the supplementary index, a table of deaths occurring in the trial is reported. The table is reproduced below for ease of reference.

Reported Cause of Death[a]	BNT162b2 (N=21,926) n	Placebo (N=21,921) n
Deaths	15	14
Acute respiratory failure	0	1
Aortic rupture	0	1
Arteriosclerosis	2	0
Biliary cancer metastatic	0	1
COVID-19	0	2
COVID-19 pneumonia	1	0
Cardiac arrest	4	1
Cardiac failure congestive	1	0
Cardiorespiratory arrest	1	1
Chronic obstructive pulmonary disease	1	0
Death	0	1
Dementia	0	1
Emphysematous cholecystitis	1	0
Hemorrhagic stroke	0	1
Hypertensive heart disease	1	0
Lung cancer metastatic	1	0
Metastases to liver	0	1
Missing	0	1
Multiple organ dysfunction syndrome	0	2
Myocardial infarction	0	2
Overdose	0	1
Pneumonia	0	2
Sepsis	1	0
Septic shock	1	0
Shigella sepsis	1	0
Unevaluable event	1	0

Table S4 | Causes of Death from Dose 1 to Unblinding (Safety Population, ≥16 Years Old). a. Multiple causes of death could be reported for each participant. There were no deaths among 12–15-year-old participants.

157. The table reports that there were 15 deaths in the vaccine arm, and 14 deaths in the placebo arm. On the face of it, there is little problem with those figures. They appear to be balanced which presents no problem.

158. Because 15 and 14 are so close numerically, it appears that the assumption can be made that the vaccines were not causing more harm than good – and that there was no cause for further investigation. But the facts below expose this table as containing inaccurate data.

158.1. First, by the date of Pfizer's six-month report, there were in fact 20 deaths in those who had received the vaccine – not 15. This appears from the article to which the appendix is attached. There it states:

> *"During the blinded, placebo-controlled period, 15 participants in the BNT162b2 group and 14 in the placebo group died; during the open-label period, 3 participants in the BNT162b2 group and 2 in the original placebo group who received BNT162b2 after unblinding died."*

158.2. It is important to understand the above statement. In the trial, the participants were randomly assigned in a 1:1 ratio to receive two 30-μg intramuscular injections, 21 days apart, of the vaccine or saline placebo. However, starting in December 2020, after the vaccine became available under EUA, participants 16 years of age or older who became eligible for Covid-19 vaccination according to national or local recommendations were given the option to learn their trial assignment.

158.3. Those who had been randomly assigned to receive placebo were offered the vaccine. After unblinding of the group assignments, participants were followed in an open-label trial period. I have set this out above already.

158.4. The point of relevance here is that it appears that the death figures in the table above only report deaths prior to placebo participants having been offered the vaccine but exclude the additional deaths that followed vaccination of the unblinded placebo arm.

158.5. At the time of the report, they knew of 20 vaccinated deaths but in the table they only reported on 15. That means that, if the table presented were accurate, it would have record 20 deaths in the vaccine arm and 14 deaths in the placebo arm. Those figures would have been statistically significant, warranting further investigation and would have alerted regulatory authorities to a possible serious safety signal.

158.6. The question that arises, once again, is why did Pfizer not provide this data in the article instead of putting it into the easily accessible table?

158.7. But there are further flaws. After stating in the article that 20 people in total died after having received the vaccine, the article proceeds to state:

> *"None of these deaths were considered to be related to BNT162b2 by the investigators."*

158.8. But that, too, is unmasked as inaccurate when cross-referenced with the table. The last line item on the table states that the cause of death in at

least one instance was an "unevaluable event". That means that the cause of death is unknown. How can the authors state, on the one hand, in the article that "*none of the deaths were considered to be related to the BNT162b2 vaccine*" while simultaneously conceding that at least one death had an unknown cause?

158.9. Furthermore, the authors give no details as to how they established that there was no causal link between the deaths and the vaccines. Autopsies, together with detailed review of medical records, would have been the objective mechanism by which to determine causality, but there is no indication anywhere in Pfizer's report that autopsies or reviews of medical records were conducted.

158.10. Another bizarre item in the table is line item 11, which states that a "*cause of death*" is "*death*". That makes no sense. What was the actual cause of that death? Was it also unknown?

158.11. There is another problem. When physicians catalogue "causes of death", the cause of death must be reported by referencing the immediate cause of death, and not underlying health conditions.

158.12. As a medical practitioner, I am qualified to write a death certificate, and I have direct knowledge of how those certificates are written and the contents of those certificates.

158.13. On death certificates, in terms of the diagnosis, the physician will list the immediate cause of death, and then separately list any underlying causes that may have contributed to the death. The point is that the underlying health conditions are not causes of death, so they cannot be listed as such. I also annex as "**HE30**" a document titled "*cause of death certification*" which was published by the statistician general in South Africa.

158.14. Based on international standards, it sets out guidelines for how deaths are to be reported and explains clearly that the "*immediate cause of death is the final disease, injury or complication directly causing the death*".

158.15. Underlying health conditions, referred to in the guide as "*an underlying cause of death*" is "*the disease or injury that started the sequence of events leading directly to death*". In this respect too, table 4 on page 11 of the supplementary index is misleading. The table lists a number of "*underlying conditions*" as "*causes of death*". Examples of this are arteriosclerosis, cardiac failure congestive, chronic obstructive pulmonary disease, dementia, and hypertensive heart disease. Serious vaccine adverse events may well have been the final disease, injury or complication directly causing the death in any or all of these cases – but these would not have been noted or investigated because the underlying cause was reported instead of the immediate cause of death.

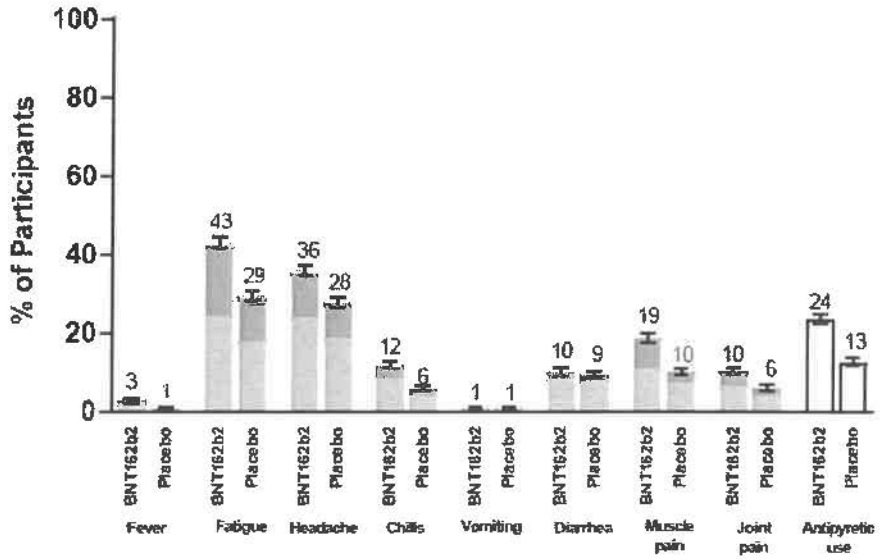
159. I now move onto the efficacy claims made, and the problems with those claims.

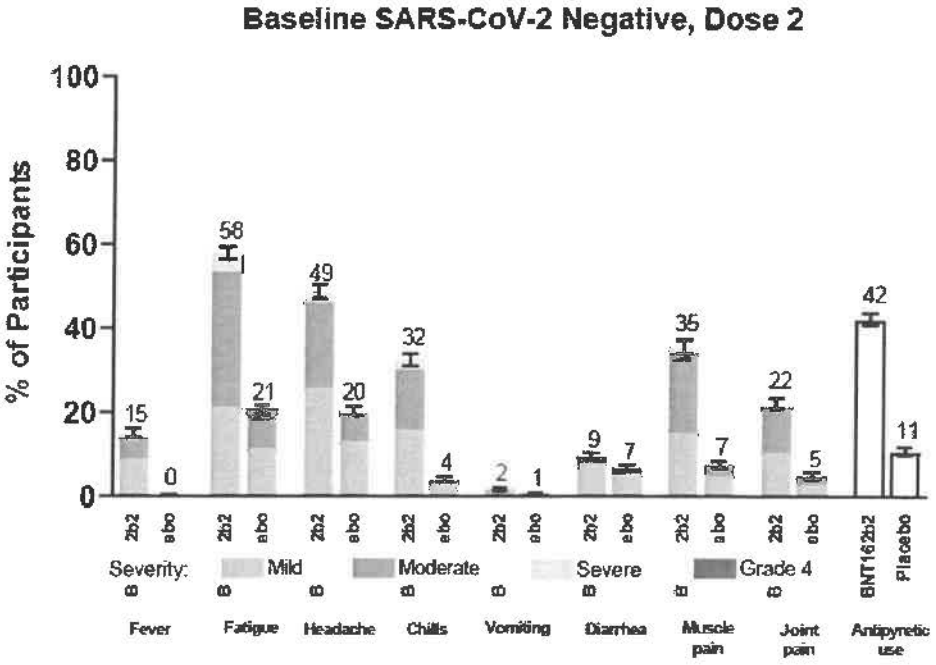
160. The six-month report claims an efficacy "against Covid" of 91.3% (down from the 95% efficacy claim in the two-month report). Any rational person would interpret this to mean that, not only would they have a 91.3% chance of being protected from contracting Covid-19 – but that they would be spared the symptoms of Covid-19.

161. The problem for Pfizer is that the data in the supplementary appendix places the efficacy claim in doubt because it shows that the trial subjects in the vaccine arm were getting more Covid-like symptoms (even through their PCR tests were negative or were not tested) than those in the placebo group.

162. This data emerges from two tables in the supplementary appendix to the six-month report. Those tables appear on page 17 and they are reproduced below for the Court's ease of reference:

Baseline SARS-CoV-2 Negative, Dose 1





163. What these graphs demonstrate is that many more people in the vaccine arm than in the placebo arm became ill with Covid-like symptoms. The situation becomes worse after dose two with many of the Covid-like symptoms becoming more severe in the vaccinated arm than in the placebo arm. For example, the second graph shows that after dose 2 of the vaccine:

163.1. 15% of participants in the vaccine group had fever compared to 0% in the placebo arm.

163.2. 58% of participants in the vaccine group had fatigue compared to 21% in the placebo arm.

163.3. 49% of participants in the vaccine group had headaches compared to 20% in the placebo arm.

163.4. 32% of participants in the vaccine group had chills compared to 4% in the placebo arm.

163.5. 2% of participants in the vaccine group had vomiting compared to 1% in the placebo arm.

163.6. 9% of participants in the vaccine group had diarrhea compared to 7% in the placebo arm.

163.7. 35% of participants in the vaccine group had muscle pain compared to 7% in the placebo arm.

163.8. 22% of participants in the vaccine group had joint pain compared to 5% in the placebo arm.

164. What is also significant is that the adverse events classified as "severe" (represented in the graph as orange), are worse in the vaccinated arm after the second dose as compared with the first dose.

165. The same trends (albeit less severe) can be seen in the first graph which tracks the same datapoints 7 days after dose 1. That means that in every single metric measuring Covid-like symptoms, participants in the vaccine arm got more sick, and had more symptoms than those in the placebo arm. How can one say a vaccine has high efficacy in preventing Covid if participants are getting more

sick with Covid-19 like symptoms in the treatment arm than they are in the placebo arm?

166. Despite there being more cases of symptomatic Covid-19 (defined as cases with symptoms plus a positive PCR test) in the placebo arm after the first and second doses, the rates of Covid-like symptoms are dramatically higher in the vaccine arm than the placebo arm after each injection, meaning that the vaccine was negatively effective at preventing Covid-like morbidity, the very thing the vaccines were ostensibly supposed to prevent.

167. The efficacy profile also appears to have been inflated. Pfizer took the results from their adult trial, which started in July 2020, and then added the results from the 12-15 year old trial despite the fact that the adolescent trial started four months later. The following is stated in the six-month report:

> *"Between October 15, 2020, and January 12, 2021, a total of 2306 participants 12 to 15 years of age underwent screening, and 2264 underwent randomization at 29 U.S. sites. Of these participants, 2260 received at least one dose of BNT162b2 (1131 participants) or placebo (1129), and 99% (1124 in the BNT162b2 group and 1117 in the placebo group) received the second dose. [...] [Data] for this cohort are included in the analyses of vaccine efficacy in the overall."*

168. It is well known that the efficacy of the vaccines wanes over time. Pfizer itself concedes as much in their six-month report:

> *"From its peak after the second dose, observed vaccine efficacy declined. From 7 days to less than 2 months after the second dose, vaccine efficacy was 96.2% (95% CI, 93.3 to 98.1); from 2 months to less than 4 months after the second dose, vaccine efficacy was 90.1% (95% CI, 86.6 to 92.9); and from 4 months after the second dose to the data cutoff date, vaccine efficacy was 83.7% (95% CI, 74.7 to 89.9) [...]*

Efficacy peaked at 96.2% during the interval from 7 days to less than 2 months after the second dose and declined gradually to 83.7% from 4 months after the second dose to the data cutoff date — an average decline of approximately 6% every 2 months."

169. That means that adding children in at a later stage gave a false boost to the efficacy numbers – this is especially so due to children having stronger immune systems than adults, and therefore being less susceptible to Covid-19.

170. The efficacy for these two demographics should have been reported separately, not presented as one combined result. Without this boost, the Pfizer 6-month reported efficacy would probably have been lower.

THE SOUTH AFRICAN GOVERNMENT'S AUTHORISATION OF THE COMIRNATY VACCINES AND THE "SAFE AND EFFECTIVE" NARRATIVE.

171. SAHPRA registered Pfizer's vaccine/s as follows:

171.1. On 16 March 2021, SAHPRA approved Pfizer's "COMIRNATY" vaccine under section 21 of the Medicines and Related Substances Act 101 of the 1965 ("the MARS Act").

171.2. Section 21 registrations are a special restricted authorisation category, meaning that the relevant product does not yet have full regulatory approval.

171.3. The relevant SAHPRA press release is annexed as "**HE31**".

171.4. On 8 December 2021, SAHPRA approved the use of a third (booster) dose of the Pfizer's "COMIRNATY" vaccine in individuals aged 18 years and older, as well as a third (booster) dose in individuals aged 12 years and older who were severely immunocompromised.

171.5. It is not clear from the relevant SAHPRA press release, annexed as "**HE32**", whether the registration was under section 15 or section 21 of the MARS Act – but for the purposes of this application, I assume that the registration was under section 21.

171.6. On 25 January 2022, Pfizer's "COMIRNATY" vaccine was approved under section 15 of the MARS Act, and thereby given full regulatory approval.

171.7. The relevant SAHPRA press release is annexed as "**HE33**". In terms of section 15(3)(a)(iii), SAHPRA can grant section 15 approvals (which are full regulatory approvals) for medications, including vaccines when it is satisfied that the medications are "*safe, efficacious, and of good quality [...]*", In so doing, it is empowered by section 15(3)(a) to pursue any investigation or enquiry that it deems necessary in order to satisfy itself of the requirements listed in section 15(13)(i)-(iii).

171.8. Considering what I have detailed in these papers, it is doubtful that SAHPRA could have pursued adequate investigation of Pfizer's data. I am advised that all of this will be answered when the rule 53 record is provided by SAHPRA.

171.9. On 15 November 2022, SAHPRA then registered two new Pfizer vaccines: First, Pfizer's Ready To Use (RTU) adult vaccine, and its Dilute To Use (DTU) paediatric vaccine.

171.10. Both of these vaccines have also been registered in terms of Section 15 of the MARS Act. The relevant SAHPRA announcement is annexed as "**HE34**".

171.11. No data has been publicly released about these vaccines or their trials, so it is impossible to do the forensic work on those vaccines that has been done in these papers on Comirnaty.

171.12. However, those vaccines use the same problematic mRNA technology, and were also manufactured by Pfizer/BioNTech.

172. Section 2A of the MARS Act sets out the objectives of SAHPRA. They are to provide for the monitoring, evaluation, regulation, investigation, inspection, registration and control of medicines in the public interest. SAHPRA does this, according to section 2B, by evaluating applications for medicines transparently, fairly and ensuring that evidence of existing and new adverse events, interactions, information with regard to post-authorization surveillance and vigilance is being monitored, analysed and acted upon.

173. It is at this stage unknown precisely what data SAHPRA had before it when it made the decisions to grant full section 15 authorisations to the various Pfizer vaccines.

174. What is known, however, is that at the time of the section 15 approvals, which occurred on 25 January 2022 and 15 November 2022, both Pfizer's two-month report (published on 31 December 2020), and its six-month report (published on 4 November 2021), were already publicly available.

175. SAHPRA must have had these two reports at the very least. How and why SAHPRA granted full authorisation to these products when, at a bare minimum it knew (or ought reasonably to have known) the following from the data, are questions that we call for it to answer in this case:

175.1. That global safety signals from a reliable adverse event reporting system, VAERS, was showing alarming rates of serious, life-threatening adverse events and deaths that were potentially linked to the vaccine.

175.2. That Pfizer's six-month safety data had markers of serious inaccuracies, as detailed above.

175.3. That the unblinding and cross-over of trial participants from the placebo arm to the vaccine arm torpedoed the collection of any long-term safety data of adverse events, thereby invalidating the study, and which further meant that unless they performed their own investigation as had been proposed by the Government of India, SAHPRA would not be able to effectively assess the long-term safety of the vaccines.

175.4. That the vaccine was being authorized for the most vulnerable populations (pregnant and lactating women, immunocompromised individuals with known or suspected immunodeficiency, people receiving cytotoxic agents or systemic corticosteroids, and people with other serious underlying health conditions), as well as individuals with a previous diagnosis of Covid-19, even though the vaccine's efficacy and safety had not been tested in any of those population demographics in the trial.

175.5. That the data showed that trial subjects in the vaccine arm of the study were presenting more frequent, and more severe Covid-like symptoms than those in the placebo arm.

175.6. That the vaccine had not been tested against natural immunity, and that neither its efficacy nor effectiveness compared to natural immunity were known.

176. But that is not the only criticism to be levelled against SAHPRA. Section 15 of the Medicines and Related Substances Act requires SAHPRA to satisfy itself, prior to registration, that the relevant vaccines were safe and efficacious.

177. SAHPRA did not conduct any independent trials on Pfizer's vaccine products (Comirnaty, DTU and RTU). What this means is that what SAHPRA had before it was data, and data analysis done by Pfizer.

178. The registration was done based on Pfizer's data without any external checks and balances, or verification.

179. I have set out above that Pfizer was contractually bound (in its agreement with BioNTech) to "commercialize" Comirnaty and other Covid-19 vaccine products. SAHPRA's sole reliance on the very party responsible for commercialization of these vaccines creates a significant conflict of interest, rendering the registration of the Comirnaty vaccines, the RTU vaccines, and the DTU vaccines vulnerable to attack on the basis of irrationality, either under the prescripts of or PAJA or legality. In the circumstances, SAHPRA could not have exercised its powers under the Act rationally.

180. SAHPRA's conduct is not the only conduct worthy of scrutiny. The Government has consistently (and continues to) run campaigns that the vaccines, including all of the Pfizer vaccines "*prevent transmission*" and are "*safe" and "effective*".

181. Astonishingly, Government also encourage pregnant women to take the vaccine despite Pfizer and BioNTech's admission (detailed above) that "*it is not yet known whether the use of [Comirnaty] in a parent could be harmful to an unborn baby [...]*".

182. The above narrative has been so widely publicised that the Court can take judicial notice of it.

183. To the extent that the respondents deny this, and the Court does not take judicial notice of these facts, the applicant will present further screenshots of statements made to that effect. For now, however, I annex as "**HE35**" sources

from the South Africa Government's official website (https://www.gov.za/coronavirus/faqs/vaccine) which quotations are valid and remain on the website as of the date on which this affidavit was deposed to:

183.1. First, the Government explains that the reason to get vaccinated is that the vaccine protects others – meaning it stops transmission. They say:

> *"Two key reasons to get vaccinated are to protect ourselves and to protect those around us. Because not everyone can be vaccinated – including very young babies, those who are seriously ill or have certain allergies – they depend on others being vaccinated to ensure they are also safe from vaccine-preventable diseases."*

183.2. Second, the government assures the public that the vaccines are safe and effective:

> *"The vaccine is both safe and highly effective to prevent severe COVID-19 disease and death."*

183.3. Thirdly, and most surprisingly considering that the novel Pfizer BioNTech COVID-19 vaccines are known to contain viral genetic material (mRNA) in lipid nanoparticles, the Government explains that:

> *"However, because vaccines contain only killed or weakened forms of germs like viruses or bacteria, ..."*

184. Fourth, the NICD[5] maintains its position that vaccination is safe in pregnant women. On its website it says:

> *The Vaccine Ministerial Advisory Committee (VMAC) continues to monitor the safety and effectiveness of COVID-19 vaccination during pregnancy and lactation for all vaccines included in, or considered for inclusion, in the national vaccine rollout. Although the risk is small, pregnant and postnatal women are at increased risk of severe COVID-19 disease compared to their non-pregnant counterparts. They are also at increased risk of preterm birth, and possibly other adverse obstetric outcomes. As a result of the growing body of safety evidence that supports the use of COVID-19 vaccines in pregnant women, the VMAC has recently updated its recommendations regarding administration of COVID-19 vaccines during pregnancy.*
>
> *Current recommendations are as follows (updated recommendations are shown in bold):*
>
> 1. *COVID-19 vaccination should be offered to women who are eligible to be vaccinated during any stage of pregnancy, and during lactation. As previously recommended, both the Comirnaty® (Pfizer) vaccine or the Janssen® (J&J) vaccine can be offered. Everyone 18 years and older is now eligible to be vaccinated, and women 18 years and older should therefore be offered vaccination during any stage of pregnancy, and during breastfeeding.*
> 2. *Consideration should be given to providing vaccination to pregnant and breastfeeding women during routine antenatal and postnatal visits. Where this is not possible, health care workers should encourage pregnant and breastfeeding women to access vaccination at a nearby vaccination site.*
> 3. *Health care workers are encouraged to discuss the benefits and possible risks of COVID-19 vaccination with their patients. These discussions should include the increased risk, albeit small, of severe disease in pregnant women when compared to non-pregnant women, reassurance about the growing evidence supporting the safety of vaccines in pregnant and breastfeeding women, the strong immune response following vaccination and the benefits of immune transfer to the baby, and ongoing safety monitoring of vaccine use in pregnancy. Furthermore, that there are no known risks associated with other non-live vaccines given routinely to pregnant women.*

[5] https://www.nicd.ac.za/vaccination-of-pregnant-and-breastfeeding-women-august-update/

4. *COVID-19 vaccination is strongly encouraged for non-pregnant women contemplating pregnancy.*

185. I also annex collectively as "**HE36**" screenshots from Government's official Twitter account stating that the vaccines are "*safe and effective*"[6]. This narrative continues to this day.

186. I have already cast significant doubt on both the safety and effectiveness by examining Pfizer's data, but there is more data available to demonstrate that the vaccines do not stop transmission, and that they are neither effective nor safe. Conclusive statements about safety, or more accurately stated the magnitude of risk, could not be made at this stage.

187. I now commence by dealing with the evidence pertaining to the claim that the vaccines stop transmission, and I then progress to setting out the additional evidence supporting the applicant's contention that the vaccines are neither safe nor effective.

It is not true that the vaccines stop transmission.

188. Pfizer executives admitted in the European Parliament that Comirnaty had not been tested prior to authorisation to evaluate whether it stopped transmission of the SARS-CoV-2 virus.

[6] (https://twitter.com/governmentza/status/1397840068799352834?lang=en)
https://twitter.com/governmentza/status/1532972921953652737
https://twitter.com/healthza?lang=en

189. It is, however, not necessary to rely on that admission, because the fact that the ability of the vaccine to prevent transmission was never intended to be part of the Pfizer trial, appears from its protocol already annexed above,

190. The Pfizer trial protocol sets out the objectives of the trial. Nowhere in the trial protocol is assessing the effect of the vaccine on transmission listed as a trial objective. The short title of the study states:

> *"**Short Title**: A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals."*

191. Testing for the vaccine's effect on transmission is not mentioned in the short title.

192. To the extent that further confirmation is required; the objectives of the Pfizer trial appear in detail from the table at pages 10 – 14 of the Pfizer trial protocol, and they show conclusively that the trial objectives were limited to testing for safety, tolerability, efficacy and immunogenicity.

193. It is manifest from the protocol that the effect of the vaccine on transmission of Covid-19 was not part of the trial.

194. It is further manifest from the aforementioned 2-month and 6-month studies published in the New England Journal of Medicine that the effect of the vaccine on transmission of Covid-19 was not measured.

195. The protocol, as well as these published studies, must have been available to SAHPRA, the Ministerial Advisory Committee of Covid-19, and the Government. It is inexplicable that the Government told the South African public that the vaccines stopped transmission, and that getting vaccinated would "*protect others*" when the documentary evidence did not prove that.

196. Many South Africans, even those who were vaccine hesitant, were convinced to take the vaccination under this ruse, and even to vaccinate their children.

197. Even more inexplicable is the fact that the Government has not retracted its statements on transmission to date, leaving many in the public misinformed about the vaccine and transmission.

It is not true that Comirnaty was proven "effective". Effectiveness was never tested. It is also not true that the vaccines are "safe".

198. I have already annexed evidence above to the effect that the Government's consistent stance is that the vaccines, including Comirnaty, were "*effective*".

199. The government at no stage attempted to inform the public regarding the definition of "*effectiveness*". That definitional lacuna left open the possibility for errors and shifting benchmarks – which is exactly what happened.

200. When the public were told that the vaccines were effective, they believed that meant that the vaccine was effective in real-world circumstances at preventing

infection, transmission, severe disease, hospitalisation and death from COVID-19. That, at least, was the original claim made by government authorities.

201. When the Pfizer mRNA vaccines were awarded EUA by FDA, it was widely publicised that the new mRNA technology was 95% effective at prevention of transmission of the SARS-CoV-2 virus. This claim was made on the basis of a single Pfizer trial, dated 31 December 2020, in which the authors claimed "95% efficacy" (not "95% effectiveness").

202. The crucial differences between the meanings of the words "efficacy" and "effectiveness" are set out below.

203. The subsequent 6-month data report of Pfizer, dated 15 September 2021, found a gradual decline in vaccine efficacy, at that stage claimed to be 91.3%. Whether the efficacy was 95% or 91.3%, real-world data simply does not support the claim of effectiveness.

203.1. South Africa's first wave of Covid cases peaked on 19 July 2020 at 210.10 Covid cases per million people.

203.2. South Africa's second wave of Covid cases peaked on 11 January 2021 with 317.93 cases per million people.

203.3. South Africa then commenced its national vaccination rollout in February 2021. If government's claims that vaccines were effective at stopping infection and transmission were correct, one would have expected the

reported cases in the Covid waves that followed to decrease. But that is not what happened. The reported cases in fact increased after the vaccination rollout.

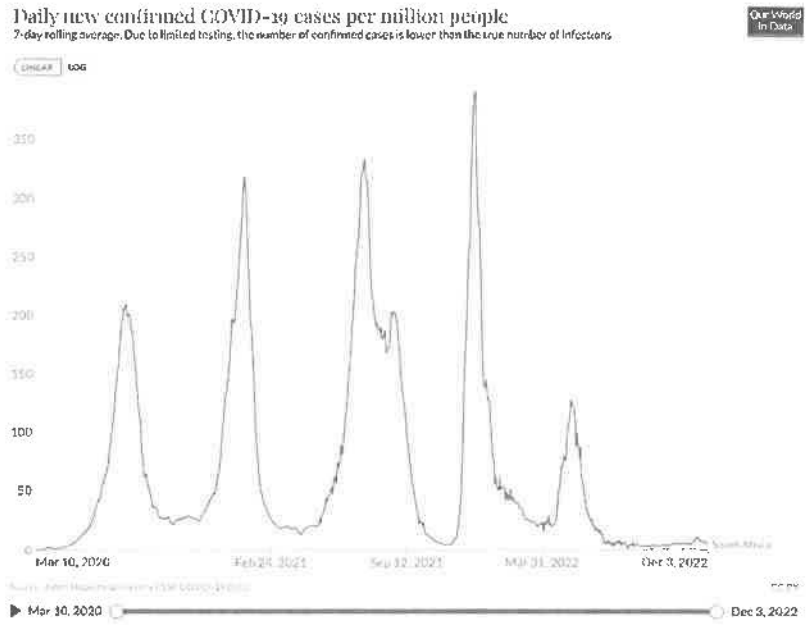
203.4. The third Covid case wave peaked on 7 July 2021, 5 months after the rollout of the vaccinations had commenced with 330.02 cases reported per million people.

203.5. Similarly, the fourth Covid case wave peaked on 17 December 2021 with 391.31 cases per million people.

204. The above data was sourced from the Our World in Data website ("**OWD**"). Their raw data on confirmed cases and deaths for all countries is sourced from the COVID-19 Data Repository of the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. It represents official government data from the relevant country (in this case obtained from the South African Department of Health).

205. The above data is graphically represented below, and the red line shows the date of the commencement of the vaccination rollout[7]:

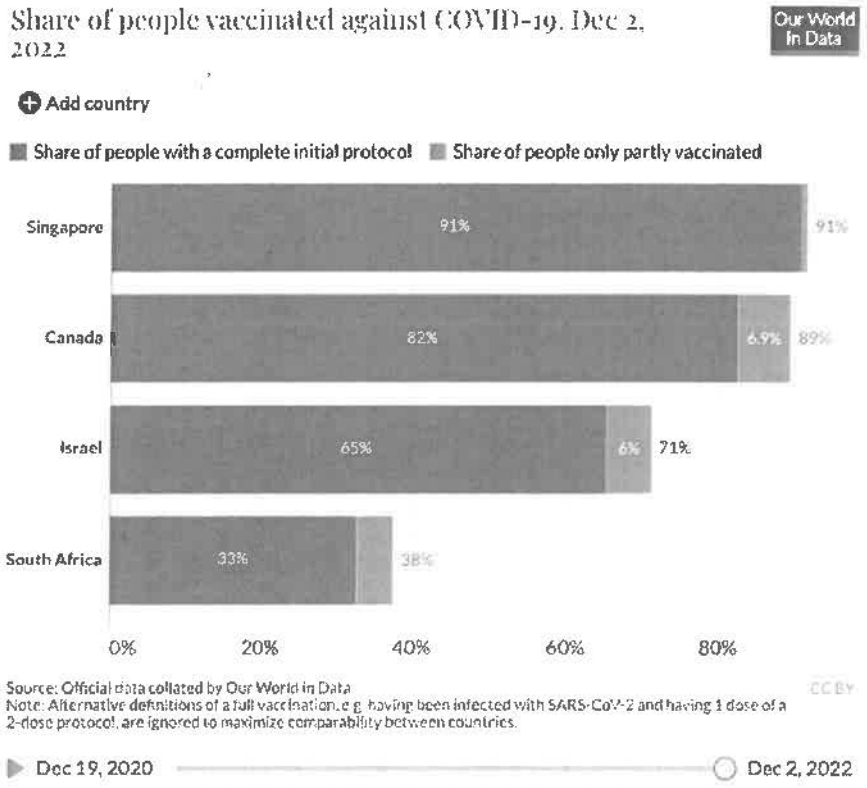
[7] Source: https://ourworldindata.org/covid-cases.



206. I accept that the above data is hampered by the relatively low percentage of vaccinated South Africans, so I turn now to assess the data (also from OWD) from a random cross-section of countries that have higher percentages of their populations vaccinated.

207. As of December 2022, Israel had 71% of their population vaccinated, Canada had 89% of their population vaccinated, and Singapore had 91% of their population vaccinated[8].

[8] Source: https://ourworldindata.org/covid-vaccinations.

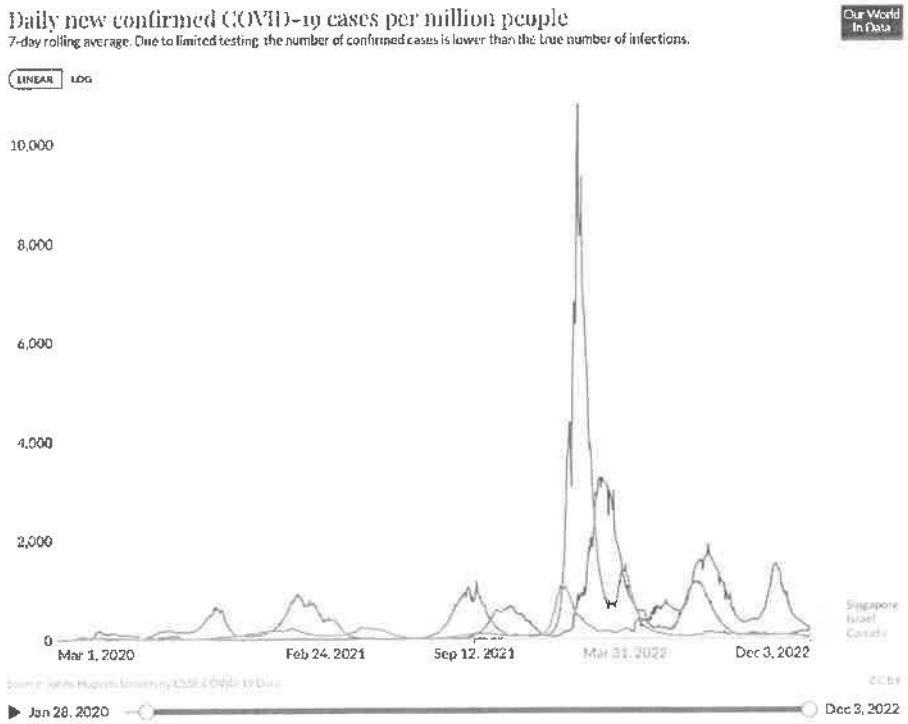


208. Similarly to South Africa, the Covid cases in the respective waves in these countries also reflect increasing case reports post-vaccination instead of decreasing case reports. This also flies in the face of the assertion that the vaccines were effective at preventing infection and transmission.

208.1. Singapore rolled out their vaccination program in January 2021. The data shows that there was little effect for 11 months, after which Singapore began experiencing spikes in case reports.

208.2. Israel and Canada both began rolling out their vaccination programs in December 2020, after which both countries reported more Covid cases

in the waves following vaccination than they had reported in the waves preceding vaccination.



209. Global authorities realized that the data was not showing that vaccines were effective at preventing infection or transmission. Having realized this, they shifted the "effectiveness" benchmark. At this juncture, they largely abandoned the claim that the vaccines prevented infection or transmission, and shifted to stating that they prevent "severe illness and death".

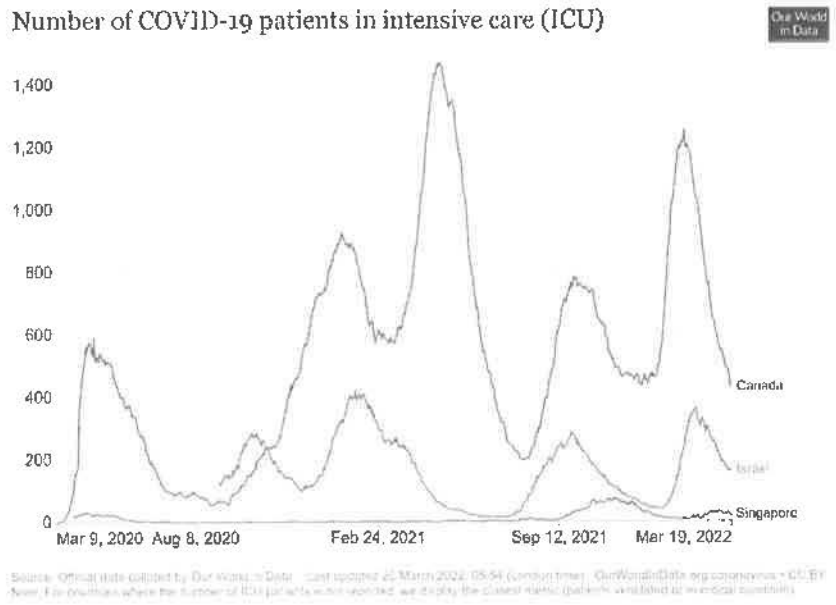
210. But the data doesn't support that either.

211. If it were true that the vaccines prevented severe illness or death in those who contracted Covid, one would expect to see real-world factual data in highly vaccinated countries such as Singapore, Canada and Israel reflecting

diminishing trends of both ICU admissions and deaths. But that is not what the data demonstrates. Here again, the data as represented in the graph below in fact shows the opposite[9]:

211.1. Singapore, which commenced its vaccination program in January 2021 saw no effect for around eight months, after which it saw spikes in Covid-related ICU admissions.

211.2. Likewise, Israel and Canada who began their vaccination programs in December 2020, saw an increase in Covid-19 related ICU admissions.

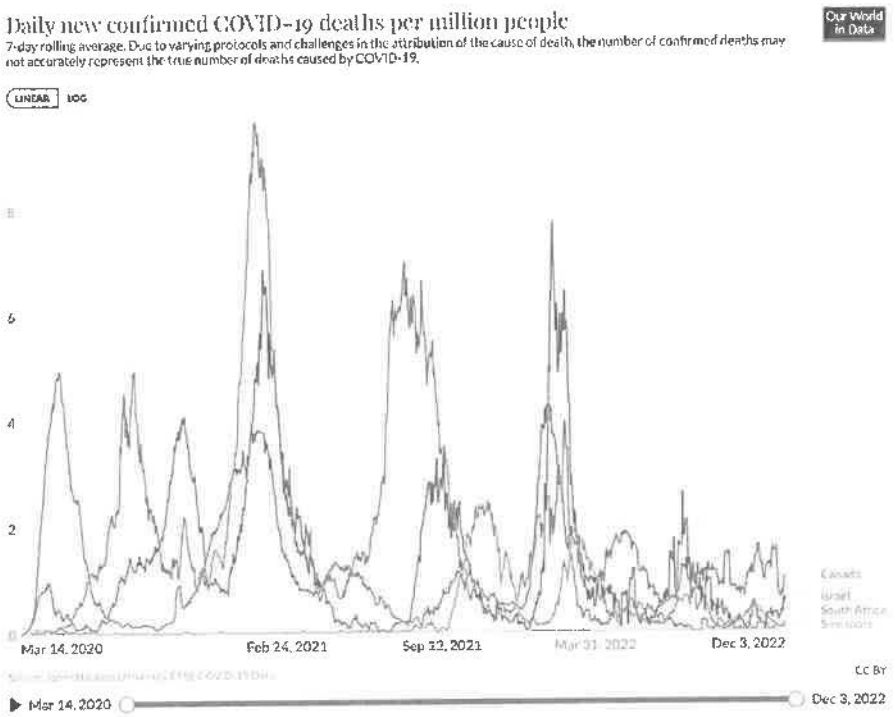


212. The same trend can be seen in Covid-19 related deaths:

212.1. The data from Singapore shows no benefit for the first 8 months, followed by an escalating trend of increasing deaths.

212.2. The data from Canada and Israel shows a transient diminishing trend for the first 11 months or so, followed by an escalating trend of increasing deaths.

212.3. In contrast, the data from South Africa, which has the lowest proportion of vaccinated individuals, does show a diminishing trend of deaths over time. This diminishing trend in South Africa is most probably the result of natural immunity that has been acquired by the 62% of the South African population who remain unvaccinated.



213. In conclusion, the real-world data contradicts the narrative of the global authorities, and the South African Government, that the vaccines prevent severe illness and death. My introduction of real-world data has been dismissed in other legal proceedings by Professors Salim Abdool Karim and Glenda Grey solely on the basis that it is not data contained in peer-reviewed journals, and is therefore neither reliable nor credible. That argument is farcical.

214. BioNTech, in its SEC (Securities and Exchange Commission) filing already annexed above, itself relies on real-world data to measure effectiveness. This is demonstrated by the extracted quotes copied below:

> *"The global distribution of BNT162b2 has also generated a vast array of real-world vaccine effectiveness data in diverse populations. Vaccine effectiveness following the primary two doses demonstrated protection against symptomatic infections, asymptomatic infections, severe infections, hospitalizations and deaths in real world vaccine effectiveness trials, mirroring the high efficacy and confirming the safety observed in our Phase 3 clinical trial.[...]*
>
> *"Real world data confirms that vaccine effectiveness decreases over time as the interval after the second dose increases, while vaccine effectiveness against hospitalization continues to be high. Waning vaccine effectiveness observed in the real-world setting coincided with the global spread of the Delta variant. Real world evidence also shows that high vaccine effectiveness is restored with a third dose booster, both against severe disease, as well as confirmed infection, including infections caused by the Delta variant. [...]"*

215. I note that the BioNTech SEC filing makes the claim that the real-world data demonstrates vaccine effectiveness. I do not know on what source data they base that conclusion because they do not disclose it, but I deny that those

conclusions are correct based on the real-world data that I have reproduced above. Pfizer is cited in this application. I invite them to produce the real-world data that their manufacturing partner, BioNTech, say supports the claim that the vaccines are effective.

216. In any event, the point is simply that real-world data is credible. If it was not, BioNTech would not themselves reference it in effectiveness assessments.

217. There is further real-world evidence that, in my respectful opinion, demonstrates that the Pfizer vaccines are neither safe nor effective. This data comes from official data published by the Government in the United Kingdom – specifically, data published by The Office for National Statistics ("ONS")[10]. The Pfizer vaccines were the most widely used of all registered vaccines in the United Kingdom.

218. The graph below shows the number of deaths caused by Covid-19 in England from August 2021 to December 2021. Green bars show deaths among people who were unvaccinated, red bars show the cumulative Covid deaths among the vaccinated, and yellow and mauve bars show deaths among people who received one or two doses of the vaccine. It shows clearly that, in every month, there were significantly more Covid-19 deaths amongst the vaccinated than there were amongst the unvaccinated (compare primarily the green and red bars). That is clear evidence that the vaccinations are not effective at either

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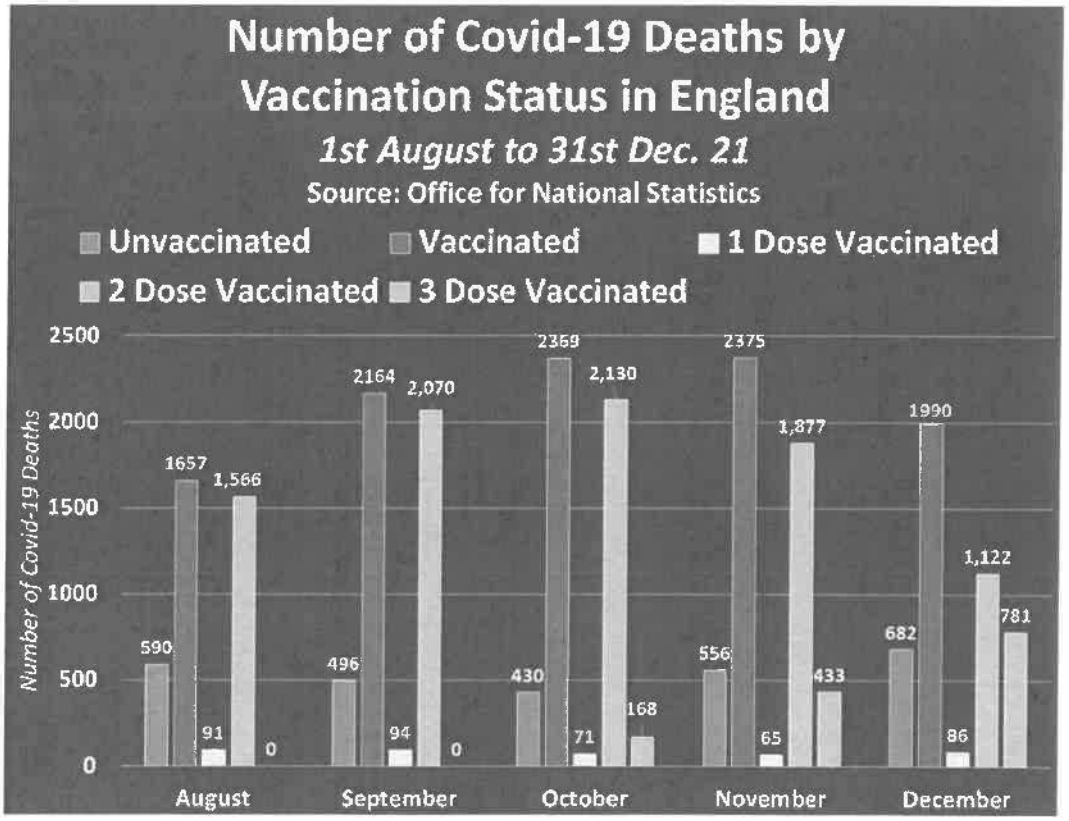
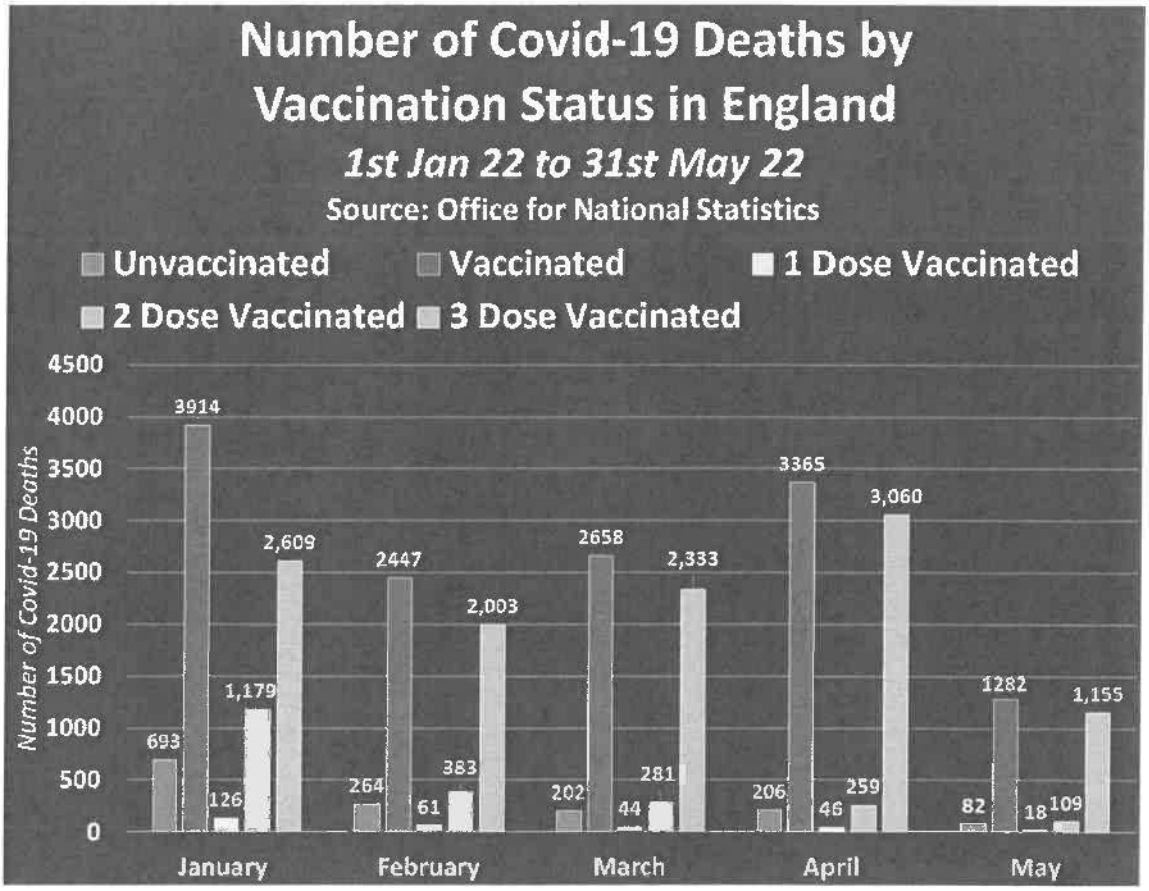
10 Source site: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregisteredweeklyinenglandandwalesprovisional/weekending9december2022.

preventing the contraction of Covid, hospitalisation from Covid, or death from Covid.



219. The trend in the above table continues into the period 1 Jan 2022 to 31 May 2022. But the later data shows another interesting trend: The Covid-19 death statistics in the unvaccinated decline steadily over the five month period, possibly reflecting the acquisition of herd immunity in the unvaccinated.

220. The relevant graph appears below:



221. Of course, the number of deaths in the vaccinated and unvaccinated arms must be calculated as a percentage of the relative percentages of the UK population that are both vaccinated and unvaccinated. Both Our World in Data (referenced and sourced above) and the United Kingdom's Health Security Agency (UKHSA) provide figures of 20% unvaccinated, and 80% vaccinated in the UK. Having a population of 56 million, that means that approximately 11 200 000 individuals are unvaccinated, and approximately 44 800 000 individuals are vaccinated in the UK.

222. If one looks at the individual months on the source data (referenced and sourced above), the trend is clear: individuals in the vaccinated arm have a higher percentage probability of death.

223. I have done these calculations in multiple months and have observed the same trends but, in order to not overburden the court, I use only one month as an example. I have chosen May 2022 (the last month reflected in the abovementioned dataset).

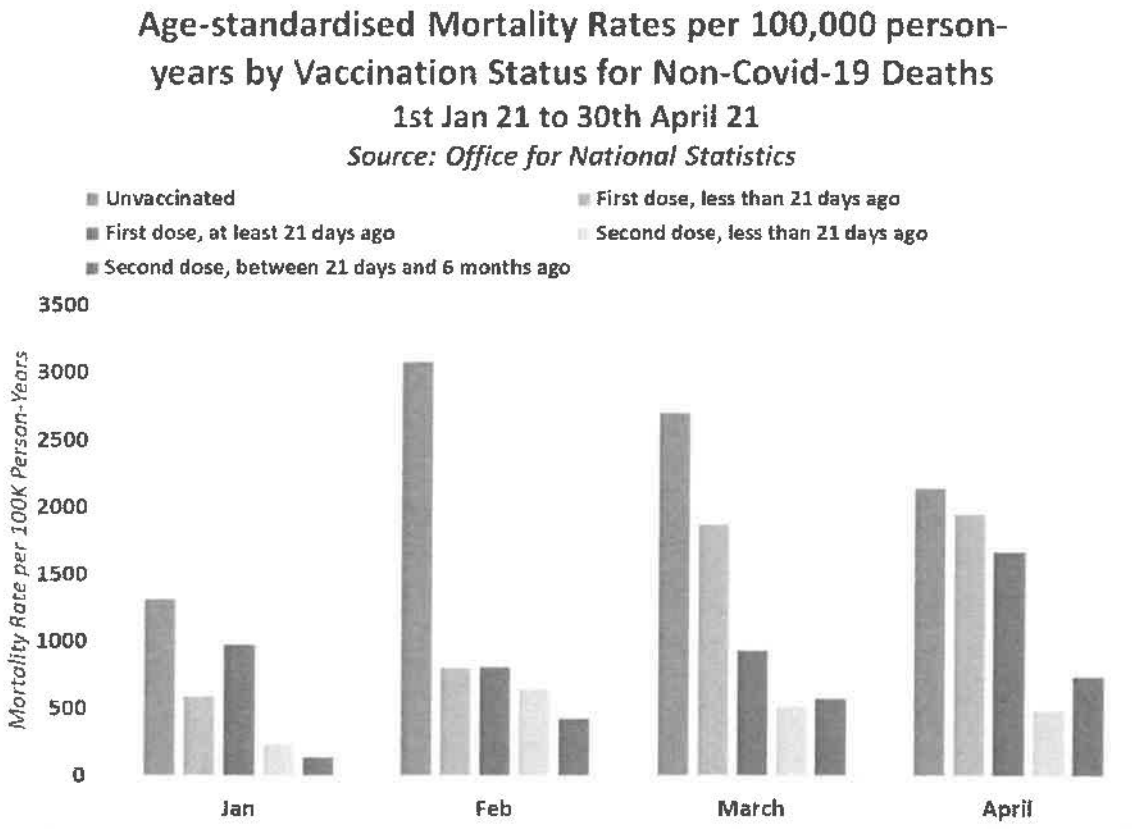
223.1. In May 2022, 82 people died out of the 11 200 000 unvaccinated individuals. That works out to a percentage of 0,00073%. Conversely, 1282 people died out of the 44 800 000 vaccinated individuals.

223.2. That works out to a percentage of 0,0029%. What that means is that, in May 2022, the vaccinated had a 4x greater chance of dying of Covid-19 than did the unvaccinated. That trend tracks through most months of available data. That is a deadly blow to vaccine effectiveness arguments.

224. Further an analysis of official ONS data reveals that, even in non Covid-related deaths, deaths were increasing in the vaccinated to the extent that they surpassed the deaths in the unvaccinated.

225. Approximately five months after each dose of the Covid-19 vaccine was administered, the non Covid-related mortality rates among the vaccinated rose significantly compared to the unvaccinated in each age group. The following charts were created using data extracted from table 1 of the Office for National Statistics dataset on 'Deaths by vaccination status (Jan 2021 to May 2022).

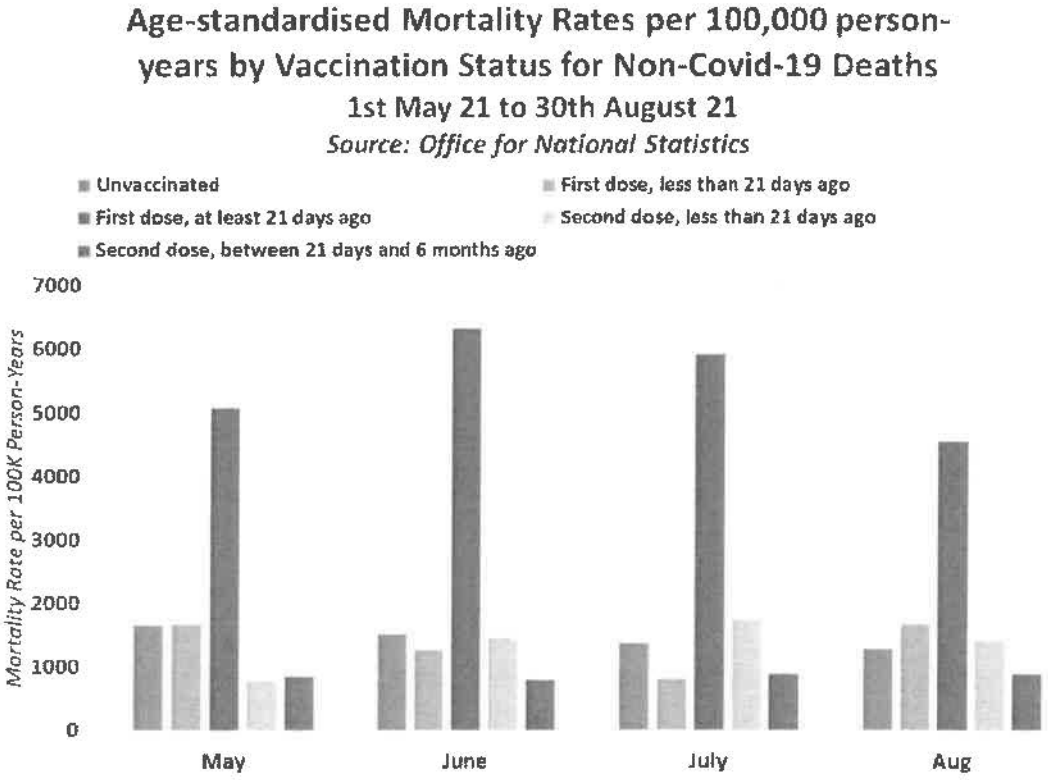
226. The first chart shows the age-standardised non Covid-related mortality rates by vaccination status between 1 January 2021 and 30 April 2021.



227. At face value the above bar chart appears to show that non Covid-related mortality rates were initially highest among the unvaccinated. However, were the brown, red, yellow and purple bars to be stacked on top of one another, to indicate total deaths in vaccinated individuals, the picture changes.

228. By the end of April 2021, five months after the first Covid-19 injection was administered in the UK, things became, and remained, manifestly worse for the vaccinated,.

229. The below chart shows the age-standardised non Covid-related mortality rates for the next four months: 1 May 2021 to 31 August 2021. They reveal that the mortality rate among the vaccinated began to escalate significantly, while revealing a some gradual decrease in mortality rate among the unvaccinated.

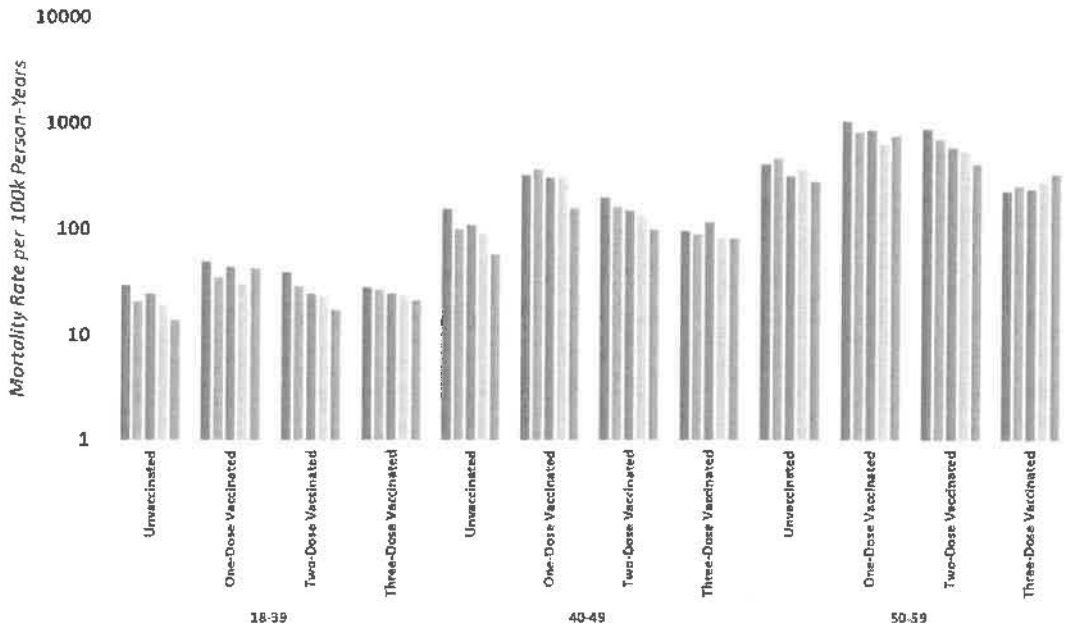


230. Unfortunately, a follow-up report published by the ONS on 6 July 2022, proves that things did not improve for the vaccinated population. By the end of May 2022, mortality rates for Non-Covid-19 deaths were lower among the unvaccinated than among the vaccinated in every age group between 18 and 90+ years in England.

Monthly Age-Standardised Mortality Rates by Vaccination Status by Age Group for Non-Covid-19 Deaths in England

January to May 2022

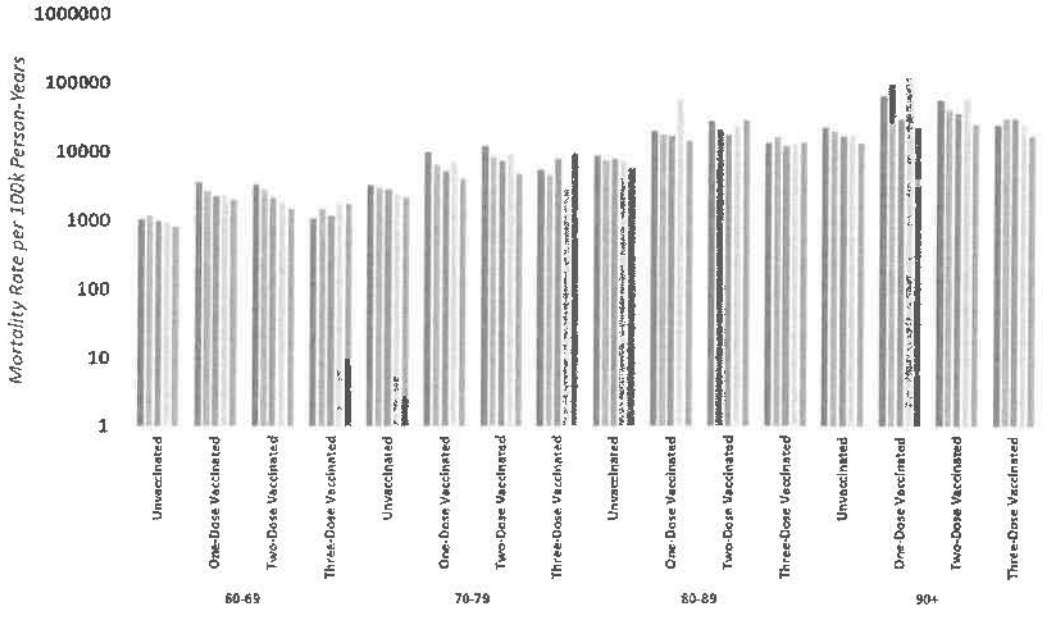
Source: (UK Gov.) Office for National Statistics



Monthly Age-Standardised Mortality Rates by Vaccination Status by Age Group for Non-Covid-19 Deaths in England

January to May 2022

Source: (UK Gov.) Office for National Statistics



231. The above data offers compelling evidence that the Pfizer vaccines are neither effective nor safe .

232. Furthermore, data from a UK Health Security Agency (UKHSA) presentation to the UK Parliament's Joint Committee on Vaccine and Immunization on 25 October 2022 is important.

232.1. The data contains a table titled "*Table 3: NNV (number needed to vaccinate) for prevention of hospitalization [...]*". The table shows the number of people that need to be vaccinated, in different age groups, in order to keep one person out of hospital for Covid-19. The table, reproduced below for ease of reference, shows that:

232.1.1. In age cohorts 5 – 11, 34200 people need to be vaccinated in order to keep one person out of hospital;

232.1.2. In age cohorts 12 – 15, 31400 people need to be vaccinated in order to keep one person out of hospital;

232.1.3. In age cohorts 16 – 19, 11200 people need to be vaccinated in order to keep one person out of hospital;

232.1.4. In age cohorts, 20 -29, 13300 people need to be vaccinated in order to keep one person out of hospital;

232.1.5. In age cohorts 30 – 39, 9900 people need to be vaccinated in order to keep one person out of hospital.

232.1.6. In age cohorts 40 – 49, 10000 people need to be vaccinated in order to keep one person out of hospital.

232.1.7. In age cohorts 50 – 59, 3000 people need to be vaccinated in order to keep one person out of hospital.

232.1.8. In age cohorts 60 – 69, 1200 people need to be vaccinated to keep one person out of hospital.

232.1.9. In age cohorts 70+, 300 people need to be vaccinated to keep one person out of hospital.

Table 3: NNV for prevention of hospitalisation for different programmes

	Programme			
Age	Primary	Booster (2+1)	Autumn 2022 boost	Spring 2023 boost
5 to 11	34200			
12 to 15	31400			
16 to 19	11200	76000	73500	
20 to 29	13300	17600	40900	
30 to 39	9900	15300	35900	
40 to 49	10000	9600	20600	
50 to 59	3000	3000	8000	
60 to 69	1200	1000	3600	
70+	300	500	800	
In a risk group	Primary	Booster (2+1)	Autumn 2022 boost	Spring 2023 boost
20 to 29	2400	3400	7500	7500
30 to 39	1600	3100	7800	7800
40 to 49	2200	2500	6000	6000
50 to 59	800	1200	3100	3100
No risk group	Primary	Booster (2+1)	Autumn 2022 boost	Spring 2023 boost
20 to 29	19900	33900	168200	
30 to 39	21700	53800	210400	
40 to 49	21700	44900	92500	
50 to 59	10900	15800	43600	

233. The same trend, albeit worse, is apparent for the prevention of severe hospitalisation. The relevant graph is reproduced below:

Table 4: NNV for prevention of severe hospitalisation for different programmes

	Programme			
Age	Primary	Booster (2+1)	Autumn 2022 boost	Spring 2023 boost
5 to 11	112200			
12 to 15	162600			
16 to 19	106500	193500	185100	
20 to 29	166200	418100	275200	
30 to 39	87600	188500	217300	
40 to 49	53700	40600	175900	
50 to 59	18700	16200	48300	
60 to 69	5700	9200	27300	
70+	2500	10400	7500	
In a risk group	Primary	Booster (2+1)	Autumn 2022 boost	Spring 2023 boost
20 to 29	11400	43500	59500	59500
30 to 39	10700	28600	40500	40500
40 to 49	9400	10600	49800	49800
50 to 59	5600	6100	18600	18600
No risk group	Primary	Booster (2+1)	Autumn 2022 boost	Spring 2023 boost
20 to 29	no cases	no cases	706500	
30 to 39	318400	no cases	no cases	
40 to 49	186800	190400	932500	
50 to 59	51600	107000	256400	

234. On the face of it, these numbers are concerning because they are so high, but the real impact, and the risk/benefit ratios, become more apparent when these numbers are compared to the numbers of serious adverse events of special interest (serious AESIs) published in the peer-reviewed journal "Vaccine", and annexed as "**HE37**".

235. The relevant article, which is titled "*Serious adverse events of special interest following mRNA Covid-19 vaccination in randomized trials in adults*", finds that in the Pfizer trial, the excess risk of serious AESIs in vaccinated participants vs placebo participants was 10.1 per 10,000.

236. This means that vaccinating 10,000 individuals resulted in about 10 individuals suffering serious adverse events. Serious adverse events are defined as medical events that result in death, life-threatening conditions, permanent disability or hospitalization. Comparison to the above NNV table, finds that vaccination of 10,000 individuals, to keep one out of hospital with severe Covid-19, occurs at the cost of far higher numbers of serious adverse events (death, life-threatening conditions, permanent disability or hospitalization). I ask rhetorically, is that a vaccine with a favorable safety profile or risk/benefit ratio?

237. Furthermore, the article itself, without comparison to data from any other source, concludes as follows under the heading "harm benefit considerations":

> *"In the Pfizer trial, the excess risk of serious AESIs (10.1 per 10,000) was higher than the risk reduction for COVID-19 hospitalization relative to the placebo group (2.3 per 10,000 participants)."*

238. In lay terms, what that means is that for every 2.3 individuals that are kept out of hospital due to vaccination, that same vaccination gives 10.1 people serious adverse events, which include death, life-threatening conditions, permanent disability and/or hospitalization.

239. There is, however, another reason that the Government's claims of 95%, alternatively 91.3% effectiveness of the Pfizer vaccines was inaccurate and needed to be retracted. That reason is this: not even Pfizer claimed 95% effectiveness in their official data and reports. What they claimed was 95%, alternatively 91.3%, efficacy.

240. "Effectiveness" and "efficacy" are two different scientific terms with two wholly different definitions, and the distinction is important in terms of conveying accurate information to the South African public. What the South African government appears to have done is rely on inaccurate data on the efficacy as effectiveness, which ultimately convinced more people to take the vaccine.

241. I explain the difference between "effectiveness" and "efficacy" immediately below with reference to an article annexed as "**HE38**", titled *"What is the difference between efficacy and effectiveness?"* and published by the Global Alliance for Vaccines and Immunity ("GAVI").

241.1. Efficacy is defined in the GAVI article in the following terms:

> *"Efficacy is the degree to which a vaccine prevents disease, and possibly also transmission, under ideal and controlled circumstances – comparing a vaccinated group with a placebo group."*

241.2. Effectiveness is defined in the GAVI article in the following terms:

> *"Effectiveness meanwhile refers to how well [the vaccine] performs in the real world."*

241.3. The article proceeds to explain that efficacy measured in trials does not always translate into effectiveness. The reality is that efficacy measurements can significantly overestimate a vaccine's impact in practice. This is because, in clinical trials, the trial participants are often healthy without underling health conditions.

241.4. I have already demonstrated that that was exactly the case in the Pfizer trial. When a vaccine is then given to the population, factors, such as the medication people are taking, underlying chronic illnesses, age, and how the vaccine is stored and administered under everyday conditions, can reduce how effective the vaccine is at preventing disease. This is why the difference between "efficacy" and "effectiveness" is so important. If trial-measured "efficacy" is reported as "effectiveness" – as it was by the South African Government – then the population is being led to believe that the vaccine has a high effectiveness when, in reality, the effectiveness was not tested in the trial.

242. In support of the GAVI article, I annex as "**HE39**" another article titled "*A Primer on Effectiveness and Efficacy Trials*". It is an important, comprehensive and well-referenced article and I humbly request this Honourable Court to read in in full.

243. That article draws the same distinctions as the GAVI article between efficacy and effectiveness. The article commences with the following introduction:

> *"Although efficacy and effectiveness studies are both important when evaluating interventions, they serve distinct purposes and have different study designs. Unfortunately, the distinction between these two types of trials is often poorly understood. In this primer, we highlight several differences between these two types of trials including study design, patient populations, intervention design, data analysis, and result reporting."*

244. The article first explains the difference between "efficacy" and "effectiveness" in the context of the study design. It explains that randomized control trials – such as the Pfizer trial are ideally suited for efficacy studies – not effectiveness studies, and that effectiveness studies are designed to examine interventions under circumstances that more closely resemble real-word conditions:

> *"Efficacy studies investigate the benefits and harms of an intervention under highly controlled conditions. Although this has multiple methodologic advantages and creates high internal validity, it requires substantial deviations from clinical practice, including restrictions on the patient sample, control of the provider skill set and limitations on provider actions, and elimination of multimodal treatments. A placebo controlled randomized controlled trial (RCT) design is ideal for efficacy evaluation because it minimizes bias through multiple mechanisms, such as standardization of the intervention and double blinding. RCTs generally eliminate issues of access (intervention is provided free), provider recommendation, and patient acceptance and adherence.*
>
> *Effectiveness studies (also known as pragmatic studies) examine interventions under circumstances that more closely approach real-world practice, with more heterogeneous patient populations, less-standardized treatment protocols, and delivery in routine clinical settings. Effectiveness studies may also use a RCT design; however, the intervention is more often compared with usual care, rather than placebo. Minimal restrictions are placed on the provider actions in modifying dose, the dosing regimen, or co-therapy, allowing tailored therapy for each subject. Although effectiveness studies sacrifice some internal validity, they have higher external validity than efficacy studies."*

245. The article proceeds to explain the difference between "efficacy" and "effectiveness" studies in the trial population. Efficacy trials have high exclusion rates. They often exclude people that are unlikely to respond to the intervention such as people with co-morbidities.

246. Again, I have already demonstrated above that this is exactly what occurred in the Pfizer trial.

247. Effectiveness trials, on the other hand, have high rates in inclusivity, including more individuals with co-morbidities, more elderly individuals, or more patients in vulnerable groupings within the population. This means that effectiveness trials give more reliable data about the real-world performance of any medical intervention – including (as in this case) vaccines.

248. Bearing in mind the difference between "efficacy" and effectiveness", I proceed now to evaluate whether the Pfizer trial was designed to test "efficacy" or "effectiveness" of Comirnaty.

249. My analysis refers to the Pfizer trial protocol already annexed above and concludes that it was a trial designed to test efficacy, and not effectiveness.

250. My conclusions rest on the following extracts from the Pfizer trial protocol:

250.1. First, the title of the protocol indicates that the study tests for "efficacy":

> *"A phase 1/2/3, placebo-controlled, randomized, observer-blind, dose-finding study to evaluate the safety, tolerability, immunogenicity, and efficacy of SARS-CoV-2 RNA vaccine candidates against covid-19 in healthy individuals."*

250.2. Second, the study rationale on page 9 of the Pfizer protocol states that the study was intended to investigate the safety, immunogenicity, and efficacy of the vaccine candidates.

250.3. Third, under table headed "Objectives, Estimands and Endpoints for phase 1" commencing on page 10 of the Pfizer protocol, the objectives are stated as testing for "efficacy". There are no objectives listed to test for "effectiveness".

250.4. Fourth, under the heading "study design" on page 36 of the Pfizer trial protocol, the overall design is described as testing for, amongst other criteria, efficacy. Again, there is no mention of effectiveness.

250.5. Fifth, under the heading "study population" commencing on page 40 of the Pfizer trial protocol, numerous exclusions spanning three pages are listed. The trial was heavily controlled, and only healthy individuals were enrolled. This accords with the definition for "efficacy studies" in the aforementioned article and does not accord with the definition of an "effectiveness study".

250.6. Sixth, clause 8.1 of the protocol is headed "Efficacy and/or Immunogenicity Assessments", again indicating that the Pfizer study was an efficacy study.

250.7. Seventh, Pfizer's two-month data report clearly show "vaccine efficacy" of 95%. The relevant portion of the table is reproduced below for convenience (the highlighting is my own), but the full original table appears on page 2613.

Table 3. Vaccine Efficacy Overall and by Subgroup in Participants without Evidence of Infection before 7 Days after Dose 2.

Efficacy End-Point Subgroup	BNT162b2 (N=18,198)		Placebo (N=18,325)		Vaccine Efficacy, % (95% CI)†
	No. of Cases	Surveillance Time (No. at Risk)*	No. of Cases	Surveillance Time (No. at Risk)*	
Overall	8	2,214 (17,411)	162	2,222 (17,511)	95.0 (90.0–97.9)

250.8. It is important to pause here and assess the table above in the context of the representations made by our Government about effectiveness. What the table shows is the following:

250.8.1. 36 523 (18 198 in the vaccine arm + 18 325 in the placebo arm were part of the study) participants were injected in the trial. That is a significant number of trial participants.

250.8.2. But the 95% efficacy statistic was not calculated with reference to all 36 523 trial participants. It was calculated with reference to 170 trial participants. The 95% efficacy is calculated as follows: the number of Covid cases in the vaccine arm (8) was subtracted from the number of Covid cases in the placebo arm (162) equaling 154. 154 was then divided by 162, and multiplied by 100 to reach the 95% efficacy statistic. So, the reality is that our government made the claim of "95% effectiveness" based on "efficacy" data from 170 of the 36 523 trial participants.

250.8.3. It is not possible from the data to get a proper effectiveness statistic. That is because, as explained above, that would require data from a much broader patient cohort, including patients with underlying health conditions, patients in vulnerable groups, and patients on medication over a much longer duration. But one can get some indication of effectiveness by dividing the number of participants that the vaccine prevented from getting Covid (154) by the number of participants given the vaccine (18 198). That gives a result of 0.84%, which is known as the "absolute risk reduction" (ARR). The authors of this report failed to comply with the requirement of the FDA (see paragraph 63 above) to provide absolute risk reduction, not just relative risk reduction.

250.8.4. That perfectly highlights the problem with relying on efficacy studies and erroneous effectiveness studies. It is simply wrong.

251. The conclusion that can be drawn from the above is a simple one: the Pfizer trial was not intended to, nor did it, test for effectiveness. It tested for efficacy. The Government's claim that the Pfizer vaccine is 95, alternatively 91.3% effective is a not accurate. It is correct to say that the Pfizer vaccine had an efficacy of 95% at 2 months and 91.3% at 6 months. Effectiveness of the vaccine was never tested in the trial. One has found no data released by Pfizer to date capable of lending itself to effectiveness calculations.

252. It is not clear how the Government misinterpreted the objective of the Pfizer trial to this extent. It is crystal clear from a perusal of the trial protocol that the Pfizer trial did not test for effectiveness – but that it only tested for efficacy. How and why, under the circumstances, the thirty-three person-strong team (including the esteemed Glenda Gray, Claudina Loots, Harry Moultrie, Tom Moultrie, Emile Stipp, Debbie Bradshaw, Rob Dorrington, Shabir Madhi, Lucille Blumberg, Cheryl Cohen, Wolfgang Preiser, James McIntyre, Ian Sanne, Moherndran Archary, Dean Gopalan, Angelique Coetzee, Eftyhia Vardas, Francesca Conradie, Francois Venter, Helen Rees, Jacqui Miot, Lynn Morris, Silingene Ngcobo, Nombulelo Magula, Prakash Jeena, Lufuno Mathivha, Shabir Banoo, Shaheen Mehtar, Simon Nemutandani, Sitembiso Velaphi and Wendy Stevens) advised government that is was appropriate to tell the public that a vaccine that had <u>not</u> been tested for effectiveness was, in fact, 95%, alternatively 91.3% effective is unclear. The is astonishing.

253. We call on the government respondents in this application to account for the apparent errors.

254. The Government ought to retract the statement the Pfizer vaccines are 95%, alternatively 91.3% effective, and instead explain to the public that the vaccines were only tested for efficacy. To the extent that they do not retract this statement every official who made the statement about "effectiveness" is likely guilty of an offence under the MARS Act.

255. There is another document in which BioNTech admits that both the safety and efficacy of Comirnaty is, at the very least, still in question. That appears from their official filing to the United States of America's Securities Exchange Commission ("**SEC**") dated 24 April 2022, and annexed as "**HE40**". In that filing, the following is stated:

> *"We may not be able to demonstrate sufficient efficacy or safety of our COVID-19 vaccine and/or variant-specific formulations to obtain permanent regulatory approval in the United States, the United Kingdom, the European Union, or other countries where it has been authorized for emergency use or granted conditional marketing approval.*
>
> *Our COVID-19 vaccine has been granted full U.S. FDA approval for individuals 16 years and older, emergency or limited use authorization in a number of countries and approval for use in certain other countries. Our COVID-19 vaccine has not yet been approved by regulatory authorities in many of such countries. We and Pfizer intend to continue to observe our COVID-19 vaccine and other variants of a COVID-19 vaccine candidate in global clinical trials. It is possible that subsequent data from these clinical trials may not be as favorable as data we submitted to regulatory authorities to support our applications for emergency use authorization, marketing or conditional marketing approval or that concerns with the safety of our COVID-19 vaccine will arise from the widespread use of our COVID-19 vaccine outside of clinical trials. Our COVID-19 vaccine may not receive approval outside of the emergency use setting in the countries where it is not currently approved, which could adversely affect our business prospects.*

256. The above is an outright admission by BioNTech that the global monitoring of the vaccine may disprove both the safety and efficacy profiles previously presented by Pfizer.

257. In circumstances where BioNTech itself admits that there is insufficient data to adequately assess the safety and efficacy of the vaccine as it is rolled out to the public, and that global data collection may change the safety and efficacy

profiles, then on what basis has the South African government assured the public that Comirnaty is "safe and effective"?

REPORTS FROM LOCAL DOCTORS SEEING ADVERSE EFFECTS OF THE PFIZER VACCINE PROCDUCTS

258. Across the country, doctors are seeing and reporting adverse events (the same as, or similar to those highlighted by Dr Jessica Rose in her VAERS statistical analysis).

259. These adverse events, as catalogued below, have manifested in otherwise healthy patients with strong temporal associations between the dates on which they received their vaccines, and the dates on which their symptoms began to manifest.

260. In medical terms, a "*temporal association*" refers to a relationship between two events or conditions that occur in a specific order in time. For example, a temporal association between a headache and an onset of nausea could indicate a certain type of headache or a certain cause of the headache.

261. A temporal association is used as a diagnostic tool, as well as a means of understanding the progression of a disease or condition. It is a way to detect patterns and link causes and effects in medical conditions.

262. I have included details from two such doctors for the benefit of the court: Dr Anton Janse Van Rensburg and Dr Maré Olivier.

263. The majority of the vaccine injuries detailed below are listed in the post-authorisation adverse event report, already annexed above commissioned by Pfizer as actual reported adverse events, and/or as "*adverse events of special interest*" (AESIs) potentially related to Pfizer's "COMIRNATY" vaccine.

264. These conditions include – but are not limited to - motor-neurone disease, heart attacks, blood clotting disorders, and neuropathy.

265. The fact that these AESIs coincide with post-vaccination events now presenting in South African patients such as those catalogued below, does not of itself establish causation – but does establish correlation. This correlation, together with consistency, specificity, temporality, plausibility and analogy (Bradford Hill criteria for causation), strongly suggests causation, or proves causation on the balance of probability, between administration of Pfizer's "COMIRNATY" vaccine and the relevant conditions. These were factors that were considered in reaching the diagnoses referred to below.

Dr Maré Olivier

266. Dr Maré Olivier, whose supporting affidavit is annexed as "**HE41**" has provided examples of six vaccine injured patients. Her supporting affidavit contains the rationale for her diagnoses and the Court may refer to that affidavit to the extent that it requires supplementation of the below summary. I now summarize those patients below:

266.1. The first patient was a previously healthy, fit 57-year-old. Prior to his death, he had been Dr Oliver's patient for the past fifteen years, and she can attest to the fact of his health (prior to the Covid-19 vaccine) as well as his clean family medical history. It was a difficult journey watching this patient's deterioration after his Pfizer vaccine on 7 September 2021 to his ultimate and untimely death on 24 January 2023. This patient suffered enormous pain, physical degeneration, and a loss of dignity as he slowly died. This notwithstanding, he photographically documented his journey and gave me permission to share those photographs in legal proceedings (even after his death) if ever asked to do so.

266.2. This patient's first and only Pfizer injection was on 7 July 2021. He began presenting with symptoms a mere four days later. By 11 July 2021, he was presenting with pain in his right eye and temporal area. He saw a neurologist in November 2021, and she requested an MRI, the results of which came back as "normal". She made the diagnosis of Bell's Palsy (unilateral facial paralysis/paresis) and trigeminal neuralgia. She prescribed pain medication to manage the trigeminal neuralgia.

266.3. I pause here to note that facial paralysis/paresis and trigeminal neuralgia are listed as adverse events of special interest in the Pfizer post-authorization report, and were reported as actual adverse events of vaccination within the initial 2½ month data collection period.

266.4. Dr Olivier saw the patient for the first time after his MRI, in February 2022. By this stage he told her that the pain tablets were not working

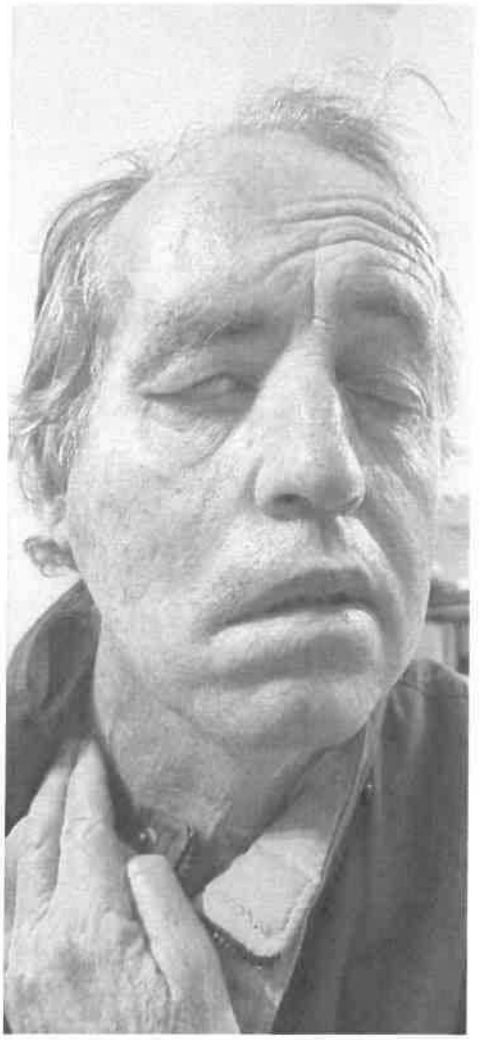
adequately, and that his symptoms were worsening. At that point, he had spent in excess of ZAR 160 000 trying to find out what was wrong with him, and to procure effective treatment – but had failed.

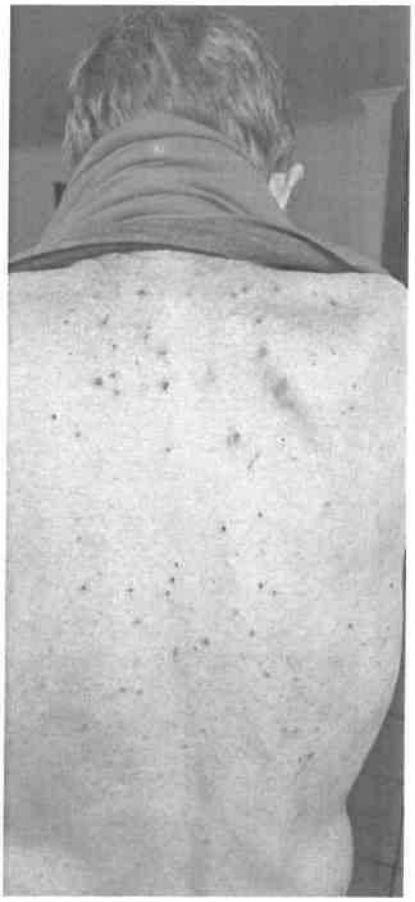
266.5. Dr Olivier saw him again in the beginning of August 2022. By this time, he had severe wasting, and he presented with a palpable hard mass in his right external ear canal. The hard mass obstructed his entire ear canal which, in turn, prevented a physical examination. Dr Olivier sent the patient for a CT scan which showed a mass in his parotid gland, spreading to different cranial nerves and facial muscles responsible for chewing. He then underwent a biopsy at Tygerberg hospital, and he was diagnosed with basaloid carcinoma of the parotid gland. Basaloid carcinoma is a type of cancer that affects the parotid gland, which is one of the major salivary glands located in the cheek near the jaw. It is a rare form of cancer that is often aggressive and may spread to other parts of the body.

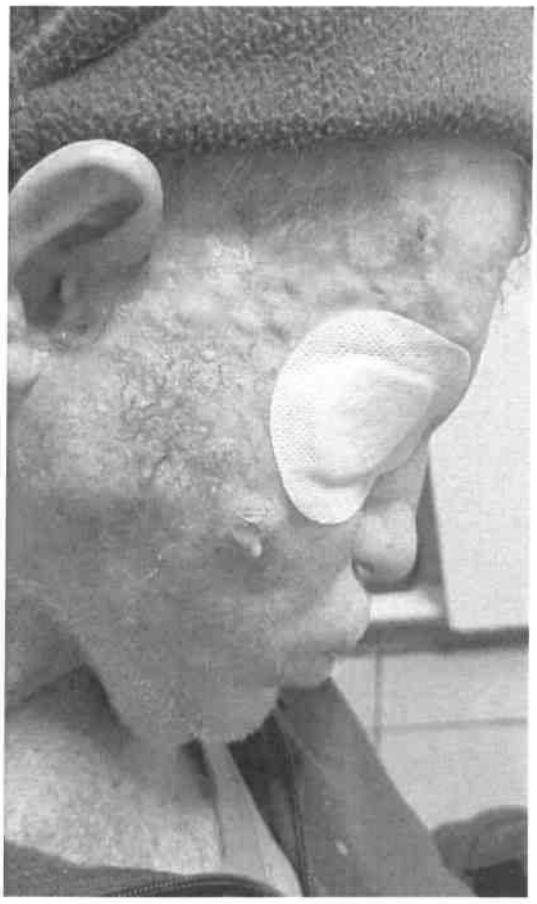
266.6. He died from this cancer on 24 January 2023.

266.7. The sudden and unexplained onset of this patient's condition, together with its rapid progression, and the close temporal association to the vaccine led Dr Olivier to conclude that this patient was probably injured by the Pfizer vaccine. The facts that facial paralysis/paresis and trigeminal neuralgia are listed in the Pfizer 2½ month post-authorization adverse events report (see above), as well as the fact that longer term

VAERS data show a huge increase in cancer cases related to the Pfizer/BioNTech vaccine (see paragraph 42.6 above), were further factors that she considered in reaching her conclusion. Photographs of this patient until the month of his death appear immediately below.







266.8. A second otherwise healthy patient had two doses of the Pfizer vaccine. Two weeks after her second vaccine, she presented with a thrombosis (formation of a blood clot inside a blood vessel, which obstructs and may cut off the flow of blood in the vessel) on the left forearm with increased D-dimers.

266.9. It is important to understand what raised D-dimer levels mean. A D-dimer is a blood test that measures the level of a protein fragment that is produced when a blood clot breaks down. Elevated levels of D-dimers may indicate the presence of a clot or an increased tendency for clotting, which can be due to a variety of underlying medical conditions, such as deep vein thrombosis, pulmonary embolism, or stroke.

266.10. By 17 September 2021, she had developed acute pulmonary tuberculosis ("**TB**"). At this juncture, her wasting was severe. She was admitted to hospital, where she subsequently died on 1 January 2022. For similar reasons to those set out above, Dr Olivier diagnosed this patient as probably having been injured by the Pfizer vaccine.

266.11. A third otherwise healthy patient received two doses of the Pfizer vaccine. A year later (in July 2022), she was diagnosed with aggressive colon cancer (despite her previous health and no family history of this disease). The cancer spread rapidly, killing her on 5 August 2022. For similar reasons to those set out above, Dr Olivier diagnosed this patient as probably having been injured by the Pfizer vaccine.

266.12. A fourth otherwise healthy patient received two doses of the Pfizer vaccine. On 30 November 2021, just after her second dose of the Pfizer vaccine, she had a mammogram which returned normal results.

266.13. However, by March 2022 (a mere 4 months later), she had presented with a lump in her breast and had another mammogram which subsequently confirmed the presence of a carcinoma. On 11 April 2022, a biopsy confirmed the presence of breast cancer.

266.14. The patient is currently receiving chemotherapy. For similar reasons to those set out above, Dr Olivier diagnosed this patient as probably having been injured by the Pfizer vaccine.

266.15. A fifth otherwise healthy patient received two doses of the Pfizer vaccine. One month after her second Pfizer vaccine, the patient consulted with Dr Olivier at her practice. She presented with a change in her stools and blood when defecating. She screened her for cancer. Both her CEA (carcinoembryonic antigen) and D-Dimer counts were found to be elevated. Because of this, Dr Olivier referred her for a colonoscopy, which subsequently confirmed colon cancer. While she was in hospital for treatment of the cancer, the patient also suffered a heart attack. This patient had no family history of colon cancer, and there were no medical markers present for the development of this disease. The patient is stable at present, and on treatment for her cancer. For similar reasons to those set out above, Dr Olivier diagnosed this patient as probably having been injured by the Pfizer vaccine.

266.16. A sixth otherwise healthy patient was a 15-year-old adolescent. He received one dose of the Pfizer vaccine. Within three months, he was presenting with severe abdominal pains. Within nine months after his Pfizer injection, he was diagnosed with macroscopic haemorrhagic cystitis (visible presence of red blood cells in the urine).

266.17. Haemorrhagic cystitis is a condition in which the bladder becomes inflamed and experiences bleeding. The important factor here was that the test she conducted showed a negative culture for infectious organisms.

266.18. Haemorrhagic cystitis with a negative culture refers to a situation where there is visible blood in the urine, but no bacterial or fungal growth is present in a urine culture. This suggests that the cause of the bladder inflammation and bleeding is not due to an infection, but rather due to other factors such as chemotherapy, radiation therapy, or an underlying medical condition or inflammation. The problem was, of course, that this young child had no such underlying causes that could have resulted in his condition.

266.19. Over and above this, haemorrhagic cystitis is uncommon in healthy men – and particularly uncommon in healthy adolescents. For similar reasons to those set out above, Dr Olivier diagnosed this patient as probably having been injured by the Pfizer vaccine.

Dr Anton Janse Van Rensburg

267. Dr Anton Janse Van Rensburg, whose supporting affidavit is annexed as "**HE42**" has provided examples of six vaccine injured patients. His supporting affidavit contains the rationale for his diagnoses and the Court may refer to that affidavit to extent that it requires supplementation of the below summary.

268. I summarize five of those patients below. In the clinical scientific process of reaching his diagnoses, Dr Janse Van Rensburg had regard to the Pfizer 2½ month post-authorization adverse events report (see above), as well as to the longer term VAERS data (see above) and the Bradford Hill criteria (see above). In brief:

268.1. One otherwise healthy patient received two doses of the Pfizer vaccine. Within 20 days of the administration of the second Pfizer vaccine, the patient was experiencing stiffness in his hands.

268.2. By December 2021, the patient started losing sensation in his left leg. This was followed by a progressive loss of motor function in both legs, and he was ultimately diagnosed in March 2022 with motor neurone disease by a neurologist. He was referred to Dr Janse Van Rensburg for palliative care and management of his condition. It is a medical certainty that this condition will eventually kill the patient, following a long period of muscular degeneration and horrendous suffering. Dr Janse Van

Rensburg diagnosed this patient as probably having been injured by the Pfizer vaccine.

268.3. A further otherwise healthy patient received one dose of the Pfizer vaccine. Within three days of having received the vaccine, the patient presented with vertigo, severe ear pain, diarrhoea, and vomiting. Her symptoms persisted, untreated by doctors who refused to consider vaccine injury, until she saw Dr Janse van Rensburg in October 2022.

268.4. In April 2022 she developed severe tinnitus due to suspected vestibulocochlear neuropathy. Dr Janse Van Rensburg diagnosed the patient as probably having been injured by the Pfizer vaccine.

268.5. A third otherwise healthy patient had received two doses of the Pfizer vaccine. Within two weeks of receiving the second dose of the Pfizer vaccine, the patient presented with signs of olfactory and trigeminal neuropathy.

268.6. In lay terms, he presented with severe nervous problems related to smell and facial sensory perception. His symptoms include severe fragrance hypersensitivity, unbearable facial pain (described by those who suffer from it as suicidally painful), burning skin and a skin rash. Dr Janse Van Rensburg diagnosed this patient as probably having been injured by the Pfizer vaccine.

268.7. A fourth patient received one dose of the Pfizer vaccine. Within five days of having received the Pfizer vaccine, the patient developed obstructive jaundice.

268.8. Obstructive jaundice is a specific type of jaundice, where symptoms develop due to a narrowed or blocked bile duct or pancreatic duct, preventing the normal drainage of bile from the bloodstream into the intestines. It may be severe or even fatal. He also developed hyper-coagulability, which is a high clotting risk, with clot formation, and reported developing abscesses in multiple sites of his body. His pre-existing Parkinson's symptoms also worsened. Dr Janse Van Rensburg diagnosed this patient as probably having been injured by the vaccine.

268.9. A fifth otherwise healthy patient received two doses of the Pfizer vaccine. Within 24 hours after the first dose of the vaccine, the patient had an acute anaphylactic reaction, which is a severe, deadly allergic reaction. She was given injectable and oral cortisone by a general practitioner to manage the attack. Had it not been for that intervention, the patient would likely have died. Dr Janse Van Rensburg diagnosed this patient as probably having been injured by the vaccine.

A SUMMARY OF THE GROUNDS OF REVIEW

269. It is against the facts set out above, that I summarise the provisions of law relied upon by the applicant for purposes of this application. These are:

269.1. Section 6(2)(a) of PAJA;

269.2. Section 6(2)(b) of PAJA;

269.3. Section 6(2)(c) of PAJA;

269.4. Section 6(2)(d) of PAJA;

269.5. Section 6(2)(e)(i) of PAJA;

269.6. Section 6(2)(e)(ii) of PAJA;

269.7. Section 6(2)(e)(iii) of PAJA;

269.8. Section 6(2)(e)(vi) of PAJA;

269.9. Section 6(2)(f) of PAJA;

269.10. Section 6(2)(h) of PAJA;

269.11. Section 6(2)(i) of PAJA.

270. In the alternative to the above provisions of law, the applicant also relies on the principle of legality as a basis for the review. As demonstrated in this affidavit, the impugned decisions are clearly irrational.

271. The rights implicated in this case include the rights protected in the following constitutional provisions:

271.1. section 10 of the Constitution;

271.2. section 11 of the Constitution;

271.3. section 12 of the Constitution; and

271.4. section 33.

272. As is evident from what I have stated in this affidavit, the rights infringed by the impugned decisions are not only those of the applicant and its members, but those of the broader public as well.

CONCLUSION

273. The applicant humbly requests the Court to grant the relief sought in the notice of motion in the interests of the health of the South African public.

WHEREFORE on behalf of the applicant, I pray for an order in terms of the notice of application to which this affidavit is attached.

HERMAN JACOBUS EDELING

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me at PRETORIA on this the 22 day of MARCH 2023, the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

COMMISSIONER OF OATHS

Name:

Address:

Position:

PETRUS GERHARDUS LOUWRENS KOEN
COMMISSIONER OF OATHS Ex Officio
PRACTISING ATTORNEY
REPUBLIC OF SOUTH AFRICA
LOFTUS VERSVELD NORTHERN PAVILION (Gate No. 12)
SECOND FLOOR, OFFICE NO. 4
416 KIRKNESS STREET, ARCADIA, PRETORIA, 0002
Tel: 087 0010 793 Fax: 086 276 4377

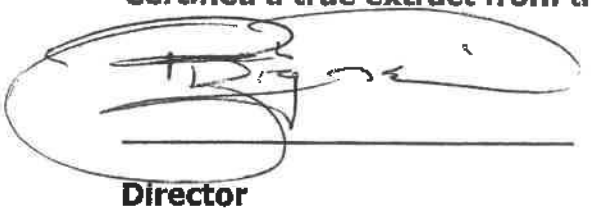
RESOLUTION PASSED BY THE BOARD OF FREEDOM ALLIANCE OF SOUTH AFRICA NPC ("FASA") ON THE 15th DAY OF MARCH 2023.

It is resolved that –

a) **FASA** institutes a semi-urgent application to the High Court against the Minister of Health and several other Respondents, in order to seek the relief as set out in the attached Notice of Motion marked as annexure **"X"**.

b) **DR HERMAN JACOBUS EDELING** is hereby authorised to depose to any affidavits and to sign any documents that may be necessary to give effect to the resolution passed herewith.

Certified a true extract from the minutes of the meeting.



Director

Dr Paolo Brogneri

"HE2"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF HEALTH	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent

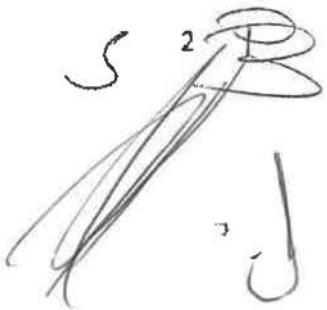
1

MEMBER OF THE EXECUTIVE COUNCIL: LIMPOPO DEPARTMENT OF HEALTH	Twelfth Respondent
MPUMALANGA DEPARTMENT OF HEALTH	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: MPUMALANGA DEPARTMENT OF HEALTH	Fourteenth Respondent
NORTHERN CAPE DEPARTMENT OF HEALTH	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTHERN CAPE DEPARTMENT OF HEALTH	Sixteenth Respondent
NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

CONFIRMATORY AFFIDAVIT

I, the undersigned

DR PAOLO BROGNERI



do hereby make oath and state that:-

1. I am an adult male dentist, domiciled at 49 Victoria Road, Camps bay, Cape Town. I am also a director of the applicant in this application, the Freedom Alliance of South Africa ("FASA"). I confirm that the institution of this application, as well as the full prosecution thereof, has been authorized by the Board of FASA as per the resolution already annexed to the founding affidavit.

2. The facts in this affidavit are, to the best of my knowledge, both true and correct, and, unless the contrary appears from the context of this document, they fall within my personal knowledge. Where I make legal submissions, I do so on the advice of the legal team in this case, and I accept their advice as correct.

3. FASA is a non-profit company duly registered and incorporated in terms of the Company laws of South Africa, with specific focus on human rights.

4. FASA's objectives include the promotion of equal rights, the expansion of freedoms, access to information without censorship and one-sided narratives, and equality and protection in general for all independent men and women of South African, in relation to the South African Constitution.

5. FASA's core values include but are not limited to:

   5.1. A belief that everyone is equally valuable because they live and are deserving of dignity.

5.2. FASA is a non-sexist, non-racist, non-discriminatory organisation, and within this context FASA is open for membership to all irrespective of race, creed, social, religious, and economic circumstances, literacy levels and educational attainment. The organisation respects historical, cultural, belief systems and social traditions, and it pursues integrity, honesty and accountability.

5.3. FASA believes in empowering the poor and the voiceless, and it recognises and respects everyone's personal choices and freedoms.

5.4. FASA believes that all are equal before the law and believe further in upholding justice and righteousness. The organisation supports moral and ethical behaviour.

5.5. FASA believes that leadership should be capable in their functions, and that they should serve to benefit all the free and independent people of South Africa

6. The above objectives are fulfilled by, *inter alia*, pursuing litigation to promote, protect, achieve and fulfill FASA's objectives and core values. The Board of FASA has the power to authorize the institution and prosecution of litigation where that litigation promotes FASA's objectives and values, and they have the authority to institute legal proceedings in the interests of the organisation, in the interests of the organization's members, and/or in the public interest.

7. FASA, its membership, its steering committee and its Board are gravely concerned about Pfizer's Covid-19 mRNA vaccine branded "Comirnaty", as well as its new

"Ready to Use" adult vaccine, and "Dilute to Use" pediatric vaccine ("the Pfizer vaccines").

8. Particularly, FASA is concerned for the safety of South African citizens (particularly some of the most vulnerable amongst us – pregnant women, yet unborn children, and the elderly), which directly implicates its core objectives as set out in paragraph 4 above. Pfizer's own trial data, and publicly available safety data suggest serious safety signals associated with Pfizer's vaccines.

9. Furthermore, FASA is opposed to the one-sided, heavily censored narrative in the mainstream media concerning the safety, efficacy and effectiveness of the Pfizer vaccines. The narrative is unbalanced and appears to be immune to facts that stand in opposition to the narrative, as well as growing scientific consensus on the harms and risks of mRNA technology. Here, too, FASA's interest in promoting and protecting South African's citizen's right of access to information (which includes a right to accurate, and complete sets of information) is directly implicated.

10. Lastly, as set out in Dr Edeling's affidavit, this case implicates, at a bare minimum, the Constitutional rights to life, dignity, and bodily integrity. That, too, falls within FASA's purview as an organisation principally dedicated to human rights.

11. For these reasons, FASA authorized this application. It humbly requests the Court to intervene where it appears, *prima facie*, that SAHPRA and the Government have failed to act with due care, and in the public interest.

DR PAOLO BROGNERI

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me at RONDEBOSCH on this the 21 day of MARCH 2023, the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

COMMISSIONER OF OATHS

Name: MTINGENI

Address: CHURCH STREET, RONDEBOSCH

Position: SERGEANT

SUID-AFRIKAANSE POLISIEDIENS
COMMUNITY SERVICE CENTRE
21 MAR 2023
RONDEBOSCH
SOUTH AFRICAN POLICE SERVICES

"HE3"

DR. HERMAN J. EDELING

NEUROSURGEON / MEDICO-LEGAL PRACTITIONER / MEDIATOR

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2041

Gauteng - Republic of South Africa

Telephone : 011-648-5101

Email : edeling@emlct.com

ABBREVIATED CURRICULUM VITAE 2022

QUALIFICATIONS AND CAREER

Matric	Grey College Bloemfontein	1969
M.B.,B.Ch.	Witwatersrand University	1975
Internship	Bloemfontein Academic Hospitals	1976
Medical Officer	SADF National Service	2 yrs
Neurosurgical Medical Officer /Registrar	Princess, Old Johannesburg General and Baragwanath Hospitals	2 yrs
Private General Practice	Parys-Kimberley-Sandton	1981 - 1990
Neurosurgical Registrar	Johannesburg and Baragwanath Hospitals	1990 - 1992
FCS Neurosurgery	South African College of Medicine	1992
Consultant Neurosurgeon and Lecturer	Johannesburg Hospital and Witwatersrand University Medical School	1993 - 1994
Private Neurosurgical and Medico-legal Practice	Johannesburg and Sandton (Neurosurgical Operative Practice ceased in 2008)	1993 - current
CIME	American Board of Independent Medical Examiners	2009
Appeal Tribunal Member/Chair	HPCSA	2012 – 2016
Accredited Mediator	UCT/MiM	2016
Medical Mediator	Johannesburg	2017 - current

CURRENT MEMBERSHIPS / PROFESSIONAL ACTIVITIES

Covid-19 – SA "Vaccine" Injury Medico-Legal Study Group (SAVIMS) – Founder

Covid-19 – Childrens Health Defence (CHD) Africa

Covid-19 – SAVAERS Advisor-Advocates

Covid-19 – Pandemics – Data & Analytics (PANDA)

South African Medico-Legal Association (SAMLA) - Honorary Life Member

Road Accident Fund (RAF) - Leader of Mediation Pilot Project obo SAMLA

Association for the Protection of Road Accident Victims (APRAV) Solutions Task Team Medical Committee – Chairperson

Society of Neurosurgeons of South Africa (SNSA)

South African Spine Society (SASS)

Colleges of Medicine of South Africa (CMSA)

South African Medical Association (SAMA) – Life Membership 2017

PREVIOUS AND OTHER PROFESSIONAL ACTIVITIES

South African Medico-Legal Association (SAMLA) – Director 2005 to 2020 (Exco Portfolios - Deputy Chairperson - Faculty Principal – Mediation – Clinical Negligence – Administration and Comunication)

Medical Mediators SA – Co-Founder / Deputy Chairperson

South African Medico-Legal Coalition Task Team – Co-Founder and Peer Review Standing Committee Chairperson

International Ethics Research Project – Dr W Moore – Stellenbosch University Faculty of Medicine and Health Sciences

Regular Attendance at Congresses, Instructional Courses, Seminars and Meetings of Various Professional Societies and Associations

South African Clinical Neuropsychological Association (SACNA) – Associate Member and Regular Invited Speaker

Lectures to Nursing Staff at Milpark-, Sunninghill-and Kenridge Hospitals

Wits / Donald Gordon Medical Centre Accredited Practitioner and Lecturer

Advanced Trauma Life Support (ATLS) Instructor

Sunninghill Hospital Medical Ethics Committee

Founder/Director of MediCity Kimberley Private Hospital

Member of Kimberley Provincial Hospital Medical Committee

Secretary of Griqualand West Branch of Medical Association of SA

Treasurer of Students Medical Council University of the Witwatersrand

Chairman of Men's Residence House Committee University of the Witwatersrand

PUBLICATIONS

PER - The Road Accident Fund And Serious Injuries: The Narrative Test – Slabbert & Edeling (2012)

SAMJ – HPCSA Guidelines to The Narrative Test – Edeling, Mabuya, Engelbrecht, Rosman & Birrell (2013)

OBITER - Serious Injury Claims Rejected By The Road Accident Fund: The Appeal Process – Slabbert & Edeling. (Accepted for publication in Volume 1 - June 2016)

SELECTED ARTICLES / PRESENTATIONS / SUBMISSIONS

Covid-19 – St Vincent and the Grenadines Class Action – Reserved as Expert Witness – 2022

Covid-19 – Commission for Conciliation, Mediation and Arbitration (CCMA) – Reserved as Expert Witness for Various Hearings – 2022

Covid-19 – Informed Consent for "Vaccination" – Author - 2022

Covid-19 – SA Constitution - What Does Section 36 Really Say? – Author – 2022

Covid-19 – Questions for Vax Pushers – Author – 2022

Covid-19 – ACDP v Minister of Health and DG of Health – Amendment of Health Regulations – Expert Affidavit – 2022

Covid-19 – SA Rugby MyPlayers – Vaccine Mandates/Efficacy/Safety – Invited Panellist – 2022

Covid-19 – Vaccine Efficacy – Analysis of Factual and Scientific Medical Evidence – Author – 2022

Covid-19 – Various Medical Reports for "Vaccine" Exemption – 2022

Covid-19 – Truth Conference – Invited Panellist – 2022

Covid-19 – ACDP Verious Events – Invited Speaker – 2022

Covid-19 – SA VAERS Presentation to KZN SACP – Invited Panellist – 2022

Covid-19 – World Council for Health - Understanding Vaccine Causation Conference – Invited Panellist – 2022

Covid-19 – SA VAERS Presentation to KZN Provincial Legislature – Invited Panellist – 2022

Covid-19 – Ministerial Appointment to Appeal Committee ito Section 24A of Medicines and Related Substances Act – Free the Children v SAHPRA – 2022

Covid-19 – Free State for Choice v University of the Free State – Case No 131/2022 – Expert Report and Affidavits – 2022

Covid-19 – Vaccine Mandates – Medical Analysis With Reference to Criteria Specified in Section 36 of the Bill of Rights of the SA Constitution – Author – 2022

Covid-19 – Regular Scientific Online Meetings – 2021 & 2022

Covid-19 – Various Radio and TV Interviews – 2021 & 2022

Covid-19 – Medical Advisor to National Employers Association of SA (NEASA) – 2021

Covid-19 – ACDP and Others v Minister of Health and Others – "Vaccination" of Children – Case No 55070/2021 – Expert Affidavit – 2021

Covid-19 – Pan African Bar Association of SA (PABASA) Webinar – Invited Panellist – 2021

Covid-19 – Hope 2021 Indaba – Invited Panellist – 2021

Covid-19 – Sakeliga KragDag – Ethical Perspectives – Invited Panellist– 2021

Covid-19 Pandemic – Health and Economic Crises – Open Letter to the RSA Minister of Health – Author – 2021

Covid-19 Pandemic – Health and Economic Crises – Open Letter to President Ramaphosa – Author – 2021

Covid-19 – The Good News about Covid-19 – Author – 2021

Covid-19 – Televised Debate – Elephant in the Room – Invited Panellist – 2021

Covid-19 – Blind Faith or Open Minds – Critical Thinking in Times of Crisis – Author – 2021

Road Accident Fund (RAF) – Stakeholder Roundtable Meetings – Invited Panellist – 2022

Educational Psychology Association of South Africa (EPASSA) - 2021 - Invited Speaker "The Educational Psychologist Working As A Medico-Legal Expert – Traumatic Brain Injury"

University of the 3rd Age (U3A) - 2020 - Invited Speaker "South African Medico-Legal Overview & Developments"

SAMLA Guidelines and Protocol for Mediation of RAF Personal Injury Disputes – Author

SAMLA Medical Mediation Pilot Project Plan – Co-Author

SAMLA Guidelines and Protocol for Medical Mediation – Co-Author

SAMLA Seminars and Expert Witness Training Workshops – Regular Presenter and Syndicate Leader

SAMLA Mock Trials – Regular Participant (Commentator – Expert Witness)

MD-INK Symposium - 2019 - "Monitoring & Eradicating Medical Errors"

Chris Hani Baragwanath Hospital Academic Day Ethics - 2019 - Invited Speaker "Medicolegal Pearls"

Educational Psychology Association of South Africa (EPASSA) - 2019 - Invited Speaker "Traumatic Brain Injuries - What the Educational Psychologist Needs to Know"

Pretoria Advanced Advocacy Training Workshop 2018 – Expert Witness

Parliamentary Portfolio Committee on Transport 2018 – Submissions on RABS (Road Accident Benefit Scheme) Bill

Society for Educational Psychologists in SA (SEPSA) - PsySSA Congress – "The role of the Educational Psychologist in medico-legal work - Head injuries with TBI (traumatic brain injury) in Children"

Society for Industrial & Organisational Psychology SA (SIOPSA) 2018 – Invited Speaker "TBI (traumatic brain injury)"

Gauteng DoH – Medico-Legal Advisor 2017 - 2018 (Patient Safety / Litigation / Peer Review / Mediation)

University of South Africa (UNISA) - 2017 - External Examiner for LLD Thesis

Clinix Annual Doctor's Conference 2017 – Invited Speaker "Clinical Negligence and Ethics"

Conflict Dynamics – Training Course on Mediation Skills for Medical Negligence and Personal Injury Claims 2017 – Participant

National DoH – Contantia – Hogan Lovells - Medical Malpractice Workshop 2017 – Panel 1 Chairperson

Medical Mediation Showcase 2016 – SAMLA / Conflict Dynamics – Developer/Chair

ANC Legal Research Group – 2016 - Workshop on Medical Negligence and Bleeding of the Public Purse 2016 – Invited Participant

COMOC 2016 (Combined Orthopaedic Associations Congress) – "Negligence In Spinal Surgery - How To Stay Out Of Trouble With The Law – Ethics"

Lecture to UP - MPHIL: PBL 812 (Medical Law And Ethics) "Drafting of Medical Malpractice Reports"

Lectures to Gauteng Department of Health - 2016 - "Avoidance of Medical Negligence"

National Department of Health (DoH) – 2015 - 2016 – Written Submissions to Medico Legal Summit – Rapporteur of Patient Safety Commission – Submissions obo SAMLA Board to Ministerial Task Team

South African Clinical Neuropsychological Association (SACNA) Conference - 2014 - Presentations on "Assessment of mTBI (mild traumatic brain injury)" - "Assessment of PTA (post-traumatic amnesia)"

Road Accident Fund (RAF) - 2014 - Invited Proposals for List of Serious Head Injuries

Minister of Transport - 2014 - Comment on Draft RABS Bill obo SAMLS

IIR – Medical Malpractice Conference – 2013 – "RAF4 Legislation, Narrative Test, Appeal Tribunal Guidelines, Malpractice by Medical Experts"

Affidavits to Constitutional Court - 2009 & 2010 - LSSA & Others v Minister of Transport - RAF Amendment Act (Medical Tariffs)

Medical Association of Namibia Congress - 2007 - Invited Speaker "Multidisciplinary Disability Assessment" and "The Expert Witness"

Department of Transport Regulatory Steering Committee - 2006 - Serious Injury Assessment Proposals

SNSA and SASS – Spinal Surgery Risks Survey - 2005 - Article on Whiplash Injuries

MEDICO-LEGAL EXPERIENCE

Medico-Legal Reports > 3719

Pre-Trial Expert Meetings > 1345

Meetings with Counsel > 795

Expert Evidence in Court > 235 matters

Mediations > 42

"HE5"

DR. HERMAN J. EDELING

NEUROSURGEON / MEDICO-LEGAL PRACTITIONER / MEDIATOR

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His Excellency the Honourable President Cyril Ramaphosa
The President of the Republic of South Africa

10 August 2021

COVID-19 PANDEMIC – HEALTH AND ECONOMIC CRISES

Dear Mr President,

We approach you in the spirit of Thuma Mina, in full confidence that you have the interests, livelihoods, health and lives of all the people of South Africa at heart. In this open letter we address you specifically in regard to safe and effective means of prevention and treatment of COVID-19.

The new long walk to freedom that will restore human health and dignity must begin now. The road leading to happy, successful individuals, families and communities may be challenging, but will be rewarding. To achieve this you, Mr. President, will have to make hard and unpopular decisions now, to release the people of South Africa from medical authoritarianism, economic hardship and avoidable illness and death.

1. BACKGROUND AND CONTEXT

1.1. Since the onset of the COVID-19 pandemic the people of South Africa have suffered a major health crisis as well as a major economic crisis. The harmful effects of these crises, which have included widespread fear, confusion, feelings of helplessness, loss of freedoms, overwhelmed healthcare practitioners, insufficient hospital beds and equipment, loss of employment, financial ruin, severe physical and mental illness, disability and death, are massive and incalculable.

1.2. These harmful effects have been aggravated by official South African COVID-19 narratives, which seem in blind faith to echo the official narratives of the WHO, FDA, CDC as well as European, American, Canadian and Australian governments, inter alia.

1.3. The official South African COVID-19 narratives are strongly and repeatedly communicated by yourself and members of your national and provincial executives, as well as by representatives of institutions such as public health departments, universities, etc. that are directly or indirectly under your control or influence.

1.4. The mainstream media have jumped onto the bandwagon and continue to amplify these official narratives.

1.5. The mRNA "vaccines" in current use are now scientifically linked to rising breakthrough infections, hospitalizations and deaths (see Israeli study breakthrough infections - see covid statistics Iceland). In effect, the cure may become worse than the illness. Despite being denied by officials and mainstream media this news has spread via social media, and is one of the leading reasons for "vaccine hesitancy".

1.6. We wish to applaud you and your Acting Health Minister, Mmamoloko Kubayi, for stating publicly that getting the COVID-19 "vaccination" is not mandatory in South Africa and will not be. She is on record as having stated: "*We have been very clear and the President has been very clear that we should never force people [to 'vaccinate']. It's voluntary. That's why we do the work that we're doing to make sure that there's enough information for people to decide whether they want to 'vaccinate' or not.*" Our concern in this regard is that this important message is not communicated as strongly or repeatedly by those under your authority, the mainstream media and big business (refer press report).

1.7. Elements of the official South African COVID-19 narratives include, but are not limited to:

1.7.1. The PCR test in current use identifies persons who are infected with SARS-CoV-2.

1.7.2. Those who have a positive PCR test and who become sick, are admitted to hospital or die; have become sick, been admitted to hospital or died due to COVID-19.

1.7.3. There is no effective or safe medical treatment for the early phases of COVID-19.

1.7.4. People should not use the home-based treatments that have not been officially authorized, even if these are recommended by doctors and scientists.

1.7.5. Instead, if you have a PCR test and become ill, you should isolate at home and wait to either become well or become so ill that you need to go to hospital.

1.7.6. The coronavirus "vaccines" in current use are effective and safe.

1.7.7. COVID-19 can only be prevented by lockdowns, social distancing, hand sanitization, masks and "vaccines". There are no other medical means of preventing COVID-19.

1.7.8. Everybody has a duty to be "vaccinated" in order to protect themselves and everybody else.

1.8. In the light of the following reported facts and opinions, which are relevant to the health and economic well-being of South Africans, and which are ignored and/or suppressed by those acting under your authority, the abovementioned official South African COVID-19 narratives appear to be harmful by virtue of being false, misleading or irrational:

1.8.1. The coronavirus PCR test is non-specific and yields false positive results, as it has no capacity to differentiate between SARS-CoV-2 and a variety of viruses that cause flu or the common cold. This has finally been acknowledged by the CDC (Centre for Disease Control) in the USA, who have declared that PCR testing will be withdrawn in December 2021 (refer CDC issue lab alert on PCR tests).

1.8.2. Logically therefore, published statistics about COVID-19 positive cases, hospitalizations and deaths are overstated to a degree that cannot be determined.

1.8.3. There is good evidence for safe and effective medical methods of preventing COVID-19 (refer to GOOD NEWS document).

1.8.4. There is good evidence for safe and effective medical treatment for the early phases of COVID-19 (refer to GOOD NEWS document).

1.8.5. The coronavirus mRNA "vaccines" are the product of experimental scientific research that has not met accepted international standards to be declared safe or effective in animal or human subjects. This is why they have not been approved for use in human subjects, but have been released under emergency use authorization (EUA) for use in a large experiment (refer to SAHPRA press release).

1.8.6. The experimental coronavirus mRNA "vaccines" are different to traditional vaccines (weakened or killed bacteria or virus) that the world has grown to know and trust (refer CDC understanding mRNA COVID-19 vaccines).

1.8.7. Logically therefore, by naming them "vaccines", instead of experimental genetic interventions, people instinctively associate their safety and efficacy with the traditional vaccines they have grown to know and trust.

1.8.8. For the above reasons the definition of the word "vaccine", as it has always been known, has recently been changed in order to accommodate the experimental coronavirus mRNA injections (refer Merriam-Webster).

1.8.9. Health authorities do not know whether the experimental coronavirus mRNA "vaccines" are safe, nor how effective they may be or how long any immunity from them may last "*Available evidence indicates that eligible COVID-19 vaccines have an acceptable short-term safety profile. Additional studies and long-term population-level surveillance are strongly encouraged to further*

define the safety profile of COVID-19 vaccines" (refer Evaluation of the safety profile of COVID-19 vaccines: a rapid review).

1.8.10. Despite widespread use of the term "acceptable" safety profile, results of early voluntary reporting indicate increased risks of harm and death associated with the experimental coronavirus mRNA "vaccines" as compared to traditional vaccines (refer Guetzkow VAERS – Israel – Iceland).

1.8.11. Despite the fact that the "vaccine" is experimental, and despite the above reports, transparency by the South African government is not yet evident as it has not, to date, encouraged reporting of vaccine adverse events by members of the public and healthcare professionals, nor has it published tracked statistics about "vaccine" related side effects, serious illness, disability or death.

1.8.12. Anyone who suffers harm or dies as a result of the experimental coronavirus mRNA "vaccines" will not have any legal claim against the manufacturer as the South African government has granted the manufacturers immunity from liability (refer Fund to Protect Pharm Companies).

1.9. Elements of the official narrative also contain inexplicable double standards, such as the contrast between:

1.9.1. One standard. Those who have a positive PCR test and who become sick or are admitted to hospital or die; have become sick, been admitted to hospital or died due to their COVID-19. Contrasting standard. Those who have had a SARS-CoV-2 "vaccine", and who become sick or are admitted to hospital or die, may have become sick or been admitted to hospital or died for reasons unrelated to the "vaccine"; and are being investigated to determine the real cause of their sickness, hospital admission or death.

1.9.2. Another standard. Ivermectin should not be used for prevention or treatment of COVID-19 because the available evidence does not meet the required standard of peer reviewed prospective randomized double blind controlled trials (refer NEMLC rapid review on Ivermectin). Contrasting standard. People

are urged to take the experimental coronavirus mRNA "vaccines", despite the fact that the available evidence does not meet the required standard of peer reviewed prospective randomized double blind controlled trials, and despite the fact that the short-term trials that have been relied upon for the EUA, and which have been conducted by the manufacturing companies, have not been independently reviewed or reproduced (refer SAHPRA).

1.9.3. Another standard. Vaccination is voluntary and not mandatory (see paragraph 1.6 above). Contrasting standard. Pressure is exerted on people to be "vaccinated". In line with official narratives many companies are now coercing their employees to be "vaccinated".

1.10. We are also concerned about ad hominem attacks against those doctors and scientists who, in line with years of consistent teaching, speak up about what they know, understand and question, and what they believe to be their ethical duty.

1.11. We are of the opinion that mass prevention regimes and early treatment regimes, with nutraceuticals and proven medications (see GOOD NEWS document), together with a caring non-fear inducing environment, would greatly reduce the numbers of sick, disabled and dead South Africans.

2. OUR PLEA TO YOU AS THE PRESIDENT OF SOUTH AFRICA

2.1. In the light of the seriousness of the COVID-19 crises, and in line with your duty to all the people of South Africa, we plead with you to:

2.1.1. Encourage everyone, and especially the Departments of Health, to make use of known and available medical methods for prevention and treatment of COVID-19 (refer to GOOD NEWS document).

2.1.2. Ensure that properly informed consent is obtained by all who administer "vaccines" before "vaccinating" anyone (refer to Informed Consent documents).

2.1.3. Admit that science is not an institution to be proclaimed by authority, but that it is independent of authority, dependent only upon free and uncensored application of the scientific method. This includes observation, questioning, research, forming hypotheses, experimentation, logical analysis, conclusion, communication with others and replication by others (refer to Blind Faith document).

2.1.4. Stop censorship of medical and scientific information and conclusions that are contrary to official policy and stop ad hominem attacks against those who hold opposing views. Encourage open debate and the sharing of information and ideas in both public and private fora (refer to Blind Faith document).

2.1.5. Change the official narrative to exclude all misleading statements, to include all relevant truths, and to apply uniform standards throughout (see paragraphs 1.7 to 1.9.3 above).

2.1.6. Track and publish daily statistics on the numbers (and proportions) of vaccinated individuals who (a) have any serious health issue; (b) have been admitted to hospital for any reason; and (c) who have died for any reason; as well as (d) the number (and proportion) of hospitalized individuals who have been vaccinated.

2.1.7. Direct the authorities to immediately ensure full transparency in the collection of data and the reporting of adverse events, as well as numbers of all deaths, the causes thereof and contextual information, such that simple, easy to understand reports become openly available on the official SA Coronavirus website on a daily and annualized basis

2.2. Mr President, when you announced the first lockdown with all of the measures such as hygiene regimes, masks, social distancing, etc. you led the charge and became responsible for a fear-inducing campaign. We respectfully suggest that you now bear the responsibility of undoing the fear, and restoring peace and calm to the people of South Africa.

2.3. Mr President, it is long past midnight and unless you act swiftly and decisively, many more unnecessary deaths and other harm will continue to occur on your watch.

2.4. We and other like-minded professionals are more than willing to present, in an open public debate, the evidence and supporting science for our standpoints and views. This should take place at the very earliest opportunity so as to "save lives and livelihoods".

2.5. We look forward to your urgent acknowledgment of receipt and the communication of an appropriate forum and time for such presentation and debate.

Yours faithfully

Dr Herman Edeling
M.B.,B.Ch.(Wits) : F.C.S.(S.A.)(Neuro)
Neurosurgeon/Medico-Legal Practitioner/Mediator

CJ Edeling

Dr Hannetjie (CJ) Van-Zyl Edeling
B.Sc. Dietetics : M.A. Counselling Psychology : D. Lit et Phil. Psychology
Counselling Psychologist/Mediator

Jané Bekker
B.A. Counseling Psychology: N. Dip. Speech & Drama
Practice Manager/Mediation Pilot Project Co-Ordinator/SEO Specialist/Student

John Henry Taylor
B.Sc. (Engineering)
Businessman

Herman Quartus Edeling
B.Com Accounting : B.Com (Hons) Property Valuation & Management
Businessman/Managing Trustee/Mediator

Riekie Erasmus
Bluris; LLB; LLM (Constitutional Practice)
Attorney in Private Practice

Dr Naseeba Kathrada
M.B.,CH.B (Natal)
General Practitioner

Dr George Coetzee
M.B.,CH.B (UP)BMedSci
General Practitioner

At the time of submission this letter is supported by

(see Annexure A - confirmatory emails)

Dr Anton Janse Van Rensburg, M.B.,B.Ch.(UP) : MSc Nutrition (UP) - Dr Nomangesi Judith Ngcakani, FCP (SA) - Dr. M.Y. Dangor, BChD PDD (UWC) - Dr Tracey Brandt M.B.,B.Ch.(Wits) – Dr Yahya Nagdee, M.B.,B.Ch. - Engela Herbst, BA Unisa - Ntombifuthi Fundzo - Francois Van Wyk - Judith (Van Zyl) Jansen - Dr. Eugene Meyer - Caron Viljoen - Debra Belinda O'Riordan - Dr ME Bezuidenhout - David Coetzer - Yolande Nel - Linda Hauptfleisch - Elmarie Barnard - Tracy King - Andre Terblanche - Jannes van Ryssen - Naomi Moller - Richard en Yolande Phyfer - Clara Isabella Green - Colette Goedhals - Deon Mushavi Huysamen, NDT, HNDE, BCom, MM, DCom.

Herman Jacobus Edeling

From:	Herman Jacobus Edeling <edeling@emlct.com> on behalf of Herman Jacobus Edeling
Sent:	10 August 2021 12:59
To:	presidentrsa@presidency.gov.za
Cc:	Robert@presidency.gov.za; Makhosini@presidency.gov.za; Nomusa@presidency.gov.za; PortiaM@presidency.gov.za; minister@health.gov.za; malebo@presidency.gov.za
Subject:	Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES
Attachments:	COVID-19-LetterTo President-HJE et al Final.pdf; Annexure A - EdelingLetterToPresident-SupportEmails25.pdf

His Excellency the Honourable President Cyril Ramaphosa
The President of the Republic of South Africa

Dear Mr President,

As patriotic citizens of South Africa we respectfully address you in relation to the COVID-19 PANDEMIC, with its associated HEALTH AND ECONOMIC CRISES.

Please see attached our open letter, signed by me and 7 co-signatories, and supported at this stage in writing by 26 other South Africans (see attached Annexure A).

We have been in contact with many more individuals and interest groups who have expressed the same views. Having sent this open letter to you, we will distribute it more broadly and will provide you in due course with details of others who support our serious concerns and requests.

As the contents of the letter refer not only to yourself, but also to members of your national and provincial executives, as well as to representatives of institutions such as public health departments, universities, etc. that are directly or indirectly under your control or influence, we respectfully request that your office distributes copies thereof, at your discretion, to all relevant persons and institutions.

Your faithfully,

Dr Herman Edeling
Neurosurgeon M.B.,B.Ch.(Wits) : F.C.S.(S.A.)(Neuro) : HPCSA Reg No: MP 180408 : PR 2401002
Medico-Legal Practitioner / Mediator

edeling@emlct.com
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+27 (11) 648-5101

EMLCT
Edeling Medico-Legal Consultancy Trust

PO Box 1158, Houghton 2041, Gauteng RSA

Herman Jacobus Edeling

From: President RSA <PresidentRSA@presidency.gov.za> on behalf of President RSA
Sent: 10 August 2021 13:01
To: Herman Jacobus Edeling
Subject: RE: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES

We acknowledge with thanks, receipt of your correspondence addressed to the President of the Republic of South Africa, His Excellency, President Cyril Ramaphosa

Going forward, the Presidential Hotline (Email: President@presidency.gov.za) will respond to all Service Delivery related issues. The contact number for the Presidential Hotline is 17737.

All other matters referred to PresidentRSA@presidency.gov.za will receive the required attention and a response will be communicated soonest.

Thank you

http://www.thepresidency.gov.za/content/legal-disclaimers

Herman Jacobus Edeling

Subject: FW: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES

From: Herman Jacobus Edeling <edeling@emlct.com>
Sent: 17 August 2021 16:31
To: 'presidentrsa@presidency.gov.za' <presidentrsa@presidency.gov.za>
Cc: 'Robert@presidency.gov.za' <Robert@presidency.gov.za>; 'Makhosini@presidency.gov.za' <Makhosini@presidency.gov.za>; 'Nomusa@presidency.gov.za' <Nomusa@presidency.gov.za>; 'PortiaM@presidency.gov.za' <PortiaM@presidency.gov.za>; 'minister@health.gov.za' <minister@health.gov.za>; 'malebo@presidency.gov.za' <malebo@presidency.gov.za>
Subject: RE: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES

His Excellency the Honourable President Cyril Ramaphosa
The President of the Republic of South Africa

Dear Mr President,

In follow-up of our letter addressed to you one week ago, and in accordance with our undertaking to provide you with details of others who support our serious concerns and requests, it is our pleasure to inform you that to date 2756 persons have responded in support of our letter.

Please take this link to a real-time updated online repository that tracks and stores the growing numbers of supporters and their full comments:

https://emlct.com/index.php/supporters-letter-to-president/

We thank you for the acknowledgement of receipt of our previous email of 10 August 2021 (see below), and eagerly anticipate your response to our requests.

Yours fathfully,

Dr Herman Edeling
Neurosurgeon M.B.,B.Ch.(Wits) : F.C.S.(S.A.)(Neuro) : HPCSA Reg No: MP 180408 : PR 2401002
Medico-Legal Practitioner / Mediator

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EMLCT
Edeling Medico-Legal Consultancy Trust

PO Box 1158, Houghton 2041, Gauteng RSA

Herman Jacobus Edeling

From: President RSA <PresidentRSA@presidency.gov.za> on behalf of President RSA
Sent: 17 August 2021 16:31
To: Herman Jacobus Edeling
Subject: RE: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES

We acknowledge with thanks, receipt of your correspondence addressed to the President of the Republic of South Africa, His Excellency, President Cyril Ramaphosa

Going forward, the Presidential Hotline (Email: President@presidency.gov.za) will respond to all Service Delivery related issues. The contact number for the Presidential Hotline is 17737.

All other matters referred to PresidentRSA@presidency.gov.za will receive the required attention and a response will be communicated soonest.

Thank you

http://www.thepresidency.gov.za/content/legal-disclaimers

Herman Jacobus Edeling

Subject: FW: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES
Attachments: Report for Presidency - POPI compliant 26 Aug 2021-.pdf

From: Herman Jacobus Edeling <edeling@emlct.com>
Sent: 26 August 2021 22:44
To: presidentrsa@presidency.gov.za
Cc: Robert@presidency.gov.za; Makhosini@presidency.gov.za; Nomusa@presidency.gov.za; PortiaM@presidency.gov.za; minister@health.gov.za; malebo@presidency.gov.za
Subject: RE: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES

His Excellency the Honourable President Cyril Ramaphosa
The President of the Republic of South Africa

Dear Mr President,

In follow-up of our letter addressed to you on 10 August 2021, and further email communication on 17 August 2021, to which we have received acknowledgements of receipt by your office, we are concerned at not yet having received the courtesy of any response to our expressed concerns and requests.

It is now our pleasure to inform you that to date 3338 persons have responded in support of our letter. Please take this link to a real-time updated online repository that tracks and stores the growing numbers of supporters and their full comments:

https://emlct.com/index.php/supporters-letter-to-president/

For your convenience we attach hereto a copy of the comments submitted by the 3338 persons who support our pleas for you to respond to the serious and urgent requests set out in paragraphs 2.1.1 to 2.1.7 of the letter. These are:-

1. Encourage everyone, and especially the Departments of Health, to make use of known and available medical methods for prevention and treatment of COVID-19 (refer to GOOD NEWS document).

2. Ensure that properly informed consent is obtained by all who administer "vaccines" before "vaccinating" anyone (refer to Informed Consent documents).

3. Admit that science is not an institution to be proclaimed by authority, but that it is independent of authority, dependent only upon free and uncensored application of the scientific method. This includes observation, questioning, research, forming hypotheses, experimentation, logical analysis, conclusion, communication with others and replication by others (refer to Blind Faith document).

4. Stop censorship of medical and scientific information and conclusions that are contrary to official policy and stop ad hominem attacks against those who hold opposing views. Encourage open debate and the sharing of information and ideas in both public and private fora (refer to Blind Faith document).

5. Change the official narrative to exclude all misleading statements, to include all relevant truths, and to apply uniform standards throughout (see paragraphs 1.7 to 1.9.3 above).

6. Track and publish daily statistics on the numbers (and proportions) of vaccinated individuals who (a) have any serious health issue; (b) have been admitted to hospital for any reason; and (c) who have died for any reason; as well as (d) the number (and proportion) of hospitalized individuals who have been vaccinated.

7. Direct the authorities to immediately ensure full transparency in the collection of data and the reporting of adverse events, as well as numbers of all deaths, the causes thereof and contextual information, such that simple, easy to understand reports become openly available on the official SA Coronavirus website on a daily and annualized basis.

We thank you for the acknowledgement of receipt of our previous emails and eagerly anticipate your response to our requests.

Yours faithfully,

Dr Herman Edeling

Neurosurgeon M.B.,B.Ch.(Wits) : F.C.S.(S.A.)(Neuro) : HPCSA Reg No: MP 180408 : PR 2401002

Medico-Legal Practitioner / Mediator

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EMLCT

Edeling Medico-Legal Consultancy Trust

PO Box 1158, Houghton 2041, Gauteng RSA

Herman Jacobus Edeling

From: President RSA <PresidentRSA@presidency.gov.za> on behalf of President RSA
Sent: 26 August 2021 10:44 PM
To: Herman Jacobus Edeling
Subject: RE: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES

We acknowledge with thanks, receipt of your correspondence addressed to the President of the Republic of South Africa, His Excellency, President Cyril Ramaphosa

Going forward, the Presidential Hotline (Email: President@presidency.gov.za) will respond to all Service Delivery related issues. The contact number for the Presidential Hotline is 17737.

All other matters referred to PresidentRSA@presidency.gov.za will receive the required attention and a response will be communicated soonest.

Thank you

http://www.thepresidency.gov.za/content/legal-disclaimers

Herman Jacobus Edeling

From:	Herman Jacobus Edeling
Sent:	07 September 2021 15:42
To:	'minister@health.gov.za'; 'DG@health.gov.za'
Cc:	'presidentrsa@presidency.gov.za'
Subject:	FW: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES
Attachments:	COVID-19-LetterTo Minister of Health.pdf; COVID-19-LetterTo President-HJE et al Final.pdf; Report for Presidency - POPI compliant 7 Sep 2021.pdf; COVID-19-BlindFaithOrOpenMinds-LH.pdf; UNPROTECTED MASS VACCINATION TRIGGERS COVID19 WAVES WORLDWIDE.pdf; VACCINATION vs COVID Morbidity Mortality Correlation - Countries.pdf; COVID-19 - GOOD NEWS - July 2021 -RefD.pdf

The Honourable Dr Mathume Joseph 'Joe' Phaahla,
The Minister of Health of the Republic of South Africa.

Dear Dr Phaahla,

We respectfully refer you to the trailing correspondence between ourselves and the Presidency, all of which has been copied to you at minister@health.gov.za.

Four weeks later, and not having received any meaningful response to our serious concerns and requests, which relate to the saving of lives and livelihoods of South Africans, we now urgently plead with you in the terms set out in the accompanying letter.

We trust that you will treat this matter with the dedication and urgency required of your position, as guardian of the health and lives of South Africans, and eagerly anticipate your response to our requests.

Yours faithfully, Obo the 3510 individuals who have written in support of our pleas to the President

Dr Herman Edeling
Neurosurgeon M.B.,B.Ch.(Wits) : F.C.S.(S.A.)(Neuro) : HPCSA Reg No: MP 180408 : PR 2401002
Medico-Legal Practitioner / Mediator

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+27 (11) 648-5101

EMLCT
Edeling Medico-Legal Consultancy Trust

PO Box 1158, Houghton 2041, Gauteng RSA

Herman Jacobus Edeling

From:	Herman Jacobus Edeling
Sent:	07 September 2021 16:12
To:	'presidentrsa@presidency.gov.za'
Cc:	'Robert@presidency.gov.za'; 'Makhosini@presidency.gov.za'; 'Nomusa@presidency.gov.za'; 'PortiaM@presidency.gov.za'; 'malebo@presidency.gov.za'; 'minister@health.gov.za'
Subject:	FW: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES
Attachments:	COVID-19-LetterTo Minister of Health.pdf; COVID-19-LetterTo President-HJE et al Final.pdf; Report for Presidency - POPI compliant 7 Sep 2021.pdf; COVID-19-BlindFaithOrOpenMinds-LH.pdf; UNPROTECTED MASS VACCINATION TRIGGERS COVID19 WAVES WORLDWIDE.pdf; VACCINATION vs COVID Morbidity Mortality Correlation - Countries.pdf; COVID-19 - GOOD NEWS - July 2021 -RefD.pdf

From: Herman Jacobus Edeling <edeling@emlct.com>
Sent: 07 September 2021 16:01
To: 'presidentrsa@presidency.gov.za' <presidentrsa@presidency.gov.za>
Cc: 'Robert@presidency.gov.za' <Robert@presidency.gov.za>; 'Makhosini@presidency.gov.za' <Makhosini@presidency.gov.za>; 'Nomusa@presidency.gov.za' <Nomusa@presidency.gov.za>; 'PortiaM@presidency.gov.za' <PortiaM@presidency.gov.za>; 'malebo@presidency.gov.za' <malebo@presidency.gov.za>; 'minister@health.gov.za' <minister@health.gov.za>
Subject: FW: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES

His Excellency the Honourable President Cyril Ramaphosa
The President of the Republic of South Africa

Dear Mr President,

In follow-up of our letter addressed to you on 10 August 2021, and further email communications on 17 August 2021 and 26 August 2021, to which we have received acknowledgements of receipt by your office, we are concerned at not yet having received the courtesy of any response to our expressed concerns and requests.

It is now our pleasure to inform you that to date 3511 persons have responded in support of our letter. Please take this link to a real-time updated online repository that tracks and stores the growing numbers of supporters and their full comments: https://emlct.com/index.php/supporters-letter-to-president/

Four weeks later, we have now turned to the Honourable Minister of Health to assist with this serious and urgent matter (please see trailing email and attached letter).

We however continue to trust that you, in your capacity as President of all South Africans, will respond to this matter with the necessary dedication and urgency.

Yours faithfully, obo the 3511 individuals who have written in support of our pleas,

Dr Herman Edeling

Herman Jacobus Edeling

From: President RSA <PresidentRSA@presidency.gov.za> on behalf of President RSA
Sent: 07 September 2021 16:17
To: Herman Jacobus Edeling
Subject: RE: Public Concern - COVID-19 PANDEMIC - HEALTH AND ECONOMIC CRISES

We acknowledge with thanks, receipt of your correspondence addressed to the President of the Republic of South Africa, His Excellency, President Cyril Ramaphosa

Going forward, the Presidential Hotline (Email: President@presidency.gov.za) will respond to all Service Delivery related issues. The contact number for the Presidential Hotline is 17737.

All other matters referred to PresidentRSA@presidency.gov.za will receive the required attention and a response will be communicated soonest.

Thank you

http://www.thepresidency.gov.za/content/legal-disclaimers

"HE6"

DR. HERMAN J. EDELING

NEUROSURGEON / MEDICO-LEGAL PRACTITIONER / MEDIATOR

M.B.,B.Ch.(Wits) : F.C.S.(S.A.)(Neuro) : HPCSA Reg No: MP 180408 : PR 2401002

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85 St Patrick Road
Houghton
Johannesburg.

Postal Address
PO Box 1158
Houghton
2041

Gauteng - Republic of South Africa

Telephone : 011-648-5101

Email : edeling@emlct.com

The Honourable Dr Mathume Joseph 'Joe' Phaahla, 7 September 2021
The Minister of Health of the Republic of South Africa

COVID-19 PANDEMIC – HEALTH AND ECONOMIC CRISES

Dear Dr Phaahla,

1. On 10 August 2021 we addressed an open letter to His Excellency the Honourable President Cyril Ramaphosa, in which we expressed very serious concerns and requests relating to the saving of lives and livelihoods of South Africans. A copy of this letter COVID-19 PANDEMIC – HEALTH AND ECONOMIC CRISES Open Letter to President Ramaphosa (copy attached), under cover of an email dated 10 August 2021, was also sent to you at minister@health.gov.za. In follow up of the issues raised therein we now address this open letter to your good self.

2. Our letter and email to the President have been followed up by further emails and documents on 17 August 2021 and 26 August 2021, all of which have also been sent to you at minister@health.gov.za. We have received acknowledgements of receipt from the Presidency to each of these 3 email messages, each one of which states that the matter "will receive the required attention and a response will be communicated soonest". Considering the magnitude of the Covid-19 crises, and the devastating effects thereof of the health, lives and livelihoods of South Africans, we note with serious concern that we have not received any response other than the acknowledgements of receipt.

3. Please see attached confirmation that our pleas to the President have by now been supported by 3510 concerned persons. Please also note the seriousness of the concerns and frustration that are evident in the text of most of the comments directed at the President.

4. As the contents of the letter refer not only to the President, but also to members of his national and provincial executives and to the Department of Health inter alia, we respectfully requested the President or his office to distribute copies thereof to relevant persons and institutions. We assume that by now the President will have asked you, in your capacity as Minister of Health, to attend to the health aspects referred to therein.

5. Not yet having received any response from the President or from your good self, we now urgently and seriously plead with you in the following terms:-

   5.1. Please read, consider and respond to the pleas set out in paragraphs 2.1 to 2.1.7 of our well-intentioned and patriotic letter to the President.

   5.2. In our view each of these pleas is of a medical nature, therefore in your field of expertise, and each falls within the scope of your responsibility and power to promote the health of South Africans.

   5.3. To the extent to which any plea relates in whole or in part to the scope of responsibility or power of another Minister, we would urge you to communicate this to the President and to your relevant colleague/s.

6. Further to the above Minister, we are sure you will agree on the importance of relying on Evidence Based Medicine in making plans and decisions.

   6.1. In this regard please see a brief explanation in COVID-19 – Blind Faith or Open Minds Critical Thinking in Times of Crisis (copy attached).

   6.2. We have recently become aware of startling and disturbing international statistics, as analysed and presented in Unprotected Mass Vaccination Triggers Covid19 Waves Worldwide (copy attached); and VACCINATION vs COVID Morbidity Mortality Correlation – Countries (copy attached).

6.3. We urgently request that you consider the importance of these statistics that show post-vaccination surges in COVID-19 cases and deaths worldwide.

6.4. In the light of these findings, as well as those referred to in our letter to the President, you will understand our concerns about recent statements by yourself and others in relation to vaccine mandates.

6.5. We propose suspension of the vaccination roll-out in South Africa until proper studies have satisfactorily determined the real risks and efficacy of COVID-19 vaccinations.

6.6. We simultaneously propose protection and treatment of South Africans by use of the safe and effective methods summarized in the GOOD NEWS about COVID-19 (copy attached) and set out in detail in the source documents referred to therein.

7. We and other like-minded professionals are more than willing to present, in a private meeting or in an open public debate, the evidence and supporting science for our standpoints and views. This should take place at the very earliest opportunity so as to save lives and livelihoods.

8. We look forward to your urgent acknowledgment of receipt, as well as your communication of an appropriate forum and time for such meeting or presentation and debate.

Yours faithfully,

Dr Herman Edeling
M.B.,B.Ch.(Wits) : F.C.S.(S.A.)(Neuro)
Neurosurgeon/Medico-Legal Practitioner/Mediator

Obo the 3510 individuals who have written in support of our pleas to the President

"HE8"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF HEALTH	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: LIMPOPO DEPARTMENT OF HEALTH	Twelfth Respondent

MPUMALANGA DEPARTMENT OF HEALTH	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL, MPUMALANGA DEPARTMENT OF HEALTH	Foudeenth Respondent
NORTHERN CAPE DEPARTMENT OF HEALTH	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTHERN CAPE DEPARTMENT OF HEALTH	Sixteenth Respondent
NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICA HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

SUPPORTING AFFIDAVIT

I, the undersigned

DR JESSICA ROSE

do hereby make oath and state that:-

1. I am an adult female Applied Mathematician, Immunologist, Computational Biologist, Molecular Biologist and Biochemist residing in Israel.

2. I make this statement of my own volition, based on my personal knowledge, education, and experience, and under penalty of perjury. The facts in this affidavit are, to the best of my knowledge and belief, both true and correct. I ask the Court to note that I have no conflicts of interest that would in any way jeopardize or compromise my objectivity in presenting evidence to this Court. The opinions I have reached have been so reached based on my scientific expertise, and research and analysis of the relevant data sets, and are wholly independent of any external influencing factors or conflicts of interest.

3. I have read the founding affidavit deposed to by Herman Jacobus Edeling ("Edeling"). For the reasons set out in this affidavit, I support the contents of that affidavit insofar as he concludes that the Pfizer Covid-19 vaccines are neither safe nor effective.

4. I am competent to testify in this affidavit as an expert to the facts and matters set forth. The facts and matters set forth in this affidavit are the types of facts and matters medical experts and health care professionals rely upon to reach expert conclusions.

My qualifications and experience

5. I pursued a Bachelor of Science in Applied Mathematics at Memorial University of Newfoundland (MUN) and a Master of Science in Medicine in Immunology at MUN. I continued with my studies in Israel, having been invited to pursue a PhD

in Computational Biology (Viral Kinetic studies on Cytomegalavirus (CMV) and Hepatitis B Virus (HBV)) at Bar Ilan University. Since its completion, I have successfully completed two Post-Doctoral degrees in Molecular Biology, with a focus on Rickettsiology at the Hebrew University of Jerusalem, and Biochemistry with a focus on Anisotropic Network modelling of ATP Cassette-Binding Transporter molecule mechanisms at the Technion Institute of Technology. Since completion of my second Post Doctorate in December 2019 and the declaration of the global pandemic, I have been analysing the Vaccine Adverse Event Reporting System (VAERS) data of the United States. I have published my findings twice in the journal "Science, Public Health Policy and the Law" and have authored a third publication co-authored with Dr. Peter McCullough. The first publication is a general analysis, the second is a critical appraisal of VAERS pharmacovigilance and the third is an analysis of myocarditis adverse events reported to VAERS in the context of the Moderna, Pfizer and Janssen COVID-19 injectable products.

6. I consistently present updates of my VAERS data analyses to the Canadian COVID Care Alliance (CCCA), Vaccine Choice Canada (VCC), the World Council for Health (WCH) and many other organizations in the form of live/recorded video presentations[1]. I also gave two three minute live video presentations at the 167th and 176th VRBPAC (Vaccines and Related Biological Products Advisory Committee) meetings to discuss the administration of vaccine booster shots and giving shots to children aged five to eleven, respectively[2]. The VRBPAC voted

16 to 2 against rolling out boosters into individuals under 65 years of age due to my testimony, and others' testimonies.[4]

7. The Vaccine Adverse Events Reporting System ("VAERS") was created in the United States in 1990 by the Food and Drug Administration (FDA) and Centres for Disease Control and Prevention (CDC) to receive reports of Adverse Events ("AE") that may be associated with any vaccine that goes to market. It is widely known as one of the World's foremost adverse events reporting systems.

8. VAERS was created because vaccines can cause adverse events, including death, that may not have been detected in clinical trials. Many times, serious adverse effects of vaccines only emerge once they have been released onto the market. The main goal of VAERS is to act as an early warning system for these events. The reports onto the system are filed primarily by medical practitioners (approximately 70%) who have, as a result of their medical expertise and in their best judgments, concluded that the relevant adverse effect was related to the vaccine. The remaining reports stem primarily from family members. In analysing the below data, I ask the Court to bear in mind that false reporting to VAERS would constitute making a false and misleading statement to the US Government which is, in turn, a federal crime according to title 18 of the United States Code. False reporting is simply not incentivised in any way. If anything, the risk is of under-reporting - not over-reporting. In any event, the data once filed is vetted by data analysts hired specifically for that purpose. Only those reports that are fully vetted

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[4] https://www.hhs.gov/advisory-committees/advisory-committee-on-immunization-practices-acip/index.html, advisory committee meeting 22 October 2021 meeting announcement.

make it onto the front-end system, which is where I access it and subsequently analyse it.

9. Despite the fact that the National Childhood Vaccine Injury Act of 1986 (NCVIA) requires health care providers and vaccine manufacturers to report to the Department of Health and Human Services specific AEs following the administration of vaccines outlined in the Act, under-reporting is a known imperfection of the VAERS system. There is no consensus on the exact rate of under-reporting – but there is a consensus on the fact that under-reporting exists.

10. Prior to setting out my findings in analysing VAERS, I wish to provide some context. A typical timeframe for a newly designed biological product (such as the Covid Pfizer vaccines) meant for human use is between 5 and 15 years - from design, animal testing, Phase I-III trials to post-trial Phase IV monitoring to FDA approval and human use. In the context of the Pfizer trials, exclusion criteria lists are long for each of the clinical pre-market trial phases (I-III) and exclude pregnant women, lactating women, children less than 12 years old (NCT04368728), and people with co-morbidities and autoimmune diseases, for example. The accelerated timeline of the COVID-19 products and the 6-9-month duration of the Phase III clinical trial (NCT04368728), precludes the generation of safety data for these groups. To my knowledge, prior to the EUA authorization of these vaccines (and the authorisation given to these vaccines in South Africa), there was no safety data generated for pregnant women, lactating women, children less than 12 and people with co-morbidities or autoimmune conditions. Dr Herman Edelling has detailed this in his affidavit, and I agree with the facts he sets out, and the conclusions he draws.

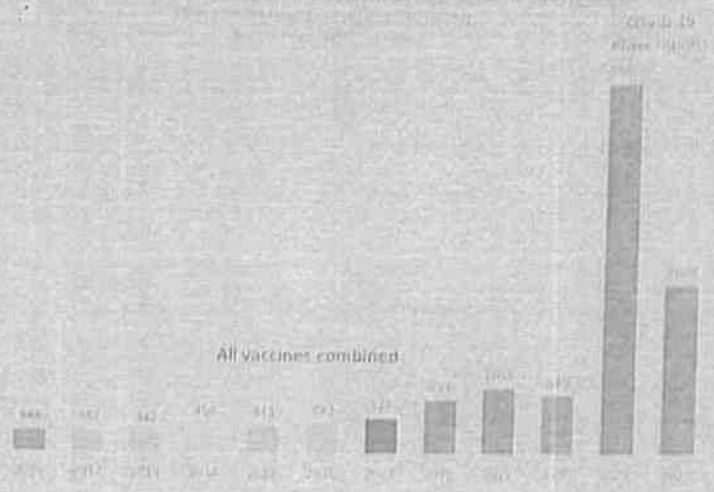
11. I have been studying VAERS data on Covid 19 vaccines for 2 years and I have found alarming results. The Covid-19 Pfizer vaccine reports show higher rates of adverse events than all other vaccines combined over the past decade in every metric analysed. For example:

11.1 The severe adverse event reports for Pfizer/BioNTech's Covid-19 vaccine in 2021 and 2022 are 1,727% higher than all other vaccines combined from 2011 to 2020. This data is still being updated for 2022.

11.2 Death reports for the Pfizer/BioNTech Covid-19 vaccine in 2021 and 2022 are 2,768% higher than all other vaccines combined from 2011 to 2020. The data is still being updated for 2022. According to the precautionary principle, when a death is linked to a biological or pharmaceutical product, it should be removed from distribution. The precautionary principle is a risk management approach that states that when an action or policy has the potential to harm human health or the environment, in the absence of scientific consensus, the burden of proof falls on those advocating for the action or policy. This principle calls for

cautious action to be taken to prevent harm, even if the cause-and-effect relationships are not fully established scientifically. In the context of the vaccine report, it suggests that if a death is associated with a vaccine, the vaccine should be removed from distribution as a precautionary measure.

11.3 Reports of disability after receiving the Pfizer/BioNTech Covid-19 vaccine in 2021 and 2022 are 875% higher than all other vaccines combined from 2011 to 2020. The data is still being updated for 2022. Disability can include serious conditions such as a loss of walking ability or tremors from neurological damage, and they often persist.

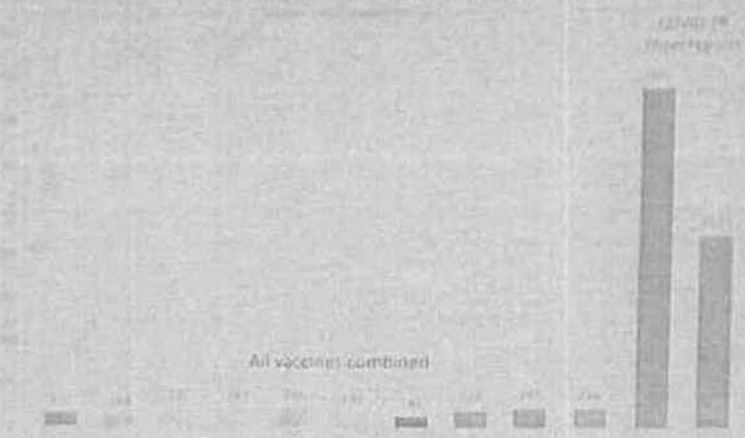


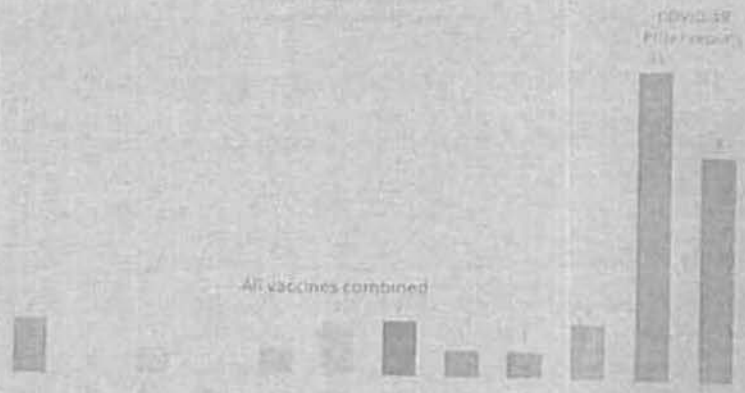
11.4 VAERS reports of Creutzfeldt-Jakob Disease ("CJD"), a serious brain disease, have skyrocketed 2,900% for the Pfizer/BioNTech COVID-19 vaccine compared to all vaccines combined from 2011-2020. CJD is a rare, degenerative, and fatal brain disorder that usually affects about one in every one million people worldwide. Since the roll-out of the Pfizer vaccines, it is affecting many more.

11.5 This is extremely concerning as the number of reports far exceeds the background reporting rate for CJD in the U.S. The National Institute of Health (NIH) website states that the average number of reports of CJD, per year, per million individuals in the United States is 1. This is verified in Wikipedia. Thus, if we consider that ~270,000,000 people have been injected at least once with one of the COVID-19 injectable products, then we would expect 270 people in the U.S. to report CJD as a background number of cases. The combined number of reports of CJD in the VAERS

domestic data set is 16, thus if we consider an underreporting factor of 91 (it has also been estimated that only 1% of adverse event reports get filed to VAERS) then we are already at 226 individuals above background. That's more than 2.1 times more cases already originating only from VAERS domestic data. These findings are cause for alarm and further investigation is needed.

11.6 VAERS reports show a 1,754% increase in cancer cases related to the Pfizer/BioNTech vaccine compared to all vaccines combined from 2011-2020. Rare cancers such as Acute Lymphocytic Leukaemia and male breast cancers are also being reported in older individuals. Data is still being updated for 2022.





11.7 VAERS reports show a 737% increase in serious pregnancy-related issues (spontaneous abortion, miscarriages, stillbirths) when comparing the mean number of reports for all vaccines from 2011-2020 to a single product (Pfizer/BioNTech) in 2021 and 2022. Reports are still being updated for 2022. Dr Herman Edeling has analysed the post-marketing

surveillance data and noted serious fertility concerns. I confirm this conclusion because it tracks with my own observations.

11.8 Further, VAERS reports show a 155% increase in adverse events in children after receiving Pfizer/BioNTech vaccine in 2021 compared to all vaccines combined from 2011-2020. This may correlate to data as children have not been vaccinated for as long as adults. This data is based on reports since the CDC Emergency Use Authorization of the vaccine in children.

12. My analysis of VAERS is weighty in its own terms. However, as the learned Judge will realise upon a further perusal of the papers, my findings tie up with: (i) the dangers associated with mRNA vaccine technologies as described by Dr Kyriakopoulos, and, more disturbingly with Pfizer's own lists adverse events of special interest ("AESI") listed in the post authorisation marketing data already annexed to Dr Edeling's papers. An AESI refers to a specific type of adverse event or side effect associated with a medical product or treatment that is closely monitored by regulatory agencies and medical communities due to its potential severity or seriousness. AESIs are typically selected based on current scientific knowledge and understanding of the medical product or treatment, and they may be considered high priority or red flag events that warrant prompt investigation and reporting. Examples of AESIs include serious adverse events such as death, life-threatening conditions, hospitalization, or disability, as well as events that are unexpected or may indicate a safety risk associated with a medical product or treatment.

13. A base criticism that I have received in the past, in an attempt to discredit the VAERS reports, is the assertion that the numbers of adverse events reports are higher for Covid-19 injectable products simply because more of them have been administered as compared to other vaccines.

14. That "argument" holds no water. It is compatible neither with available data, nor basic math.

15. If we compare the death rates reported to VAERS in the context of all vaccines combined for the past 30 years, to the death rate in 2021 for the COVID-19

products only, we observe an over 10,000% increase in death reports. Granted, many doses of the COVID-19 injectable products have been administered. But the combined amount of vaccines administered for all vaccines combined is comparable to the number of doses administered for the COVID-19 vaccines in the United States.

16. If one excludes all vaccines except the flu vaccine, and performs some basic math, the following is apparent:

16.1 According to the CDC, 193.8 million doses of flu vaccine have been distributed in the United States as of February 26, 2021 (for the 2020-2021 flu season) - *the highest number of doses in a single flu season*[5] and 558 million doses of COVID-19 vaccines were administered in the United States from December 14, 2020, through March 21, 2022[6].

16.2 Those numbers track a 462 day period. A flu season is a year (365 days), so it is fair to assume that if 193.8 million doses of flu vaccine were administered in 365 days then ~245 million doses would have been administered in 462 days.

16.3 On that basis, I make the assumption that we have 2.3 times more doses of COVID product administered than for the flu for the same time period of 462 days. It would make sense then, that the rate of reporting in

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[5] https://www.cdc.gov/flu/season/faq-flu-season-2020-2021.htm
[6] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html

VAERS (for the same range of adverse events as reported for the flu) should be about twice for COVID than for flu. Twice as many doses, a proportional number of reporting, equals twice as many reports. But that is not what we see.

17. As of March 25 2022, according to the CDC's system, there were 1,696 different types of adverse events and 45,650 total adverse events reported to VAERS in the context of the 14 variations of flu vaccines. Also according to the CDC's system, there were 10,526 different types of adverse events and 5,368,444 total adverse events reported to VAERS in the context of the 3 variations of the COVID-19 products used in the United States (These counts do not represent the individuals who experienced an adverse event but the total number of events reported).

17.1 There were twice as many COVID shots than flu shots.

17.2 There were 6.2 times as many types of adverse event types reported in the context of the COVID shots.

17.3 There were 117.6 times as many reports of adverse events in the context on the COVID shots.

18. I omitted all the other vaccines (there are 82 other types of vaccines) and I still reach the conclusion that there is no comparison with regard to the number of vaccines and the relationship to the number of adverse events occurring and being reported, and I certainly do not see the anticipated doubling of the reports as we would have expected if the injection to adverse event ratio was proportional for flu and COVID products.

19 I stand in support of the relief sought in the notice of motion.

DR JESSICA ROSE

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me by way of Zoom on this the 21st day of February 2023 the regulations contained in Government Notice No. R1258 of 21 July 1972 as amended, and Government Notice No. R1648 of 19 August 1977 as amended, having been complied with.

COMMISSIONER OF OATHS

Name:

Address:

Position:

Margaretha Wilhelmina van Dyk
Practicing Attorney, VDMS Inc
15 Orchard Road, Bordeaux,
Randburg, South Africa
Commissioner of Oaths ex officio

"HE9"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF HEALTH	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: LIMPOPO DEPARTMENT OF HEALTH	Twelfth Respondent

MPUMALANGA DEPARTMENT OF HEALTH	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: MPUMALANGA DEPARTMENT OF HEALTH	Fourteenth Respondent
NORTHERN CAPE DEPARTMENT OF HEALTH	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTHERN CAPE DEPARTMENT OF HEALTH	Sixteenth Respondent
NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICA HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

SUPPORTING AFFIDAVIT

I, the undersigned

DR ANTHONY M. KYRIAKOPOULOS

do hereby make oath and state that: -

1. I am an adult male specially trained Medical & Molecular Microbiologist, and a Fellow of The Institute Of Biomedical Sciences in the United Kingdom. My principal place of business at 11 Sachtouri street, 18536, Piraeus, Greece.

2. The facts in this affidavit are, to the best of my knowledge, both true and correct, based on validated internationally recognized scientific literature and, unless the contrary appears from the context of this document, they fall within my personal knowledge and/or expertise. I ask the Court to note that I have no conflicts of interest that would in any way jeopardize or compromise my objectivity in presenting evidence to this Court. The opinions I have reached have been so reached based on my scientific expertise and are wholly independent of any external influencing factors or conflicts of interest.

3. I have read the founding affidavit deposed to by Herman Jacobus Edeling ("Edeling"). For the reasons set out in this affidavit, I support the contents of that affidavit insofar as he concludes that the Pfizer Covid-19 vaccines are neither safe nor effective.

My qualifications and my ability to testify as an expert on mRNA technology

4. My curriculum vitae ("CV"), annexed as "AK1", shows that I have been researching the molecular genetics of aging and cancer for more than 20 years. During this research I have used mRNA technology extensively in producing two Ph.D. theses and sustaining postdoctoral positions for other colleagues.

5. I am a Medical Microbiologist. I graduated from the Faculty of Medicine of the University of London UK. I also received a Postgraduate Diploma in Medical

Microbiology from The London School of Hygiene and Tropical Medicine London, UK, and a Master's Degree from the Faculty of Medicine, Medical School, University of London UK. In Greece, I completed medical training in Medical - Molecular Microbiology and obtained a Doctorship in Medicine, from the Medical School of the University of Athens. This is recognised after official panel examination as a Doctorship of Philosophy in Medical Microbiology from The Institute of Biomedical Sciences in United Kingdom (UK). Currently I am the President of the Hellenic Society of Taurine and Fellow of the Institute of Biomedical Sciences UK. I am a senior researcher in Biomedical Sciences at the level of Assistant Professor (h-index: 13). I have worked at postdoctoral positions and as a senior medical scientist for more than 20 years at multidisciplinary domains of science and medicine, and in tuberculosis and leprosy, medical and molecular microbiology, molecular genetics of aging and senescence and molecular and cell biology of cancer at distinguished institutions such as St Georges and the Middlesex Hospital in London UK, the Medical School of the University of Athens, the Pasteur Institute in Paris France, and the National Hellenic Research Foundation in Athens Greece amongst other places. Currently, I specialize in natural compound medicine and I develop novel medicinal patents for drugs. In this respect, I hold a portfolio of five national, one international and one US patent for medicinal preparations and medicine drugs. I founded and direct Nasco AD Biotechnology Laboratory, Piraeus Greece, where I act as a Director and Head of Research and Development. My patent portfolio concerns novel formulations and the patents are against infectious diseases, auto-immunity and cancer. I have over 2000 citations in International Peer Review Journals and 53 publications in respected peer review journals in Greece and worldwide.

6. My full academic background, the research positions I have held, and my publications are all detailed to the best of my knowledge in my CV. There are links to my professional account in research gate which detail my citations, h-index score and international peer reviewed publications.

7 Following multiple publications over the last three years, where I was the first author or a co-author in highly respected peer reviewed scientific journals of medicine and biomedical sciences, of high impact factor in the disciplines of COVID-19 epidemiology, and molecular pathology of mRNAs vaccination, used and thereon called as gene vaccines [1], it is my expert opinion that the Pfizer mRNA "vaccines" are neither safe nor effective as used against infectious diseases. In the pages that follow I detail my reasons for this conclusion.

mRNA technology

8. Pfizer's COVID-19 "vaccines" are synthetic mRNA gene "vaccines". mRNA stands for "messenger RNA". It is a molecule that acts as a blueprint for making proteins. Proteins perform many essential functions in the body. mRNA is made by copying a section of DNA, which is the genetic material that contains the instructions for making all the proteins in the body. This process is called transcription. The mRNA molecule then leaves the cell's nucleus and travels to the ribosome, which is the cellular structure responsible for making proteins. At the ribosome, the mRNA serves as a template for making the relevant protein. Another type of RNA called transfer RNA brings the building blocks of proteins (amino acids) to the ribosome,

and the ribosome links these amino acids together in the sequence specified by the mRNA to create a chain of amino acids, which folds into a functioning protein. In this way, the cellular mRNA acts as a go-between, transmitting the instructions stored in DNA to the ribosome to produce proteins.

9. Pfizer's mRNA "gene vaccines" make use of the above process providing instructions (in the form of synthetic mRNA) for the ribosomes to make a synthesized version of the virus SARS-CoV-2 producing the human disease called Covid-19 spike protein. The theory is that once the SARS-CoV-2 spike protein is produced from the synthetic mRNAs in gene "vaccines", the immune system will recognize it as foreign, and mount an immune response, ultimately killing the virus. In this way, the Pfizer gene "vaccines" are unlike traditional vaccines. Traditional vaccines contain inactivated or weakened viruses or pieces of them in order to trigger immune responses, whereas Pfizer's novel mRNA gene "vaccines" use the body's protein synthesis production as a mechanism to trigger the immune response. The mRNA in the "vaccine" is encased in a lipid nanoparticle, which helps it enter cells and be translated into the spike protein. After this, the immune system creates antibodies against the spike protein, which is supposed to provide protection against COVID-19 if the person is exposed to the virus in the future. In summary, mRNA "vaccines" are supposed to work by using the synthetic mRNA to instruct or "hijack" the cells in the human organism to make a version of the virus's spike protein, thus meant to trigger an immune response that can provide protection against COVID-19. Moreover, as I have published, the mRNAs in the gene "vaccines" are equipped with robust synthetic caps that will lead to endurance of the molecules inside the cell in unexpected way and for an unwanted duration.

This can lead, as I have also written in the peer reviewed publications, to cancer, autoimmunity and aging defects [2].

10. I can attest to the fact that mRNA technology was and still is a promising therapeutical intervention against cancer and genetic disorders. This notwithstanding, it is crucial to understand that, prior to Covid-19, mRNAs had never been trialed or tested as a weapon against infectious diseases (such as Covid-19). Recent scientific literature characterizes the mRNAs used against Covid-19 as pro-drugs or even drugs in order to describe the true safety properties in the future of these molecular compounds when administered inside the human organism [3]. Due to the lack of testing of this technology's efficacy and safety in targeting infectious diseases, the reality is that much remains unknown, and what is known creates serious doubt as to its efficacy, and more importantly, its safety. For these reasons, it is my expert opinion that the mRNA technology was used prematurely as a weapon against infectious diseases, and especially against the SARS-CoV-2 pandemic. Frankly, the product was rushed to market with grossly inadequate evaluation of either safety or effectiveness. The public was told that this product was "safe" even though mRNA technology had never before been tested for efficacy or safety in tackling infectious diseases. Even when the mRNA technology has been used (prior to the Covid-19 pandemic) for cancer treatment, there were severe detected side effects in related clinical trials prompting more safety related clinical research prior to use [4] [5]. Bell's palsy, a form of acute face paralysis, was also indicated to be a serious side effect prior to the current gene "vaccine" use [6]. Nowadays, it is widely recognized as a serious side effect due to the gene "vaccines" administration against covid-19 [7], [8]. Marketing these

"vaccines" as "safe" and "effective" under the circumstances, was (and still remains), in my expert opinion, a gross misrepresentation that has jeopardized public health and has caused severe disease and death.

11. I have read the founding affidavit deposed to by Dr Herman Edeling, and I concur with his conclusion that the Pfizer gene "vaccine" is neither safe nor effective. Fortunately, there is now a plethora of papers coming out in rapid succession that are collectively uncovering the mechanisms by which these injections cause bodily harm [9]. And another set of papers in which I am the first author or a co-author is revealing that repeated boosters have diminishing gains in protection and could even lead to increased vulnerability to the disease [10], [11].

12. In the following paragraphs I detail some of the real risks associated with the mRNA technology to buttress my view that these gene "vaccines" have, to date, not been proven "safe" or "effective". The reality is that there are still too many unknowns about how this technology operates in the human body (particularly in the context of expressing a highly toxic spike protein) to qualify this gene "vaccine" as safe.

13. While the science is complex, the immune response to these injections can be described in relatively simple terms, and it is quite distinct from the immune response to a natural infection with SARS-CoV-2 in many ways.

14. The mRNA gene "vaccine" is injected into the deltoid muscle. The injection contains a large number of mRNA molecules coding for a modified form of the Covid-19 virus' spike protein ("the spike protein"), normally produced by the virus. These mRNA molecules are packaged into lipid nanoparticles ("LNP"). These LNPs serve several roles: to protect the mRNA from rapid enzymatic breakdown,

and to facilitate its uptake into the cell and facilitate its release into the cell's cytoplasm. The LNPs also act as adjuvants to further provoke an immune response, and to promote rapid synthesis of the spike protein within the cell, according to the RNA code.

15. Essentially, these nanoparticles also hijack human host cell machinery to get it to synthesize the spike protein and present it on their surface, provoking an immune cell response.

16. It is important to understand the differences between the spike protein in the Covid-19 virus, and the spike protein in the Pfizer "vaccines". The virus (and attendant spike protein) enters cells mainly via a specific type of receptor called the ACE2 receptor [12]. Those receptors are present only in certain cell types, which means that the virus and attendant spike protein can only enter certain cells, and not others. The vaccine is different. The LNP enables the mRNA molecules to indiscriminately enter <u>all</u> cells throughout the human body, where spike protein will then be synthesized. Optimization of entry of nanoparticles into human cells involves making them small, spherical and positively charged [13]. and these are all properties of the mRNA vaccines. The net effect is that the vaccine results in a greater biodistribution of the spike protein than the virus. Notably, the injected nanoparticles are rapidly taken up by immune cells that would not normally be infected by the virus because they have no ACE2 receptors. What could logically result theoretically is an autoimmune response, in which the immune system attacks and removes its own immune cells, because they are displaying a toxic foreign protein on their surface. Prior to the use of mRNA gene "vaccines" against

COVID-19, as a coauthor, I have contributed to prognose and analyze the causality of autoimmunity due to the mRNAs in gene "vaccines" [14]. Latter publications come to prove our initial medical prognosis and re-enforce that mRNAs in gene vaccines cause elevation of autoimmune antibodies [15].

17. Enhancing the toxicity even more, the mRNA sequence coding for the spike protein itself is also very different from the sequence present in the RNA of the original SARS CoV-2 virus. Most notably, it has been "humanized" by inserting special sequences on both ends that disguise its viral origins. This results in a stealth entry mechanism that does not provoke the normal immediate response to viral mRNA that serves as an early warning system. The developers felt this was necessary because otherwise the mRNA would be destroyed before it ever got a chance to make the spike protein. This "humanization", as I described in a recent publication [16], causes the mRNA to be extremely resistant to breakdown. While most mRNA molecules only survive for a few hours after they are produced, the mRNA in these injections has been shown to still be present in the draining lymph nodes two months after vaccination. The spike protein product was also found in the lymph nodes two months later, showing that the mRNA was still active in producing the spike protein [17].

18. Following injection of the nanoparticles into the deltoid muscle, the muscle cells rapidly take up the particles and begin producing spike protein at a high rate, which is then displayed on their surface shortly thereafter. Circulating immune cells respond to the alarm signals released by the muscle cells by swarming into the arm muscle. They too can't stop themselves from taking up the nanoparticles and

also synthesizing spike protein. They rapidly begin migrating into the lymph system, congregating initially in the lymph nodes under the arms, to begin the process of informing antibody-producing immune cells of the imminent danger. Swollen lymph nodes under the arms is normally a signal for breast cancer, but it is often being observed following COVID vaccination, showing clearly that much of the action is taking place in these lymph nodes [18].

19. The limited animal tracer studies that have been done on the biodistribution of mRNA vaccine nanoparticles injected into muscle have shown that, while the bulk of the product remains localized to the injection site, a substantial amount of the mRNA ends up in the draining lymph nodes, and, detectable amounts also show up in multiple organs throughout the body. Among organs, the highest concentration is consistently found in the spleen, with the liver and ovaries not far behind, and detectable although low levels have been found in mouse brains [19].

20. In immunology, the term antigen refers to a foreign molecule (usually a protein) whose presence in the body provokes an immune response, and antibodies are the proteins that are produced by the immune cells (through interactions between B-cells and T-cells) in response to the foreign antigen. With subsequent exposures to that same antigen, the antibodies bind to the antigen and interfere with its uptake by cells, thus thwarting an infection with a virus such as SARS-CoV-2. Research has shown that immune cells in the spleen release exosomes (small lipid particles) containing the antigen into the external space, and the antibody-producing cells (B-cells and T-cells) take up those exosomes as a central and essential activity during antibody induction. In *vitro* experiments with the gene "vaccine" mRNA

nanoparticles coding for the spike protein have shown that exposed cells release exosomes containing the spike protein, along with certain microRNAs that alter protein expression in recipient cells [20]. Furthermore, this same study showed that microglia (immune cells in the brain) can take up those exosomes and react by inducing an inflammatory response (inflammation in the brain, which can lead to neurological damage) [20].

21. In the same experiment, two specific microRNAs were found: miR-148a and miR-590. These microRNAs can weaken the body's response to a signal called the type-1 interferon response, which helps the immune system fight cancer and infections. When immune cells absorb exosomes with these microRNAs, their ability to respond to type-1 interferons is reduced [20].

22. A predicted result is increased risk to cancer and infection by any pathogen. Indeed, there is a strong signal in the Vaccine Adverse Event Reporting System (VAERS), maintained by the United States CDC, for conditions such as Bell's palsy and shingles in association with the Pfizer COVID "vaccines". Many medical practitioners have reported alarming increases in cancer among their patient's following "vaccination". Particularly noteworthy is cancer that was in remission resurfacing in an aggressive form. The VAERS database also shows significantly more reports linking cancer to the Pfizer COVID "vaccines" than to all other vaccines, particularly breast cancer. In this respect, I have read Dr Jessica Rose's affidavit and I support her findings insofar as she notes increased cancer reports post-Pfizer gene "vaccination". This is what I have prognosed in my recent publication even before the cancer reports have emerged [2].

23. A likely pathway by which exosomes released by immune cells in the spleen could be taken up by microglia in the brain is via major nerves in the trunk. Exosomes are known to be able to migrate along nerve fibers as a transport system to reach distant places. The released exosomes would travel along the splanchnic nerve to a nerve center called a ganglion, whence they can continue along the vagus nerve to reach not only the brain but also the heart, the lungs, the liver and the gut.

24. VAERS contains a huge repository of vaccine adverse events related to the Pfizer vaccine. These events far outnumber events reported for other vaccines over the same time period, and many of the symptoms are typical symptoms of inflammation in the vagus nerve and other nerves, particularly in the face, such as the auditory nerve, the optic nerve, the trigeminal nerve and the facial nerve. The exosomes can also reach, via these nerve conduits, major centers in the brain stem controlling basic life functions such as heart rhythm and heart rate, blood pressure, consciousness, and breathing. Disturbances in these centers leading to an intense inflammatory response and subsequent nerve damage can have life-threatening consequences.

25. A recent peer reviewed paper published by the late Professor Luc Montegnier (Nobel prize winner for his work on the HIV virus) and colleagues discussed 26 cases, mostly in Europe, of severe Creutzfeldt Jakob Disease (CJD, essentially human MADCOW disease) associated with COVID-19 "vaccination". In all cases involving the Pfizer gene "vaccine", symptoms first appeared within one month of the second "vaccine". Progression towards paralysis was very rapid, and many of

these patients died within three months of the onset of symptoms. All except one of the original 26 are now dead. I also analyze this paper as a co-author in our recent publication [21]. This is very alarming, as CJD is very rare, with only 1 out of a million people ever diagnosed with it.

26. This rare but severe adverse reaction to the mRNA vaccine is likely due to the fact that the spike protein has prion-like properties [22]. A prion is a type of protein that can cause certain diseases in the brain and nervous system. Unlike most pathogens, such as viruses and bacteria, prions are not composed of DNA or RNA, and they do not replicate by dividing or making copies of themselves. Instead, they cause disease by changing the shape of normal proteins in the body into abnormal, infectious forms. Prion diseases, also known as transmissible spongiform encephalopathies, are a group of neurological disorders that are caused by prions. They are characterized by a gradual decline in brain function, leading to memory loss, personality changes, and eventually death. Some well-known prion diseases include Creutzfeldt-Jakob disease, kuru, and variant Creutzfeldt-Jakob disease (vCJD), which is associated with consumption of infected beef in the United Kingdom. Prion diseases are rare, but they are of great concern because they can spread from person to person, and there is currently no cure or effective treatment for these diseases.

27. CJD is a prion disease, caused by misfolding of the prion protein, a protein which normally has multiple important roles in neurons but which turns rogue when it misfolds into a toxic structure that precipitates out as a plaque. I surmise that the spike protein, given its prion-like properties, is acting as a seed to crystallize the

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prion protein into its misfolded form. There are several papers in the literature that have identified certain sequences within the spike protein that are characteristic of prion-like proteins. This property, combined with its ability to reach the brain via exosomes released from immune cells in the spleen, can likely explain many of the neurological symptoms that people are experiencing in response to these injections. Of course, the spike protein produced by the virus could cause similar problems, but an important distinction is that the virus is mostly confined to the lungs in patients with a healthy immune response, whereas the vaccine immediately breaches both the lung and vascular barriers such as the blood-brain barrier [21].

28. Furthermore, the association of mRNA-spike protein injections with multiple deadly cancers was highlighted in our recent publication [10]. Moreover, the potential molecular reasons for severe autoimmunity due to increased levels of p53 has been recently published in a paper where I was first author [11]. This paper unravels the complex reasons why the p53 levels are elevated due to the spike protein. The elevated levels of p53 will cause prion and prion related disease since they boost the production of prion proteins within the organism. In many ways, p53 is a protein that is critical for preventing the development of cancer. It acts as a tumor suppressor by regulating the cell cycle and promoting cell death (apoptosis) in cells that are damaged or have the potential to become cancerous. p53 also plays a role in the immune system by regulating the function of immune cells and promoting the activation of the type-1 interferon response, which helps the immune system fight infections and cancer. However, increased levels of p53 have been linked to autoimmunity, which is when the immune system mistakenly attacks and

damages the body's own tissues. This can occur because p53 can disrupt the normal balance of immune cells, causing them to become overactive and attack the body's own tissues. In addition, high levels of p53 can suppress the type-2 interferon response, which normally helps to control and limit the immune response, leading to further immune system overactivity and autoimmunity. Thus, the delicate balance between p53 and other immune regulatory proteins is important for maintaining a healthy immune response and avoiding autoimmunity. This homeostatic balance unfortunately is disrupted in the gene mRNA "vaccinated" sufferers that develop autoimmune diseases like multiple sclerosis and polyneuropathies as summarized in the recent publication where I am the first author [23].

29. A much more common adverse reaction to the vaccine is myocarditis (inflammation in the heart), which is especially affecting young male athletes, but also affects the rest of population, and unfortunately it can result in sudden death [24], [25], [26]. Because young people rarely suffer from severe disease when they are exposed to COVID-19, any risk from the vaccine quickly offsets any potential benefits for them. The mechanism leading to this in many ways parallels the mechanism causing neurological symptoms. Exosomes containing the spike protein can easily breach the vascular barrier in the heart via nerve fiber pathways. The spike protein, especially the S1 segment that is released following breakage at the furin cleavage site, has been shown to cause an inflammatory response in the heart, likely related in part to its ability to bind to ACE2 receptors, which are prevalent in heart muscle cells [27]. Athletes in particular are known to have significantly more ACE2 receptors in their heart than those who don't exercise vigorously [28].

Mechanistically, inflammation triggered by the S1 subunit causes the release of inflammatory cytokines. These cytokines trigger the release of reactive oxygen species (ROS), which damage the heart muscle cells. The subsequent infiltration of fibroblasts leads to the production of scar tissue replacing certain portions of the heart muscle, weakening heart function [29].

30. The presence of preexisting myocarditis due to the vaccine can be very dangerous in the context of an adrenalin rush, because the inflamed heart is less able to react appropriately to the excess load induced by the adrenalin response. This can lead to arrhythmias and cardiac arrest, which is often fatal, particularly if emergency assistance to restart the heart is not immediately available. There are now several peer-reviewed case studies and epidemiological studies linking fatal myocarditis to the vaccines, and also showing that the risk is much greater from the vaccines than it is from the disease itself] [25], [30], [31].

31. The Pfizer COVID "vaccine" may have serious side effects on platelets, causing severe blood clotting problems [32]. Most of the reports in VAERS show a strong link between the Pfizer COVID gene "vaccine" and blood clots, including a dangerous condition where a blood clot moves to the lungs [10]. This may be because the gene "vaccine" triggers the body to produce antibodies that attack platelets, leading to clumping and forming of clots. This could happen because the antibodies target the spike protein in the virus, which is similar to proteins found in platelets. There may also be a risk of other autoimmune diseases because the spike protein is similar to other proteins in the body that are associated with autoimmune diseases.

32. Further, the expression of the spike protein post gene "vaccination" in the testes and ovaries could result in an autoimmune attack against these tissues, leading to impaired fertility [33]. There is a strong signal in VAERS for miscarriages and disrupted menstrual cycles associated with these vaccines. Here, too, I support Jessica Rose's affidavit.

33. As mentioned before and more explicitly emphasized here, there is a real possibility that the mRNA in the vaccines could be translated into DNA and even integrated into the human genome and passed down to future generations [34]. A class of viruses called retroviruses are known for their ability to reverse transcribe RNA into DNA, but few people realize that human cells possess this capability as well. Not all cell types actively express the relevant proteins (proteins capable of transcribing RNA into DNA), but ones that do include cancer cells, neurons, certain immune cells, and sperm [23]. A peer-reviewed *in vitro* study showed that human liver cancer cells grown in culture and transfected with the mRNA coding for the spike protein had already converted the RNA into DNA as soon as six hours after exposure [35]. Sperm have been demonstrated to have the capability to translate foreign mRNA into DNA, release it into plasmids, and deliver it to the fertilized egg [36]. The resulting fetus can maintain the DNA in the plasmids throughout their lifespan and even pass it down to their offspring [37].

34. Although this is somewhat technical, an important point to be made is that the mRNA vaccines fail to induce an immune response to the mRNA itself, due to its stealth nature, as described above, and this is potentially very problematic. A

normal reaction to the virus involves activation of a pathway called the PI3K/Akt pathway via stimulation of a receptor called toll like receptor 3 (TLR3) by the viral RNA. The vaccines fail to activate this pathway, and this means that this signaling response doesn't happen [27], [38]. This pathway ultimately results in the induction of an anti-inflammatory cytokine called IL-10, as part of the resolution of the immune response. IL-10 can turn off the destructive inflammatory reaction to the virus and induce cellular proliferation to support restoration of new healthy cells to replace those that died [39]. Particularly when this fails to occur in the brain or the heart or the liver, the chronic inflammatory state induced by the vaccine causes continued damage over a sustained period, eventually with devastating consequences in some cases.

35. There is increasing evidence, especially recently, that the mRNA vaccines are not effective in stopping the spread of COVID-19 [40]. While they do indeed produce a strong antibody response that should protect against severe disease, at least in the short term, the benefit is short-lived, as the antibodies fade rather quickly such that repeated boosters are required to sustain antibody protection. I have already mentioned here the likely suppression of the type-1 interferon response as this was published in a recent peer reviewed publication where I am a co-author [10]. Worse than this, however, studies on the types of antibodies produced in response to the boosters are revealing an alarming class switch in the antibodies that most vaccinologists know bodes very poorly for the long-term effectiveness of the vaccines [41].

36. One major class of antibodies are the immunoglobulin G (IgG) antibodies. Within that class, researchers have identified three major subclasses categorized as

IgG1, IgG2 and IgG4. IgG2 is especially important as it is known to be very effective in stopping the virus from infecting cells. IgG4, on the other hand, is recognized as an anti-inflammatory antibody that binds to the antigen but does not prevent infection. Furthermore, it interferes with the binding of the productive antibodies like IgG2. In the study mentioned above, IgG4 made up only 0.04% of the total IgG pool following the second vaccine. But the percentage of IgG4 after the booster shot rose to nearly 20 percent on average. This was a complete surprise to the researchers, and it suggests that the vaccines are leading the immune system towards a state of anergy, possibly due to immune exhaustion. Disturbingly, high levels of IgG4 are linked to many autoimmune diseases [42]. On top of this a recent publication describing a rare case of igG4 related nephritis relapse post the mRNA gene vaccination presents a forthcoming great risk for kidney failure patients receiving the gene vaccination worldwide [43].

37. However, most importantly of all, I have to state for the plethora of emerging clinical evidence, as is being published in highly respected medical journals in recent months, of sudden deaths due to mRNA-spike protein expressing injections. Speaking as an Orthodox Christian, hereby, for the sake of the souls of our dead Brothers and Sisters I provide the references for every set of episodes I describe.

38. In a series of autopsy studies in 25 individuals who died unexpectedly from myocarditis, the major histopathological finding prevailing all others was death due to arrhythmia and heart failure. The cause of these deaths was clarified by the authors of this clinical investigation as a severe complication following the mRNA-spike protein expressing injections [25]. In relevance to the mRNA-spike protein

expressing injection-produced myocarditis study, it has been found that in all (16 out of 16) patients who received the mRNA and developed myocarditis, the full-length spike protein persisted in a concentration of 33.9±22.4 pg/mL, in their plasma post their second mRNA injection [44].

39. In a recent sudden death incident in a 22-year-old Korean patient who suffered from myocarditis 5 days after the first mRNA-spike protein shot, and died 7 days later, the main histopathological finding from the autopsy performed was extensive band necrosis in the atria and ventricles of the heart. As the authors conclude, "the primary cause of death was determined to be myocarditis, causally associated with the BNT162b2 "vaccine"[45].

40. Finally, and not least, the findings of a recent case study that corroborate studies on encephalitis and myocarditis as an adverse fatal event due to mRNA injections or as the authors conclude: "gene based COVID-19 vaccines," was sudden death due to concurrent multifocal necrotizing encephalitis in the brain and vasculitis-mild myocarditis complicated with chronic cardiomyopathy. This 76-year-old patient received three doses overall of two different COVID-19 vaccines and died three weeks after the second dose of the mRNA-BNT162b-mRNA shot [46].

41. Before closing, I would like to add that I have read the affidavits deposed to by Dr Mare Olivier and Dr Anton Janse Van Rensburg. Those patient cases are alarming and I support the diagnoses made by the two Doctors. Liver disease, gall bladder conditions, aggressive cancers, bell's palsy, neurological conditions, accelerated parkisons' symptoms and tinnitus are all conditions that can be associated to the mRNA technology. I have explained the mechanisms above.

42. In conclusion, it has become very clear that the mRNA vaccine technology is in an arms race against the virus, and the virus is clearly winning.

43. In summary, it is my expert opinion that the mRNA genetic biologics, mistakenly called "vaccines," are producing severe illnesses in a vast section of the population, and, most importantly, cancer, autoimmunity-neurodegeneration and death. They are, thus, neither safe nor effective, and therefore it does not make sense to continue to encourage the general population to get repeated boosters. The risk/benefit ratio clearly favors risk over benefit for anyone under 50 years old, and, given the ineffectiveness of the antibodies against the continually emerging new variants, and the dangerous trend of increasing production of the ineffective IgG4 with boosters, it is doubtful that even the elderly will benefit from future booster shots. It is my opinion that the mRNA technology should be reconsidered and, in many ways, can be described as a complete failure in the fight against COVID-19, and we should acknowledge this fact and stop the manufacture and sales of this biologic. A much better strategy towards protection against COVID-19 is to encourage people to use holistic medicine protocols, such as: eating wholesome organic natural foods that are rich in micronutrients, exercising regularly, and spending time out in the sunlight to boost their vitamin D and E levels, in order to maintain a strong innate immunity that can protect them from severe disease. There has been solid scientific evidence that the global population to a great extent already had a robust T cell immunity against SARS-CoV-2 due to prior SARS-CoV exposure in 2003, and that other true vaccinations such as the one for anti-hepatitis A virus infection are protective against severe COVID-19. I wonder why these

serious epidemiologic measures were not taken into account in addressing the SARS CoV-2 pandemic.

44. I stand in support of the relief sought in the notice of motion.

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https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9611676/

DR ANTHONY M. KYRIAKOPOULOS

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me at by way of MS Teams on this the 19th day of February 2023 the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

COMMISSIONER OF OATHS

Name:

Address:

Position:

Margaretha Wilhelmina van Dyk
Practicing Attorney, VDMS Inc
15 Orchard Road, Bordeaux,
Randburg, South Africa
Commissioner of Oaths ex officio

"AK1"

CURICULUM VITAE

Dr Anthony M. Kyriakopoulos, BSc (Hons), Dip.LSHTM, MSc, MD/Ph.D. FIBMS

Medical and Molecular Microbiologist

Fellow of the Institute of Biomedical Sciences in Medical Microbiology

United Kingdom

Director & Head of Research and Development Nasco A.D. Biotechnology Laboratory

11 Sachtouri str, 18536, Piraeus, Greece.

Short Biography

Dr Anthony M. Kyriakopoulos, BSc (Hons), Dip.LSHTM, MSc, MD/Ph.D.* FIBMS

Medical and Molecular Microbiologist

Fellow of the Institute of Biomedical Sciences in Medical Microbiology

*This is recognized as Ph.D. by the Institute of Biomedical Sciences UK

Medical Microbiologist graduated from the Faculty of Medicine of the University of London UK. Received a Postgraduate Diploma of The London School of Hygiene and Tropical Medicine London, UK, and a Master's Degree from the Faculty of Medicine, Medical School, University of London UK. In Athens Greece, completed medical training in Medical - Molecular Microbiology and obtained a Doctorship in Medicine, / Doctorship of Philosophy from the Medical School of the University of Athens. Currently I am the President of the Hellenic Society of Taurine and Fellow of the Institute of Biomedical Sciences UK. I am a senior researcher in Biomedical Sciences at the level of Assistant Professor (see h-index in research gate account). Worked at postdoctoral positions and as a senior medical scientist for more than 20 years at multidisciplinary domains of science and medicine, as in medical microbiology, molecular genetics of aging and senescence and molecular and cell biology of cancer at the Middlesex Hospital London UK, the Pasteur Institute of France, and the National Hellenic Research Foundation, Athens Greece amongst other places. Currently, specializing in novel medicinal patents for drugs and hold a portfolio of 5 national, one international and one US. Founded and direct Nasco AD Biotechnology Laboratory, Piraeus Greece, where I rely my patent portfolio of novel formulations and patents against infectious diseases, auto-immunity and cancer. I count over 2000 citations in International Peer Review Journals and 53 publications in respected peer review journals in Greece and worldwide.

For full details please see:

https://www.researchgate.net/profile/Anthony-Kyriakopoulos

Key words of my specialties:

Medical microbiology, tuberculosis and leprosy, PCR and molecular typing PFGE, CRISPR and mRNA technology. Infectious diseases, autoimmunity and cancer.

Academic Background

- 1993: BSc (Hons) First Class Honors Degree Biomedical Sciences University of Westminster London UK
- 1994: MSc Medical Microbiology, London School of Hygiene and Tropical Medicine, University of London, London UK
- 2000: Doctor of Philosophy / Doctorship in Medicine, University of Athens, Greece.
- 2003: Associate Member of the Institute of Biomedical Sciences in Medical Microbiology United Kingdom
- 2010: Member of the Institute of Biomedical Sciences in Medical Microbiology United Kingdom
- 2020: Fellow of the Institute of Biomedical Sciences in Medical Microbiology United Kingdom

Academic / Research Positions

- 2000-2006, Medical Researcher, Microbiology Department, Medical School, University of Athens
- 2003 - 2019 Senior Researcher – Research Collaborator, National Hellenic Research Foundation, Athens Greece
- 2012- Today: Head of Research and Development Nasco AD Biotechnology Laboratory, Piraeus Greece.

Main Scientific / Research Specialisations:

- Medical Microbiology
- Molecular Microbiology
- Molecular Genetics of Ageing and Senescence
- Molecular Genetics of Cancer and Autoimmunity
- Pharmacognosy: Development of novel natural compound medicine drugs to combat, multi drug resistant infections, autoimmune disorders, chronic inflammation and cancer.

Most important recent and relevant peer reviewer full paper publications related to COVID-19 and mRNA genetic vaccination in PubMed NCBI US library:

https://pubmed.ncbi.nlm.nih.gov/?term=Kyriakopoulos+A.M.

List of Papers:

1. Seneff S, Kyriakopoulos A M, Nigh G, et al. (February 11, 2023) A Potential Role of the Spike Protein in Neurodegenerative Diseases: A Narrative Review. Cureus 15(2): e34872. doi:10.7759/cureus.34872
2. Kyriakopoulos AM, Nigh G, McCullough PA, Seneff S. Mitogen Activated Protein Kinase (MAPK) Activation, p53, and Autophagy Inhibition Characterize the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Spike Protein Induced Neurotoxicity. Cureus. 2022 Dec 9;14(12):e32361. doi: 10.7759/cureus.32361. PMID: 36514706; PMCID: PMC9733976.
3. Kyriakopoulos AM, McCullough PA, Nigh G and Seneff S. "Potential Mechanisms for Human Genome Integration of Genetic Code from SARS-CoV-2 mRNA Vaccination: Implications for Disease." J Neurol Disord 10 (2022):519.
4. Kyriakopoulos AM, Nagl M, Gupta RC, Marcinkiewicz J. Taurine and N-Bromotaurine in Topical Treatment of Psoriasis. Adv Exp Med Biol. 2022;1370:99-111. doi: 10.1007/978-3-030-93337-1_9. PMID: 35882785.
5. Seneff S, Nigh G, Kyriakopoulos AM, McCullough PA. Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs. Food Chem Toxicol. 2022 Jun;164:113008. doi: 10.1016/j.fct.2022.113008. Epub 2022 Apr 15. PMID: 35436552; PMCID: PMC9012513.
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7. Doulberis M, Papaefthymiou A, Kotronis G, Gialamprinou D, Soteriades ES, Kyriakopoulos A, Chatzimichael E, Kafafyllidou K, Liatsos C, Chatzistefanou I, Anagnostis P, Semenin V, Ntona S, Gkolia I, Papazoglou DD, Tsinonis N, Papamichos S, Kirbas H, Zikos P, Niafas D, Kountouras J. Does COVID-19 Vaccination Warrant the Classical Principle "ofelein i mi vlaptin"? Medicina (Kaunas). 2021 Mar 9;57(3):253. doi: 10.3390/medicina57030253. PMID: 33803295; PMCID: PMC7999356.
8. Kyriakopoulos AM, Papaefthymiou A, Georgilas N, Doulberis M, Kountouras J. The Potential Role of Super Spread Events in SARS-COV-2 Pandemic; a Narrative Review. Arch Acad Emerg Med. 2020 Sep 21;8(1):e74. PMID: 33134970; PMCID: PMC7587986.
9. Baliou S, Adamaki M, Kyriakopoulos AM, Spandidos DA, Panayiotidis M, Christodoulou I, Zoumpourlis V. CRISPR therapeutic tools for complex genetic

disorders and cancer (Review). Int J Oncol. 2018 Aug;53(2):443-468. doi: 10.3892/ijo.2018.4434. Epub 2018 Jun 6. PMID: 29901119; PMCID: PMC6017271.

10. Baliou S, Adamaki M, Kyriakopoulos AM, Spandidos DA, Panayiotidis M, Christodoulou I, Zoumpourlis V. CRISPR therapeutic tools for complex genetic disorders and cancer (Review). Int J Oncol. 2018 Aug;53(2):443-468. doi: 10.3892/ijo.2018.4434. Epub 2018 Jun 6. PMID: 29901119; PMCID: PMC6017271.

For full academic peer reviewed publications that are in other than PubMed medical scholars relating to COVID-19 and mRNA technology please attend my research gate account:

https://www.researchgate.net/profile/Anthony-Kyriakopoulos

A sum of important citations other than COVID-19, and mRNA technology publications

1. Kyriakopoulos AM, Nagl M, Baliou S, Zoumpourlis V. Alleviating Promotion of Inflammation and Cancer Induced by Nonsteroidal Anti-Inflammatory Drugs. Int J Inflam. 2017;2017:9632018. doi: 10.1155/2017/9632018. Epub 2017 May 10. PMID: 28573063; PMCID: PMC5442344.
2. Kyriakopoulos AM, Nagl M, Orth-Höller D, Marcinkiewicz J, Baliou S, Zoumbourlis V. Successful treatment of a unique chronic multi-bacterial scalp infection with *N*-chlorotaurine, *N*-bromotaurine and bromamine T. Access Microbiol. 2020 Apr 24;2(7):acmi000126. doi: 10.1099/acmi.0.000126. PMID: 32974590; PMCID: PMC7497830.
3. Kyriakopoulos AM, Grapsa E, Marcinkiewicz J, Nagl M. Swift Cure of a Chronic Wound Infected With Multiresistant *Staphylococcus aureus* in an Elderly Patient With Stage 5 Renal Disease. Int J Low Extrem Wounds. 2019 Jun;18(2):192-196. doi: 10.1177/1534734619834746. Epub 2019 Apr 1. PMID: 30929522.
4. Logotheti S, Khoury N, Vlahopoulos SA, Skourti E, Papaevangeliou D, Liloglou T, Gorgoulis V, Budunova I, Kyriakopoulos AM, Zoumpourlis V. N-bromotaurine surrogates for loss of antiproliferative response and enhances cisplatin efficacy in cancer cells with impaired glucocorticoid receptor. Transl Res. 2016 Jul;173:58-73.e2. doi: 10.1016/j.trsl.2016.03.009. Epub 2016 Mar 21. PMID: 27063960.
5. Kyriakopoulos, A. M., Logotheti, S., Marcinkiewicz, J., & Nagl, M. (2016). N-chlorotaurine and N-bromotaurine Combination Regimen for the Cure of Valacyclovir-unresponsive Herpes Zoster Comorbidity in a Multiple Sclerosis Patient. International Journal of Medical and Pharmaceutical Case Reports, 7(2), 1-6. https://doi.org/10.9734/IJMPCR/2016/25476

6. Davies MJ, Gordon JL, Gearing AJ, Pigott R, Woolf N, Katz D, Kyriakopoulos A. The expression of the adhesion molecules ICAM-1, VCAM-1, PECAM, and E-selectin in human atherosclerosis. J Pathol. 1993 Nov;171(3):223-9. PMID: 7506307
7. Kyriakopoulos AM, Tassios PT, Matsiota-Bernard P, Marinis E, Tsaousidou S, Legakis NJ. Characterization to species level of Mycobacterium avium complex strains from human immunodeficiency virus-positive and -negative patients. J Clin Microbiol. 1997 Nov;35(11):3001-3. PMID:9350780
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9. Kyriakopoulos AM, Matsiota-Bernard P, Marinis E, Legakis NJ, Tassios PT. Comparison of Mycobacterium avium isolates from Greek AIDS and human immunodeficiency virus-negative patients by pulsed-field gel electrophoresis. Clin Microbiol Infect. 2000 Sep;6(9):490-5. PMID:11168183
10. Kyriakopoulos AM, Dinda B. Cornus mas (Linnaeus) Novel Devised Medicinal Preparations: Bactericidal Effect against Staphylococcus aureus and Pseudomonas aeruginosa. Molecules. 2015 Jun 17;20(6):11202-18. doi: 10.3390/molecules200611202
11. Logotheti S, Khoury N, Vlahopoulos SA, Skourti E, Papaevangeliou D, Liloglou T, Gorgoulis V, Budunova I, Kyriakopoulos AM, Zoumpourlis V. N-bromotaurine surrogates for loss of antiproliferative response and enhances cisplatin efficacy in cancer cells with impaired glucocorticoid receptor. Transl Res. 2016 Jul;173:58-73.e2. doi: 10.1016/j.trsl.2016.03.009. Epub 2016 Mar 21. PMID: 27063960.

Intellectual Property; Innovations / Patents Granted

Patent 1.

Stable Olive Oil Production Through Filtration By Cellulose Membrane. GR1008334 (B) — 2014-10-21. Inventor : Kyriakopoulos Antonios Marlou-Panagioti

http://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20141021&DB=EPODOC&locale=en_EP&CC=GR&NR=1008334B

Patent 2.

Aqueous Acid Preparation Used for Soft Alkaline Lysis, Extraction and Biochemical Treatment of the Cornus Mascula Fresh Fruit Nutritional Elements. GR1008036 (B) — 2013-11-19. Inventor : Kyriakopoulos Antonios Marlou-Panagioti

http://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20131119&DB=EPODOC&locale=en_EP&CC=GR&NR=1008036B

Patent 3.

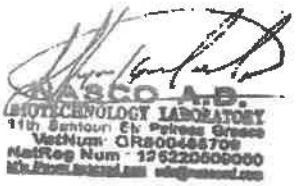
Strong Antimicrobial-Action Preparation Derived from the Biochemical Treatment of The Fresh Cornus Mascula Fruit Pulp withSodium Bromide for Acting against *Pseudomonas Aeruginosa* and *Staphylococcus aureus*. GR1008363 (B) — 2014-11-28, Inventor: Kyriakopoulos Antonios Mariou-Panagioti

http://worldwide.espacenet.com/publicationDetails/biblio?FT=D&date=20141128&DB=EPODOC&locale=en_EP&CC=GR&NR=1008363B

Patent 4.

US patent: Kyriakopoulos AM (2020) N-bromotaurine solutions and emulsions against abnormal cells. US patent number: 10,772,855 [Application Number 16/079,997] 2020.
https://uspto.report/patent/grant/10,772,855

Hereby, I confirm that information incorporated in the CV is correct to the best of my knowledge.



Dr Anthony M. Kyriakopoulos BSc (Hons), Post. Dip. LSHTM, MSc, MD/Ph.D., FIBMS

"HE10"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF	Seventh Respondent

HEALTH

MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: LIMPOPO DEPARTMENT OF HEALTH	Twelfth Respondent
MPUMALANGA DEPARTMENT OF HEALTH	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: MPUMALANGA DEPARTMENT OF HEALTH	Fourteenth Respondent
NORTHERN CAPE DEPARTMENT OF HEALTH	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTHERN CAPE DEPARTMENT OF HEALTH	Sixteenth Respondent

NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICA HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

SUPPORTING AFFIDAVIT

I, the undersigned

PROFESSOR NORMAN ELLIOTT FENTON

do hereby make oath and state that:-

1. I am an adult male Professor Emeritus of Risk at Queen Mary University of London (retired as Full Professor in December 2022) and a Director of Agena, a company that specialises in artificial intelligence and bayesian probabilistic reasoning. I am a mathematician by training with a current focus on quantifying risk and uncertainty using causal, probabilistic models that combine data and knowledge (bayesian networks). I have published 7 books and over 400 peer reviewed articles. My work covers multiple domains including especially law, forensics and health. I have been an expert witness in major criminal and civil cases, and I have been active since 2020, analysing data related to Covid risk.

2. I have the following qualifications and admissions:

   2.1. PhD (1981) in Mathematics, Sheffield University;

   2.2. MSc (1979), in Mathematics, Sheffield University;

   2.3. BSc (Class I) in Mathematics, University of London (LSE) 1978;

   2.4. CEng Chartered Engineer, Member of the IET (since 1987);

   2.5. CMath Chartered Mathematician, Fellow of the IMA (AFIMA 1988, FIMA 1998);

   2.6. FBCS Fellow of the BCS (British Computer Society) since 2005;

   2.7. FHEA Fellow of the Higher Education Academy, since June 2019;

2.8. Completed Expert Witness Training with Bond Solon under the auspices of Cardiff University Law Dept (2007-2008).

3. I have the following employment record:

3.1. 2000- Professor of Computing, Queen Mary University of London. Director of Risk and Information Management Research Group;

3.2. 1998- Director of Agena Ltd, Cambridge (CEO from 1998-2015);

3.3. 1992-2000 Professor of Computing Science, City University (CSR);

3.4. 1989-1992 Reader in Software Reliability, City University (CSR);

3.5. 1984-1989: South Bank Polytechnic (Dept Electrical & Electronic Eng): Reader and Director of the Centre for Software & Systems Engineering;

3.6. 1988 Visiting Researcher GMD, Bonn, Germany;

3.7. 1982-84 Post Doctoral Research Fellow (Mathematics), Oxford University (also member of Wolfson College);

3.8. 1981-82 Post Doctoral Research Fellow (Mathematics), University College Dublin;

3.9. 1975-76 (and part-time 1976-1979) Sales Administration, Hedges and Butler Wine Merchants.

4. I hold the following positions, and have the following affiliations:

4.1. Advisory Board Koop Technologies, since Oct 2020;

4.2. Director of Aldgate Analytics Ltd, since 2015;

4.3. Director of Agena Ltd, since 1997 (CEO from 1997-2015);

4.4. Independent reviewer (REF2013) for major UK University (details confidential) since Feb 2012;

4.5. External Assessor, University of Malaya, Kuala Lumpar, Malysia, since Dec 2012;

4.6. Scientific Committee, Knowledge Transfer Network Industrial Maths, since 2007;

4.7. Affiliated Professor to the University of Haifa, Israel since 2007;

4.8. Member of the IET (The Institution of Engineering and Technology) formerly Institute of Electrical Engineers, since 1987;

4.9. Chartered Engineer, since 1987;

4.10. Fellow of the Institute of Mathematics and Applications, (since 1998, Associate Fellow 1987-1998)

4.11. Chartered Mathematician since 2003;

4.12. Fellow of the British Computer Society since 2005;

4.13. Member of the IEEE Computer Society, since 1991

4.14. Member of EPSRC Computing College 1994-2003, and 2005 to current;

4.15. External examiner South Bank University (Electrical Engineering), 1999-2004;

4.16. External examiner of BSc in Computing, Royal Holloway and Bedford New College, 1997-2001;

4.17. External examiner for Open University MSc Software Engineering, 1997-1998;

4.18. External examiner of BSc in Computing, the American University, Richmond, 1995-1999;

4.19. Editorial Board, e-Informatica Software Engineering Journal, since 2012;

4.20. Editorial Board, Software Quality Journal, since March 1991;

4.21. Editorial Board, Journal of Empirical Software Engineering, 1995-2005;

4.22. Council Member of (National) Centre for Software Reliability, 1988-2004 (Secretary from 1991-2000);

4.23. Co-editor (with Alan Brown of SEI, Carnegie-Mellon, USA) of the Chapman & Hall Computer Science: Research and Practice book series, 1992-1996;

4.24. Member of ASM (Applications of Software Measurement) Industrial Advisory Group, 1992-1997;

4.25. Member of IEE Steering Committee on Computer Based Systems Professionals;

4.26. BSI Committee QMS 2/3/1 (Software Reliability), 1988-1995;

4.27. Member of ACM since 1993;

4.28. Member of the European Association of Theoretical Computer Science, since 1985;

4.29. Member of BCS FACS (Formal Aspects of Computer Science), since 1985;

4.30. Life Member of Wolfson College Oxford Association, since 1984; and

4.31. Life Member of London School of Economics Association, since 1983

5. The remainder of my professional resume appears in my curriculum vitae annexed as "NF1".

6. The facts in this affidavit are, to the best of my knowledge, both true and correct, and, unless the contrary appears from the context of this document, they fall within my personal knowledge and expertise. I ask the Court to note that I have no conflicts of interest that would in any way jeopardize or compromise my objectivity in presenting evidence to this Court. The opinions I have reached have been so reached based on my scientific expertise, and research and analysis of the relevant data sets, and are wholly independent of any external influencing factors or conflicts of interest.

7. I have read the founding affidavit of Herman Edeling and I agree that:

7.1. The Pfizer mRNA vaccines are not effective.

7.2. The Pfizer mRNA vaccines are not safe.

7.3. Further, it is my expert opinion that the data was not transparently and accurately presented in either Pfizer's 2-month data (see the article titled "*Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine*" published in the New England Journal of Medicine and annexed to Dr. Edeling's affidavit) or their 6-month data (see the article "*Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months*" and annexed to Dr Edeling's affidavit). Instead, it appears to have been manipulated in order to falsely inflate the safety and efficacy profiles of the Pfizer vaccine and buttress the "*safe and effective*" narrative.

8. Specifically, I would like to make the following comments:

8.1. Dr Edeling, in his affidavit, places reliance on data from the Office of National Statistics in the UK ("ONS"). His analysis, which I support, shows that after the roll-out of the vaccines, people who were vaccinated had a higher probability of dying than did those who were unvaccinated. On their face, that data is alarming but the point that needs to be made is that those statistics are, in fact, already biased in favour of vaccine effectiveness. In fact, the Statistics Regulator in the UK concedes as much.

8.2. Since July 2021, when government first started releasing data on mortality rates by vaccination status, the ONS began producing reports every two

months (up until they stopped doing it in July 2022). I believed that those reports were of great importance because they presented the first opportunity to properly and fully determine the risk-benefit of the vaccines because they'd enable one to see a comparison of all-cause mortality between the vaccinated and the unvaccinated. If the vaccines were as safe and effective as the global population had been told, then the data as released in the ONS reports should have shown a higher all-cause mortality in the unvaccinated as opposed to the vaccinated. The problem was that, right from the beginning, I (using the expertise set out above) determined that the data was flawed. I found anomalies and misclassifications plaguing the data: for example, people who were dying shortly after vaccination were being classified as "unvaccinated", there were a lot of missing deaths of people who were vaccinated, and there were under-representations of people who were unvaccinated in the relevant sample sets. I raised these issues with the ONS but I received no answers. I decided to file a complaint directly with the Statistics Regulator on 11 November 2022. In the letter of complaint, I raised two primary points. The first was that the ONS had grossly underestimated the population proportion of the unvaccinated which had the effect of making all cause deaths in the unvaccinated population reflect as higher than they were, and the second point was that mortality rates that were being reflected that were both nonsensical in various categories and completely incompatible with historical data. I made the point in the complaint that the data was so flawed that it could not be used to substantiate favourable safety and/or effectiveness profiles for the vaccines. The Statistics Regulator agreed that because of the biases, the ONS data should not be used to show favorable vaccine effectiveness or safety. What

this means practically is that the data (flawed as it is) shows that the vaccines have concerning safety and effectiveness profiles. Even these problematic profiles are biased towards vaccine effectiveness and safety, so one can only postulate how bad the true, unbiased figures would look for vaccine effectiveness and safety. I attach the Statistics Regulators response as "**NF2**"

8.3. Further, when the ONS reports all-cause mortality in vaccinated and unvaccinated people, it underestimates the percentage of unvaccinated people in the population. The effect of this is to artificially decrease the denominator in their calculations. For example the ONS, in May 2022, estimated the unvaccinated population to be 8%[1] but the true figures as published by the UKHSA (UK Health Security Agency) are closer to 20%[2].

8.4. These misclassifications have the effect of misrepresenting vaccine effectiveness in favour of vaccination.

8.5. Even with the flawed studies and biases, ONS data indicates problems with safety and effectiveness of the Pfizer mRNA vaccines.

8.6. A further flaw in the published Pfizer studies was the exclusion of participants who were infected in the first two weeks after vaccination. Dr Edeling has

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1 Source: https://www.ons.gov.uk/file?uri=/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathsbyvaccinationstatusengland/deathsoccurringbetween1january2021and31may2022/referencetable06072022accessible.xlsx

2 Source https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1088929/Weekly_Flu_and_COVID-19_report_w27.pdf

addressed this in his affidavit, and I can confirm that his observations are both correct and statistically significant. We are finding in our work that in the first two weeks after vaccination there are a significantly higher number of vaccinated people that become infected than unvaccinated people that become infected. None of this data gets reported in the published studies. By using such exclusionary techniques, it is statistically possible to prove, falsely, that a placebo is effective at preventing infection.

8.7. Another flaw in the published Pfizer studies was artificial reduction of the numbers of "confirmed Covid-19 cases" by failing to test all symptomatic cases for Covid-19. The Pfizer protocol /the 2 month report/the 6 month report annexed to Dr Edeling's affidavit makes it clear that testing of symptomatic cases was left to the discretion of the investigators.

8.8. It is important to compare the numbers of symptomatic cases in the vaccinated group and the numbers of symptomatic cases in the unvaccinated group – but the selective testing left to the discretion of the investigators means that such an exercise is impossible. All symptomatic cases should have been tested. The fact they weren't is, in my opinion, an indication of an intent to manipulate figures.

8.9. I turn now to deal with the unblinding and the cross-over in the trial as detailed by Dr Edeling in his affidavit. The Pfizer BioNTech phase 2–3 Safety and Efficacy trial was reported to be a "placebo-controlled, observer-blinded randomised control trial". In those sorts of trials, there are usually two study arms: a vaccine arm and a placebo arm. Both arms

have to be preserved to the end of the trial in order to collect comparative data that can be used to generate safety and efficacy profiles. The problem in this trial is that trial participants were unblinded from late December 2020, i.e. after collection of the two-month data, and after the FDA had granted EUA (emergency use authorisation) for use of the Pfizer BioNTech mRNA vaccines. After unblinding, the placebo recipients were offered the opportunity to receive the vaccine, i.e. the opportunity to cross over from the placebo group to the vaccinated group. I confirm Dr. Edeling's numbers insofar as he states that 88.8% of trial participants crossed over to the vaccinated arm of the trial.

8.10. The data cutoff date for Pfizer's FDA biological license application for full approval was 13 March 2021. By that cutoff date for data collection, 88.8% of the placebo arm had already received their first real dose of the vaccine.

8.11. Because of this unblinding and crossover, the conditions necessary for an RCT (randomised controlled trial) were no longer met, and it is simply a misrepresentation to continue to call the trial a "placebo-controlled, observer-blinded randomised control trial".

PROFESSOR NORMAL ELLIOTT FENTON

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me by way of MS Teams on this the 20th day of February 2023 the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

COMMISSIONER OF OATHS

Name:

Address:

Position:

Margaretha Wilhelmina van Dyk
Practicing Attorney, VDMS Inc
15 Orchard Road, Bordeaux,
Randburg, South Africa
Commissioner of Oaths ex officio

"NF1"

NORMAN FENTON CURRICULUM VITAE

Bio

I am Professor Emeritus of Risk at Queen Mary University of London (retired as Full Professor Dec 2022) and a Director of Agena, a company that specialises in artificial intelligence and Bayesian probabilistic reasoning. I'm a mathematician by training with current focus on quantifying risk and uncertainty using causal, probabilistic models that combine data and knowledge (Bayesian networks). I have published 7 books and over 400 peer reviewed articles. My works covers multiple domains including especially law and forensics(I've been an expert witness in major criminal and civil cases), and health. Since 2020 I have been active in analysing data related to Covid risk.

Education

- PhD (1981) in Mathematics, Sheffield University
- MSc (1979), in Mathematics, Sheffield University
- BSc (Class 1) in Mathematics, University of London (LSE) 1978
- CEng Chartered Engineer, Member of the IET, 1987 - 2022
- CMath Chartered Mathematician, Fellow of the IMA (AFIMA 1988, FIMA 1998)
- FBCS Fellow of the BCS (British Computer Society), 2005 - 2022
- FHEA Fellow of the Higher Education Academy, since June 2019
- Completed Expert Witness Training with Bond Solon under the auspices of Cardiff University Law Dept (2007-2008)

Employment

- 2000-2022 Professor (School of Electronic Engineering and Computer Science), Queen Mary University of London. Director of Risk and Information Management Research Group
- 1998- Director of Agena Ltd, Cambridge (CEO from 1998-2015)
- 1992-2000 Professor of Computing Science, City University (CSR)
- 1989-1992 Reader in Software Reliability, City University (CSR)
- 1984-1989: South Bank University: Reader and Director of the Centre for Software & Systems Engineering
- 1988 Visiting Researcher GMD, Bonn, Germany
- 1982-84 Post Doctoral Research Fellow (Mathematics), Oxford University (also member of Wolfson College)
- 1981-82 Post Doctoral Research Fellow (Mathematics), University College Dublin
- 1975-76 (and part-time 1976-1979) Sales Administration, Hedges and Butler Wine Merchants

Other positions

- Emeritus Professor, Queen Mary University of London since Jan 2023
- Advisory Board Koop Technologies, since Oct 2020
- Turing Fellow (Fellow of the Turing Institute) July 2018 - August 2021
- Director of Aldgate Analytics Ltd, since 2015
- Visiting Lecturer, University College London (annual MSc lecture on Bayes and the Law) since 2014
- Affiliated Professor to the University of Haifa, Israel since 2007
- Member of EPSRC Computing College 1994-2003, and 2005 to current
- Simons Fellow, Isaac Newton Institute Newton Institute for Mathematical Sciences, Cambridge University, July-Dec 2016.
- Presenter, BBC award winning Documentary "Climate Change by Numbers" 2014-2015

My publications, lectures and seminars, media appearances, legal work and risk assessment work can be accessed on https://www.normanfenton.com/full-cv.

Ed Humpherson to Norman Fenton, Martin Neil, Clare Craig and Scott McLachlan: ONS Deaths by Vaccination Status statistics

Dear Norman Fenton, Martin Neil, Clare Craig and Scott McLachlan,

ONS Deaths by vaccination Status statistics

Thank you for [redacted] and for your interest in our ONS's Deaths by Vaccination Status publication and for your patience as we have carried out our investigations. It has taken us some time to respond, for which I apologise. This is because these are important issues and we wanted to consider them carefully. I have set out our thinking on the issues below.

Our first consideration is the purpose of the ONS statistics. The Deaths by Vaccination Status publication aim to provide a broad overview of the situation regarding deaths and COVID-19 vaccinations. The analysis was developed in response to user requests during the pandemic to understand the vaccination status of people who died from COVID-19.

As ONS makes clear in its publication, this analysis is not intended to be, nor is it appropriate for, understanding vaccine effectiveness. Analyses about vaccine effectiveness and safety are covered by the weekly COVID-19 vaccine surveillance report, published by the Health Security Agency (UKHSA). We do consider that it will be important for ONS to reiterate what its Deaths by Vaccination status report is for, and is not for, in future publications.

Your paper on this topic recognised that the sample analysed in the Deaths by Vaccination Status publication is not a whole-population sample. We agree and ONS has an important point. To summarise, the publication uses data from the Public Health Data Asset (PHDA), which combines data from the 2011 census and the General Practice Extraction Service (GPES) for an individual to be included in the PHDA, they must have responded to the 2011 census and be presently registered with a GP. Approximately 78% of the population fall into this category. Those missing from the PHDA dataset are therefore not missing at random, and they are more likely to fall under one or more of the following categories:

- Younger in age
- Born outside of the UK
- Unvaccinated (as it is more difficult to obtain a COVID-19 vaccination without being registered with a GP)

We consider that it is therefore likely that the sample used in the Deaths by Vaccination Status publication is not representative of the general population. Those who are missing are, we think, more likely to be younger and unvaccinated. This is also acknowledged by ONS in its Deaths by Vaccination Status publications.

ONS is working to address some of the sampling issues present in the first six iterations of the publication. As stated in the notice at the top of the most recent publication, there is a delay in publishing the next edition. This is because ONS requires further data on subsequent booster vaccinations, and also because it is waiting for data from the 2021 Census. These data will substantially increase the sample size, meaning that the sampling frame will be much more representative of the general population. We will monitor how ONS delivers and communicates these changes as part of our ongoing review work.

In your letter to us, you state that there is a "gross underestimation of the population proportion unvaccinated present in the Deaths by Vaccination Status publication. In our view, although the number of people in each vaccination category is used in the publication, it is only used to determine the age-standardised mortality rate (ASMR) of each group. The number of people in each group is not and should not be used as a measure of vaccine uptake in the UK. This is because the sample in this publication is not random, as indicated above. Those missing from the sampling frame are more likely to unvaccinated. We will look to ONS to make this distinction clearer.

In your paper you also state that the number of deaths reported within the first 21 days of receiving the first dose of the Covid-19 vaccination is below that which could be expected in the general population, and that this difference is evidence of systematic undercounting of deaths by ONS. Our view of this question starts with the consideration that the population included is not representative of the general population, and it is therefore likely that any pattern you observe is attributable to the 'healthy vaccinee' effect. This happens when people who are ill (either due to COVID-19 or another relevant illness) are likely to delay vaccination. The result of the effect is a lower than average mortality rate within the first 21 days of receiving a vaccination. This effect is modelled by ONS in their Deaths by Vaccination Status publication.

Turning to the underlying data recording, we do not consider that there is evidence to indicate that ONS has systematically undercounted deaths within the first two weeks of receiving the COVID-19 vaccination. ONS have confirmed with us that they do receive data in these instances, and that the individual would fall into the 'vaccinated' category. We have asked that this be made clear in future iterations of this publication.

ONS has previously published [redacted] on the number of people who died after receiving the COVID-19 vaccination (up to January 2022, there were 24 deaths registered in the UK with ICD-10 code U12, 'COVID-19 vaccine causing adverse effects, on the death certificate). When we met with ONS, it confirmed that it is working on a publication that focuses on deaths after the COVID-19 vaccination, which will be published this year.

Overall, then, our view is that the Deaths by Vaccination Status publication does not provide information on vaccine effectiveness or vaccine safety, and should not be used in this way. We would advise use of the weekly COVID-19 vaccine surveillance report, published by UK Health Security Agency (UKHSA), instead. This looks at a range of measures of vaccine effectiveness, including effectiveness against infection, transmission, hospitalisation and mortality. The UKHSA publication also provides a list of other publications written by UKHSA and its collaborators, which look at the effectiveness of the [redacted].

Thank you again for contacting us about [redacted].

Yours sincerely,

Ed Humpherson
Director General for Regulation

Dated
23 January 2023

Last updated on
23 January 2023

Sent by
Ed Humpherson
Director General for Regulation, Office for Statistics Regulation

Sent to:
Norman Fenton, Martin Neil, Clare Craig, Scott McLachlan

File
Ed Humpherson to Norman Fenton, Martin Neil, Clare Craig and Scott McLachlan: ONS Deaths by Vaccination Status statistics

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Gloucestershire Hospitals NHS Foundation Trust

"NF3"

16 February 2022

Freedom of Information
Legal Services Department
Cheltenham General Hospital
Sandford Road
Cheltenham
GL53 7AN

Email: ghn-tr.foi@nhs.net

BY EMAIL TRANSMISSION

Mr Mark Wijesinghe

Dear Mark

Re: Request under Freedom of Information Act 2000 ID 6400

I am writing to you in response to your additional request for information which was received on 7 February. In your request you explained that in addition to our original response you would like the information provided at a more refined level of detail. In particular you asked for the following:

"I was hoping for daily or weekly, or even monthly data assumming over the 12 month period does not show a clear picture.
If this is not too much to ask,
Could I have weekly or monthly data or at the least, the last month's data".

This is now attached. We have added additional sheets of data.

Please could I draw your attention to any possible re-use of the above/attached information as follows:

The Freedom of Information Act (FOIA) gives people a general right of access to information held by or on behalf of public authorities that should lead to a better understanding of how public authorities carry out their duties, how the decision making process works and how they spend public money. Access to a document under a FOIA request does not give an automatic right to re-use the document. Should you wish to re-use the document please write to me and this shall be considered in light of the Re-Use of Public Sector Information Regulations. You should:

Submit requests in writing, which includes e-mail.

- Give your name and address
- Specify which documents you want to re-use
- State the purpose for which the document is to be re-used.

Re-use of information provided under the FOIA and without permission granted under the Re-use of Public Sector Information Regulations may amount to a breach of copyright and related rights.

If you need any further assistance, please do not hesitate to contact me. However I hope that this provides the information you required but if you are unhappy with the service you have received in

Chair: Peter Lachecki
Chief Executive: Deborah Lee

BEST CARE FOR EVERYONE

relation to your request and wish to request a review of our decision, you should write to me at the above address quoting the reference number.

If you are not content with the outcome of the review you may apply directly to the Information Commissioner for a decision. Generally the Information Commissioner cannot make a decision unless you have exhausted the review and complaints procedure provided by the Trust. The Information Commissioner can be contacted at: The Information Commissioner's Office, Wycliffe House, Water Lane, Wilmslow, Cheshire SK9 5AF.

Yours sincerely

Caroline Pennels
Head of Legal Services and Trust Lead for Freedom of Information
Gloucestershire Hospitals NHS Foundation Trust

Data Protection
Your information will be used by the Trust for the purposes of dealing with your request. The information you provide will also be used to monitor and review the Trust's Publication Scheme and to monitor compliance with the legislation. The information you provide will be stored in a secure shared database which will only be accessible to the Freedom of Information (FOI) Lead for the Trust to which you made the request, and their authorised FOI administrators.

"HE11"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF HEALTH	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: LIMPOPO DEPARTMENT OF HEALTH	Twelfth Respondent

JAT

MPUMALANGA DEPARTMENT OF HEALTH	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: MPUMALANGA DEPARTMENT OF HEALTH	Fourteenth Respondent
NORTHERN CAPE DEPARTMENT OF HEALTH	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTHERN CAPE DEPARTMENT OF HEALTH	Sixteenth Respondent
NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICA HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

SUPPORTING AFFIDAVIT

I, the undersigned

DR JAMES A THORP

do hereby make oath and state that:-

JAT

1. I am an adult male Obstetrician-Gynaecologist (OBGYN) practising in the sub-speciality of Maternal Foetal Medicine. I have been a practising Medical Doctor (M.D.) for forty-three (43) years. I am domiciled at 1027 Bellevue Ave Ste 205, St. Louis, MO 63117, United States of America.

2. The facts in this affidavit are, to the best of my knowledge, both true and correct, and, unless the contrary appears from the context of this document, they fall within my personal knowledge.

Introduction

3. I ask the Court to note that I have no conflicts of interests that would in any way jeopardise or compromise my objectivity in diagnosing and handling my patients, or in presenting evidence to this Court. The opinions I have reached have been so reached based on my professional expertise and are wholly independent of any external influencing factors or conflicts of interest.

4. I have read the founding affidavit deposed to by Herman Jacobus Edeling ("Edeling"). I support the contents of that affidavit insofar as he concludes that the Pfizer Covid-19 vaccines are neither safe nor effective but I limit my concurrence to my areas of specialty (fertility) and state specifically that, to the best of my knowledge and expertise, it is my expert opinion that none of the Pfizer vaccine products should be administered to (i) any woman who intends, at any stage of her life, to have children, (ii) any woman who is pregnant, (iii) any woman who is breastfeeding, or (iv) any child because they are unsafe. These conclusions accord with my own observations of objective, available medical and scientific evidence and data, and the patient cases I have dealt with in my own practice. In his affidavit,

Edeling sets out my evidence. I confirm the contents of his affidavit insofar as they pertain to me. The evidence he cites comes directly from me, and I consulted with both him and the applicant's legal team in detailing and explaining my evidence.

5. Edeling also sets out comprehensive evidence by computational biologist, Dr Jessica Rose, who has analysed the VAERS data. I concur with her findings as they pertain to pregnancy and fetal-related issues. It should be noted that my figures are slightly different to Dr Rose's as she focused solely on the Pfizer vaccines whereas I focused on all mRNA Covid-19 vaccines. The point is simply this: all mRNA vaccines, including Pfizer's vaccines, are unsafe.

My qualifications and expertise

6. I am an expert Obstetrician-Gynaecologist. The qualifications and experience on which my expertise is based are as follows:

6.1. I obtained my undergraduate degree (B.A.) in 1975 from Western Michigan University, which is in Kalamazoo, Michigan, majoring in Chemistry, with Biology minor and Math minor.

6.2. I obtained my Doctor of Medicine in 1979 from Wayne State University School of Medicine, which is in Detroit, Michigan.

6.3. I completed my internship in Obstetrics and Gynecology at the University of Colorado Health Centre located in Denver, Colorado, in 1980.

JAT

6.4. I completed my residency in Obstetrics and Gynecology at the University of Colorado / St Luke's located in Denver, Colorado, in 1983.

6.5. I completed my fellowship in Maternal Fetal Medicine at the University of Texas Medical School located in Houston, Texas, in 1988.

6.6. I was a Major in the United States Air Force from 1983 to 1986 based at K.I. Sawyer Air Force Base Hospital in Marquette, Michigan, where I was Chief of Obstetrics and Gynecology. Thereafter, I was on the Inactive Reserve Status List from 1986 to 1992 when I was honorably discharged.

6.7. I have had numerous academic appointments, which most recently include Clinical Professor, Department of Obstetrics & Gynecology, through numerous institutions including University of Texas-Houston, University of Missouri at Kansas City, University of Florida, and Florida State University College of Medicine Pensacola Regional Campus.

6.8. I have undertaken voluntary re-certification by way of Maintenance of Certification for OBGYN and Maternal Fetal Medicine through the American Board of Obstetrics and Gynecology.

JAT

6.9. The society of Maternal Fetal Medicine (SMFM) elected me to the National Board of SMFM for a three (3) year term from 2000 to 2003.

6.10. I have served as an examiner for ABOG for one year.

6.11. I have testified as an expert witness to the Bush Administration in the United States Senate in 2003. I was asked to testify for my expertise in the treatment of the fetus as a patient.

6.12. I was invited to speak at the World Council for Health's (WCH) General Assembly Meeting held on July 11, 2022, in London.

6.13. My most recent publications include:

6.13.1. Thorp JA, Renz T, Northrup C, Lively C, Breggin P, Bartlett R, et al. "*Patient Betrayal: The Corruption of Healthcare, Informed Consent and the Physician-Patient Relationship*". G Med Sci. 2022; 3(1): 046-069. https://www.doi.org/10.46766/thegms.medethics.22021403;

6.13.2. Thorp KE, Thorp JA, Thorp EM. COVID-19 and the Unraveling of Experimental Medicine – Part I. G Med Sci. 2022; 3(1): 015-045. https://www.doi.org/10.46766/thegms.pubheal.22012306

6.13.3. Thorp KE, Thorp JA, Thorp EM. COVID-19 and the Unravelling of Experimental Medicine – Part II. G Med Sci. 2022; 3(1):074. https://www.doi.org/10.46766/thegms.pubheal.22022804

6.13.4. Thorp KE, Thorp JA, Thorp EM. COVID-19 and the Unraveling of Experimental Medicine – Part III. G Med Sci. 2022; 3(1):118-158. https://www.doi.org/10.46766/thegms.pubheal.22042302

My expert opinion on mRNA covid-19 vaccines, including all Pfizer vaccine products

7. I have called for a world-wide ban and moratorium on the use of any Covid-19 mRNA vaccines, including the Pfizer vaccine products, in pregnancy until long-term safety data are irrefutable. It needs to be said here that I agree with Edeling's analysis of Pfizer's data that shows that its Comirnaty vaccine's safety was not tested in pregnant or breastfeeding women. This renders the vaccine wholly experimental in those cohorts. The fact that, despite this, the relevant Government and regulatory authority recommended the product to pregnant or breastfeeding women, or for that matter, to any woman who wants to have children violates the long-standing six-millennia golden rule of pregnancy: never use an investigational drug, a new substance, a new vaccine, in pregnancy even if there is a potential benefit.

8. To the best of my knowledge, clinical experience and research there is an increased risk of the following complications related to the COVID-19 "vaccines": menstrual irregularities, miscarriage, foetal deaths also known as stillbirths, foetal growth abnormalities, abnormal foetal testing, abnormal foetal vascular abnormalities, foetal malformations, foetal arrhythmias, and foetal cardiac arrests. This is borne out by the data in the post-marketing adverse events data already cited by Edeling and annexed to his affidavit.

9. The mRNA vaccines carry the mRNA in lipid nanoparticles (LNP's). The LNPs cross all God-made barriers including the blood brain barrier, and the placental barrier if you're pregnant. The LNP's go straight to the foetal blood and to the foetal brain and they are concentrated in the foetal ovaries. Dr Kyriakopoulos explains this in his affidavit, and I do not repeat those explanations here save to say that I concur with his reasoning, and the facts upon which that reasoning is based.

10. In contrast to the male, female ovaries have only about a million eggs (also known as ovum) formed in female foetuses prior to birth to last their entire life after birth. Following administration of a COVID-19 "vaccine", every single ovum will be exposed to concentrated amount of potentially toxic LNP and messenger RNA (mRNA), which is synthetic and man-made.

11. To the best of my knowledge, clinical experience and research, the COVID-19 "vaccines" rival the effectiveness of the abortion pill (RU486 or Mifepristone), killing and maiming women and resulting in adverse pregnancy outcomes.

JAT

Analysis of adverse event data

12. Over the course of a two (2) week period in June 2022, I personally analysed and verified data reported in the Vaccine Adverse Event Reporting System (VAERS), which is the national vaccine safety monitoring system here in the USA, which accepts reports of adverse events after vaccination.

13. I specifically compared VAERS data related to the COVID-19 mRNA "vaccines" and compared them to VAERS data related to the influenza vaccines.

14. The COVID-19 mRNA "vaccines" compared to the influenza vaccines are associated with increases in menstrual disorders, miscarriage, foetal chromosomal abnormalities, foetal cystic hygroma, foetal malformations, foetal cardiac arrest, foetal cardiac arrhythmias, foetal cardiac disorders, foetal vascular mal-perfusion abnormalities, abnormal foetal surveillance testing, abnormal foetal growth patterns, placental thrombosis, and foetal death.

15. All of the findings below are verified by independent investigators, and I verified my analysis with a Department of Defense (DOD) statistical consultant that assisted me on the condition of anonymity.

16. All of these findings are statistically and clinically significant when compared to adverse events from the Influenza vaccines that have been used in pregnancy since 1998. My findings are:

16.1. Abnormal uterine bleeding (menstrual irregularity) is 1000-fold greater;

16.2. Miscarriages are 50-fold greater;

16.3. Foetal chromosomal abnormalities are 100-fold greater;

16.4. Foetal malformation is 50-fold greater;

16.5. Foetal cystic hygroma (a major malformation) is 90-fold greater;

16.6. Foetal cardiac abnormalities are 50 fold-greater;

16.7. Foetal arrhythmia is 60-fold greater;

16.8. Foetal cardiac arrest is 230-fold greater;

16.9. Foetal vascular mal-perfusion is 130-fold greater;

16.10. Foetal growth abnormalities are 40-fold greater;

16.11. Foetal abnormal surveillance tests are 20-fold greater;

16.12. Foetal placental thrombosis is 70-fold greater; and

16.13. Foetal death is 40-fold greater.

17. None of the Pfizer vaccine products should be administered to women who intend to fall pregnant, or who are pregnant or breastfeeding. It is a matter of extreme urgency that the relevant Government and regulatory authorities warn women about the potential safety risks associate with the Pfizer mRNA vaccine products.

James A. Thorp

DR JAMES A THORP

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me at by way of Zoom on this the 22/23 day of February 2023, the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

Name:

Address:

Position:

COMMISSIONER OF OATHS

Margaretha Wilhelmina van Dyk
Practicing Attorney, VDMS Inc
15 Orchard Road, Bordeaux,
Randburg, South Africa
Commissioner of Oaths ex officio

VAL

"HE12"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF HEALTH	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent

MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent
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NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICA HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent

PFIZER Twenty-third Respondent

SUPPORTING AFFIDAVIT

I, the undersigned

DR ASEEM MALHOTRA

do hereby make oath and state that:-

1. I am an adult male Consultant Cardiologist, having qualified in 2001, currently practising at Roc Private and domiciled at Flat 1, Greenhill, Prince Arthur Rd, Hampstead, NW3 5UB.

2. The facts in this affidavit are, to the best of my knowledge, both true and correct, and, unless the contrary appears from the context of this document, they fall within my personal knowledge and expertise. I ask the Court to note that I have no conflicts of interest that would in any way jeopardize or compromise my objectivity in presenting evidence to this Court. The opinions I have reached have been so reached based on my scientific expertise, and research and analysis of the relevant data sets, and are wholly independent of any external influencing factors or conflicts of interest.

3. I have read the founding affidavit of Herman Edeling and I agree that:

   3.1. The Pfizer mRNA vaccines are not effective.

3.2. The Pfizer mRNA vaccines are not safe.

3.3. Further, it is my expert opinion that the data was not transparently and accurately presented in either Pfizer's 2-month data (see the article titled "*Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine*" published in the New England Journal of Medicine and annexed to Dr. Edeling's affidavit) or their 6-month data (see the article "*Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months*" and annexed to Dr Edeling's affidavit). Instead, it appears to have been manipulated in order to falsely inflate the safety and efficacy profiles of the Pfizer vaccine and buttress the "*safe and effective*" narrative. In this affidavit, as in my peer reviewed publications, I urge a cautious approach when confronting the official "*safe and effective*" narrative being perpetuated both globally and in South Africa.

My qualifications and expertise

4. I qualified with an MBChB from Edinburgh medical school. I have incorporated my medical training with population-based research to write multiple academic publications and help influence healthcare policy. I am a frequent expert commentator in print and TV. During the Covid-19 pandemic I was personally asked by the secretary of state for health and social care Matt Hancock to advise on the links between the virus and obesity.

5. I am an NHS trained Consultant Cardiologist, currently practising at Roc private.

6. Further, I:

6.1. Am a vising Professor of Evidence Based Medicine at the Bahiana School of Medicine and Public Health, Brazil;

6.2. I was a member of the Academy of Medical Royal Colleges Choosing Wisely Steering Group; 2014-2018

6.3. Am President of The Public Health Collaboration;

6.4. Have served a maximum of two allowed terms on the board of trustees of independent health think tank, The King's Fund from 2015-2021.

6.5. Am a honorary council member of the metabolic Psychiatry unit at the Stanford University School of Medicine.

6.6. Was, in December 2019, awarded a Fellowship to the Royal College of Physicians.

6.7. Have trained in general Cardiology and gained sub-speciality training in intervention within the North West Thames London deanery.

7. I authored a Sunday Times best-selling book; "the 21 Day Immunity plan" in 2020. My first book, The Pioppi Diet published in 2017 became an international best seller. Most recently I published my third book "A Statin Free Life" – A revolutionary plan to prevent heart disease.

8. I was a consultant clinical associate to the Academy of Medical Royal Colleges 2014-2015. My role involved the provision of a clinical perspective and input into the work of the Academy, undertaking specific projects and activities on behalf of the Academy in relation to health policy and also speaking on behalf of the Academy externally on agreed issues.

9. The main areas of work covered during that time have included the organisation of seminars for NHS England CEO, Simon Stevens, on "Delivering New Models of Care", and Improving the Health of NHS staff in relation to the Five Year Forward view. I also wrote the executive summary and co-authored a report on international Hospital Standardised Mortality Rates for medical director of the NHS Professor Sir Bruce Keogh.

10. Representing the Academy: (AoMRC Obesity campaign) I represented the Academy at various stakeholder meetings including parliamentary ones, and I was a speaker at national and international conferences.

11. Action on Sugar: Founding member and former science director. I've led work highlighting the harms of excess sugar consumption in the UK and abroad. Through both private and public advocacy including being invited by the secretary of state for health, Jeremy Hunt to give a plan to tackle child obesity, I have influenced sugar reduction strategies in the UK including the introduction of a sugar sweetened beverages levy in 2016. Earlier this year I was invited to meet the secretary of state for health, Matt Hancock, after which I delivered a keynote lecture in British parliament on the science of reversing type 2 diabetes.

12. Choosing Wisely: I conceived the idea for a joint campaign between the BMJ and the AoMRC to improve the quality of healthcare in the NHS through reducing overdiagnosis and overtreatment and the introduction of shared decision-making tools for patients and doctors. I am the first author on a BMJ publication on behalf of the AoMRC entitled " Choosing Wisely in the UK; The Academy of Medical Royal Colleges Initiative To Reduce the Harms of Too Much Medicine". (see research and publications).

The Pfizer mRNA vaccines are neither safe nor effective

13. In response to severe acute respiratory syndrome coronavirus (SARS-CoV-2), several new pharmaceutical agents have been administered to billions of people worldwide, including the young and healthy at little risk from the virus. Considerable leeway was afforded in terms of the pre-clinical and clinical testing of these agents, despite an entirely novel mechanism of action (mRNA) and concerning biodistribution characteristics. Amongst those products is Pfizer's mRNA vaccine, Comirnaty, it's Ready to Use adult vaccine ("RTU vaccine") based on the same mRNA technology, and its Dilute to Use pediatric vaccine ("DTU vaccine"), also using the same mRNA technology. No data is publicly available for the DTU and RTU vaccines, but they contain the same mRNA technology as the Comirnaty vaccine, for which there is substantial publicly available data. My scrutiny of the available data has led me to the conclusion that the Pfizer mRNA vaccine technology is unsafe and ineffective. My reasons for this conclusion follow.

14. I volunteered in a vaccine center at the commencement of the pandemic and received two doses of Pfizer's mRNA vaccine in January 2021 to prevent transmitting the virus to vulnerable patients – unaware at the time that the vaccines had not been trialed to assess whether they stopped transmission. I appeared on Good Morning Britain promoting the vaccine and received press coverage for having convinced a vaccine-hesitant film director to take the vaccine. However, after a severe personal tragedy, I critically appraised the data and spoke to eminent scientists and investigative medical journalists, leading me to conclude that the Pfizer vaccine products are not as safe and effective as I initially believed. This conclusion was reached using the framework of evidence-based medicine, and considering individual clinical expertise, best available evidence, and patient preferences and values.

15. The aforementioned personal tragedy was the loss of my Father. He was a former deputy chair of the British Medical Association. He died of a cardiac arrest in July 2021 after having taken a double dose of the Pfizer vaccine. His post-mortem findings were frankly inexplicable. Two of his three major arteries had severe blockages: 90% blockage in his left anterior descending artery and a 75% blockage in his right coronary. Given that he was an extremely fit and active 73-year-old man, having walked an average of 10–15 000 steps/day during the whole of lockdown, this was a shock to everyone who knew him, but most of all to me. I knew his medical history and lifestyle habits in detail. My father who had been a keen sportsman all his life, was fitter than most men his age. Since the previous heart scans (a few years earlier, which had revealed no significant problems with perfect blood flow throughout his arteries and only mild furring), he had quit sugar,

lost belly fat, reduced the dose of his blood pressure pills, started regular meditation, reversed his prediabetes and even massively dropped his blood triglycerides, significantly improving his cholesterol profile. It is unusual in the extreme for someone as fit and healthy as my father to have a cardiac arrest, presenting with such severe blockages, without having experienced any symptoms in the weeks or months preceding the arrest. Usually, once an individual has even one blockage over 60 or 70%, they will experience symptoms such as chest pain with or after physical exertion. This is usually a warning symptom that can lead to early, effective treatment – but my Father experienced nothing of the sort. His blockages progressed extremely rapidly, and there was no medical cause for it that I could identify.

16. Over and above this, there was no evidence of an actual heart attack preceding the cardiac arrest. My own special area of research is how to delay progression of heart disease and even potentially reverse it. Specializing in these areas, I began investigating the potential cause of my Father's death. Given the close temporal association between the administration of his Pfizer vaccines and his untimely death, I was forced to consider the vaccines as a causal agent.

17. In November 2021, I learned of a peer-reviewed study linking the Pfizer mRNA vaccine to an increased risk of coronary events in middle-aged patients. In over 500 middle-aged patients under regular follow up, using a predictive score model based on inflammatory markers that are strongly correlated with risk of heart attack, the mRNA vaccine was associated with significantly increasing the risk of a coronary event within five years from 11% pre-mRNA vaccine to 25% 2–10

weeks post mRNA vaccine. This study, although validly criticized, was sufficiently concerning to me to warrant my own personal investigation of the Pfizer data.

18. A further issue that was brought to my attention by a colleague was that the supplementary appendix of Pfizer's pivotal mRNA trial showed four cardiac arrests in those who took the vaccine versus one in the placebo group. These figures were small and did not reach statistical significance in the trial, but without further studies, it was not possible to rule out a causal relationship. These figures are detailed in Dr Edeling's affidavit, and I confirm their accuracy. To the best of my knowledge, no autopsies were done to determine whether there was a causal link between the recorded cardiac arrests and the mRNA vaccine, and so this cannot be ruled out.

Pfizer Vaccine effectiveness and safety

19. Headlines all around the world, including in South Africa, made bold claims of a Pfizer vaccine "effectiveness" of 95%. Dr Edeling, in his affidavit explains, with reference to two articles, the difference between "effectiveness" and "efficacy": efficacy speaks to a vaccine's efficacy in carefully controlled trial conditions whereas effectiveness speaks to real-world effectiveness. He explains further that the Pfizer trial was an "efficacy" trial and not an "effectiveness trial" but that, this notwithstanding, it was marketed incorrectly as an effectiveness trial. I can confirm that Dr Edeling is correct about the distinction between "efficacy" and "effectiveness".

20. It would be understandable for the lay public and doctors to interpret these "effectiveness" claims as meaning that, for example, if 100 people were vaccinated then 95% of people would be protected from getting the infection. But the original trial revealed that a person was 95% 'less likely' to catch the autumn 2020 variant of COVID-19. This is known in medical speak as relative risk reduction, but to know the true value of any treatment one needs to understand for that person, by how much is their individual risk reduced by the intervention that is, the absolute individual risk reduction.

21. Importantly, it turns out that the trial results suggest that the vaccine was only preventing a person from having a symptomatic positive test, and the absolute risk reduction for this was 0.84% (This, too, is detailed by Dr Edeling in his affidavit, and I confirm his reasoning). In other words, if 10 000 people had been vaccinated and 10 000 had not, for every 10 000 people vaccinated in the trial, 4 would have tested positive with symptoms compared to 88 who were unvaccinated. Even in the unvaccinated group, 9912 of the 10 000 (over 99%) would not have tested positive during the trial period. Another way of expressing this is that you would need to vaccinate 119 people to prevent one such symptomatic positive test.

    21.1. Here it needs to be noted that Pfizer, in their data, selectively published the relative risk reduction without publishing the absolute risk reduction even though both the WHO and the FDA require the publication of both for the purposes of obtaining informed consent from patients.

22. The numbers look even worse when calculating how many people are required to be vaccinated in order to prevent one death. Dr Edeling has summarized those

figures in his affidavit with reference to UKHSA data. I have checked that data and support his factual statements. Here, it suffices to say that depending on the relevant age cohort, the number needed to vaccinate in order to prevent one death can run into the thousands.

23. These extremely high "number needed to vaccinate" figures would only be justifiable if the Pfizer vaccine had a borderline pristine safety profile (in other words, if more people were helped by the vaccine than were harmed by adverse events associated with the vaccine) but that is not what the data is showing.

23.1. First, the adverse event reporting and cataloguing was suppressed in the Pfizer trials. This was done primarily in three ways: (i) trial participants were limited on their apps to reporting certain types of adverse events; (ii) some participants who were hospitalized after their inoculations were withdrawn from the trials and not reported in the final results; and (iii) Pfizer unblinded trial participants and crossed-over the 88.8% of the placebo arm to the vaccine arm in order to suppress the collection of long terms safety data. I again confirm Dr Edeling's facts and conclusions in respect of these issues.

23.2. Pharmacovigilance data have shown that one of the most common mRNA COVID-19 vaccine-induced harms is myocarditis. A study across several Nordic countries showed an increased risk from mRNA vaccination over background, especially in young males. Authorities have repeatedly maintained that myocarditis is more common after COVID-19 infection than after vaccination, but this is farcical because

the incidence of myocarditis rocketed from spring 2021 when vaccines were rolled out to the younger cohorts having remained within normal levels for the full year prior, despite COVID-19.

23.3. Since the vaccine rollout in the UK, almost 500,000 adverse event reports have been recorded in association with the mRNA COVID-19 vaccinations. This level of reporting is unprecedented and equals the total number of reports received in the first 40 years of the Yellow Card reporting system (for all medicines, not just vaccines) up to 2020. The yellow card reporting system is the UK's vaccine adverse events reporting system.

23.4. The US Vaccine Adverse Effect Reporting System (VAERS) has also recorded an unprecedented level of reports associated with COVID-19 vaccines. However, it has been estimated that serious adverse effects that are officially reported are a gross underestimate, and potential medium to longer-term harms may be missed. I have read Dr Jessica Rose's affidavit and support her detailed VAERS findings. They accord with my own research.

23.5. Similarly, a recent paper in "Nature Scientific Reports" revealed a 25% increase in both acute coronary syndrome and cardiac arrest calls in the 16- to 39-year-old age groups significantly associated with administration with the first and second doses of the mRNA vaccines but no association with COVID-19 infection. The authors state that:

[T]he findings raise concerns regarding vaccine-induced undetected severe cardiovascular side effects and underscore the already established causal relationship between vaccines and myocarditis, a frequent cause of unexpected cardiac arrest in young individuals.

23.6. The disturbing findings in this paper have resulted in calls for a retraction. In the past, scientists with a different view of how data should be analysed would have published a paper with differing assumptions and interpretation for discussion. Now they try to censor.

23.7. Many other concerns have been raised about potential harms from the vaccines in the mid- to long-term (these are set out more fully in Dr Kyriakopoulos' affidavit, and I do not repeat them here). Although some of these concerns remain hypothetical, it may be a grave mistake to focus only on what can be measured and not on the wider picture, especially for the young. The fact that potential concerns around mRNA technology are being ignored by authorities is even more concerning given that long term safety data collection regarding the vaccines was torpedoed by Pfizer due to the cross-over.

24. The abovementioned issues are fully canvassed and referenced in my peer-reviewed article titled "*Curing the pandemic of misinformation on Covid-19 mRNA vaccines through real evidence-based medicine – Part 1*", published in the Journal of Insulin Resistance, and annexed to this affidavit as "**AM2**".

25. My research made it clear to me that there was a significant amount of misinformation being circulated about the safety, efficacy and effectiveness of

Pfizer's mRNA vaccines. Furthermore, it appeared to me that this misinformation was not only penetrating mainstream media and influencing global medical policy – but that it was creeping into medical journals. I investigated how this phenomenon had developed and I published Part 2 of my peer-reviewed paper detailing my findings. That paper is titled "*Curing the pandemic of misinformation on Covid-19 mRNA vaccines through real evidence-based medicine – Part 2*". It was also published in the journal of Insulin Resistance, and it is annexed as "**AM3**". Some of key findings were:

25.1. There is a long-documented history (both through studies and lawsuits) of the strategies in which drug companies hide, ignore or misrepresent evidence about new drugs. Distortion of medical literature and misrepresentation of data by companies keen to expand the marketplace for their product may result in overprescribing with predictable consequences of millions of patients suffering from avoidable adverse reactions.

25.2. It appears that information is being suppressed across the board, including at academic institutions. One researcher at a prestigious UK institution contacted me to inform me that in his cardiology department a group of academics were deliberately suppressing research that revealed that the mRNA vaccine was shown to significantly increase coronary risk as determined by cardiac imaging as compared to the unvaccinated. The chair of the group expressed concerns that publishing the data may result in loss of funding from the pharmaceutical industry. After I had alluded to this on GB News, the whistleblower informed me

that non-disclosure agreement letters were sent to all members of the team involved in this area of research.

25.3. In an international survey of respondents from higher education institutions, 14% admitted to knowing a colleague who fabricated, falsified and modified data, and 34% of scientists report questionable research practices that included selective reporting of clinical outcomes in published research and concealing conflicts of interest. This information comes from an official UK parliament enquiry and can be accessed at the web address in the attached footnote.

25.4. Further, Pfizer has yet to share all the raw data from its pivotal clinical trials for the COVID-19 vaccines. The raw data from clinical trials comprises thousands of pages that have yet to be released for independent scrutiny. This lack of transparency is important because what it means is that global approval of the vaccines has been granted based on data cherry-picked by Pfizer. Transparency advocates have sued the Food and Drug Administration (FDA) to gain access to the data upon which the Pfizer (BNT162b2) vaccine was granted emergency use authorisation. The FDA wanted a US Federal court judge to allow the agency 55 years to release this data. Why would the FDA – 'which is responsible for the oversight of more than $2.7 trillion in consumption of food, medical products, and tobacco' – do this? Secrecy should never surround any public health intervention. The lawyer acting on behalf of the plaintiff Aaron Siri reported that:

[T]he government also sought to delay full release of the data it relied upon to license this product until almost every American alive today is dead. That form of governance is destructive to liberty and antithetical to the openness required in a democratic society.

25.5. Policy makers and policy influencers seemed to be drawing information about Pfizer's vaccine safety and effectiveness from media statements crafted by Pfizer themselves, rather than critically apprising the data themselves, and applying their independent minds. One such example was the admission of Rochelle Walensky, the former chair of the Centers of Disease Control (CDC), whose optimism in the efficacy of Pfizer's COVID-19 vaccine came from reading a CNN news story, which was an almost verbatim reproduction of Pfizer's own press release.

25.6. A major risk factor for failure to protect the public from the harms of data manipulation is the lack of independence of the global regulators. For example, the FDA's Centre for Drug Evaluation Research (CDER) receives 65% of its funding from the pharmaceutical industry (mainly in the form of user fees). For example, as part of the approval process for its COVID-19 vaccine, Pfizer made a wire transfer to the FDA of $2 875 842 million in May 2021. FDA approval for Pfizer's COVID-19 injection duly followed in August 2021 despite recent evidence emerging that the original randomized control trial data suggested a greater risk of serious adverse events from the vaccine than from hospitalisation because of COVID-19.

26. For all these reasons, and the reasons more fully set out in my annexed peer-reviewed papers, I am of the view that administration of the Pfizer vaccine products should be immediately suspended. I support the notice of motion and the founding affidavit deposed to by Dr Edeling.

DR ASEEM MALHOTRA

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me at WESTVILLE on this the 23 day of FEBRUARY 2023, the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

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Curing the pandemic of misinformation on COVID-19 mRNA vaccines through real evidence-based medicine - Part 1

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Background: In response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), several new pharmaceutical agents have been administered to billions of people worldwide, including the young and healthy at little risk from the virus. Considerable leeway has been afforded in terms of the pre-clinical and clinical testing of these agents, despite an entirely novel mechanism of action and concerning biodistribution characteristics.

Aim: To gain a better understanding of the true benefits and potential harms of the messenger ribonucleic acid (mRNA) coronavirus disease (COVID) vaccines.

Methods: A narrative review of the evidence from randomised trials and real world data of the COVID mRNA products with special emphasis on BionTech/Pfizer vaccine.

Results: In the non-elderly population the "number needed to treat" to prevent a single death runs into the thousands. Re-analysis of randomised controlled trials using the messenger ribonucleic acid (mRNA) technology suggests a greater risk of serious adverse events from the vaccines than being hospitalised from COVID-19. Pharmacovigilance systems and real-world safety data, coupled with plausible mechanisms of harm, are deeply concerning, especially in relation to cardiovascular safety. Mirroring a potential signal from the Pfizer Phase 3 trial, a significant rise in cardiac arrest calls to ambulances in England was seen in 2021, with similar data emerging from Israel in the 16–39-year-old age group.

Conclusion: It cannot be said that the consent to receive these agents was fully informed, as is required ethically and legally. A pause and reappraisal of global vaccination policies for COVID-19 is long overdue.

Contribution: This article highlights the importance of addressing metabolic health to reduce chronic disease and that insulin resistance is also a major risk factor for poor outcomes from COVID-19.

Keywords: COVID-19; mRNA vaccine; cardiac arrests; real evidence-based medicine; shared decision-making.

Vaccines save lives

The development of safe and highly effective vaccines during the latter half of the 20th century has been one of medicine's greatest achievements. The prominent scars on my left arm are a constant reminder of the success of our ability to curb some of the deadliest diseases such as smallpox, tuberculosis (TB), measles, mumps and rubella to name but a few. Collectively, traditional vaccines are estimated to save approximately 4–5 million lives per year.[1] The greatest success of vaccination was the global eradication of smallpox, which had a 30% mortality rate.[2]

In other words, almost one in three people who contracted it died. The development of a safe and effective vaccine after much trial and error resulted in 95 out of 100 individuals being protected from symptomatic infection from smallpox with immunity lasting five years, which by the 1970s resulted in complete eradication of the virus. Similarly, one dose of the measles vaccine is said to be '95% effective'. What is meant by this? What most people would assume is that 95 out of 100 who take the inoculation are protected from symptomatic infection, transmission and also have long-lasting immunity. Similarly, if exposed to chickenpox, only five out of 100 vaccinated children will catch it.

Vaccines are also some of the safest interventions in the world when compared to most drugs used in chronic disease management, as indeed we should expect, given that they are being administered to prevent something in healthy people, not treat an illness. It was therefore welcome

news that in the summer of 2020, several drug companies including both Pfizer and Moderna announced the results of their 2-month randomised controlled trial that they had developed a vaccine with more than '95% effectiveness' at preventing infection from what at the time was the predominantly circulating strain of the coronavirus disease 2019 (COVID-19).

A doctor's experience

Volunteering in a vaccine centre, I was one of the first to receive two doses of Pfizer's messenger ribonucleic acid (mRNA) vaccine, at the end of January 2021. Although I knew my individual risk was small from COVID-19 at age 43 with optimal metabolic health, the main reason I took the jab was to prevent transmission of the virus to my vulnerable patients. During early 2021, I was both surprised and concerned by a number of my vaccine-hesitant patients and people in my social network who were asking me to comment on what I regarded at the time as merely 'anti-vax' propaganda.

I was asked to appear on *Good Morning Britain* after a previously vaccine-hesitant film director Gurinder Chadha, Order of the British Empire (OBE), who was also interviewed, explained that I convinced her to take the jab.

But a very unexpected and extremely harrowing personal tragedy was to happen a few months later that would be the start of my own journey into what would ultimately prove to be a revelatory and eye-opening experience so profound that after six months of critically appraising the data myself, speaking to eminent scientists involved in COVID-19 research, vaccine safety and development, and two investigative medical journalists, I have slowly and reluctantly concluded that contrary to my own initial dogmatic beliefs, Pfizer's mRNA vaccine is far from being as safe and effective as we first thought. This critical appraisal is based upon the analytical framework for practicing and teaching evidence-based medicine, specifically utilising individual clinical expertise and/or experience with use of the best available evidence and taking into consideration patient preferences and values.

A case study

Case studies are a useful way of conveying complex clinical information and can elicit useful data that would be lost or not be made apparent in the summary results of a clinical trial.

On 26 July 2021, my father, Dr Kailash Chand OBE, former deputy chair of the British Medical Association (BMA) and its honorary vice president (who had also taken both doses of the Pfizer mRNA vaccine six months earlier) suffered a cardiac arrest at home after experiencing chest pain. A subsequent inquiry revealed that a significant ambulance delay likely contributed to his death.[3] But his post-mortem findings are what I found particularly shocking and inexplicable. Two of his three major arteries had severe blockages: 90% blockage in his left anterior descending artery and a 75% blockage in his right coronary. Given that he was an extremely fit and active 73-year-old man, having walked an average of 10–15000 steps/day during the whole of lockdown, this was a shock to everyone who knew him, but most of all to me. I knew his medical history and lifestyle habits in great detail. My father who had been a keen sportsman all his life, was fitter than the overwhelming majority of men his age. Since the previous heart scans (a few years earlier, which had revealed no significant problems with perfect blood flow throughout his arteries and only mild furring), he had quit sugar, lost belly fat, reduced the dose of his blood pressure pills, started regular meditation, reversed his prediabetes and even massively dropped his blood triglycerides, significantly improving his cholesterol profile.

I couldn't explain his post-mortem findings, especially as there was no evidence of an actual heart attack but with severe blockages. This was precisely my own special area of research. That is, how to delay progression of heart disease and even potentially reverse it. In fact, in my own clinic, I successfully prescribe a lifestyle protocol to my patients on the best available evidence on how to achieve this. I've even co-authored a high-impact peer-reviewed paper with two internationally reputed cardiologists (both editors of medical journals) on shifting the paradigm on how to most effectively prevent heart disease through lifestyle changes.[4] We emphasised the fact that coronary artery disease is a chronic inflammatory condition that is exacerbated by insulin resistance. Then, in November 2021, I was made aware of a peer-reviewed abstract published in *Circulation*, with concerning findings. In over 500 middle-aged patients under regular follow up, using a predictive score model based on inflammatory markers that are strongly correlated with risk of heart attack, the mRNA vaccine was associated with significantly increasing the risk of a coronary event within five years from 11% pre-mRNA vaccine to 25% 2–10 weeks post mRNA vaccine. An early and relevant criticism of the validity of the findings was that there was no control group, but nevertheless, even if partially correct, that would mean that there would be a large acceleration in progression of coronary artery disease, and more importantly heart attack risk, within months of taking the jab.[5] I wondered whether my father's Pfizer vaccination, which he received six months earlier, could have contributed to his unexplained premature death and so I began to critically appraise the data.

Questioning the data

I recalled a cardiologist colleague of mine informing me, to my astonishment at the time, that he had made a decision not to take the vaccine for a number of reasons, including his personal low background COVID-19 risk (see Table 1)[6] and concerns regarding unknown short- and longer-term harms. One thing that alarmed him about Pfizer's pivotal mRNA trial published in *The New England Journal of Medicine* was the data in the supplementary appendix, specifically that there were four cardiac arrests in those who took the vaccine versus only one in the placebo group.[7] These figures were

TABLE 1: Infection fatality rate of ancestral variants of COVID-19 pre-vaccination by age.

Age	Median IFR %	Median IFR (absolute)	Survival rate estimate (%)
0–19	0.0027	1 in 37 037	99.9973
20–29	0.0140	1 in 7143	99.9860
30–39	0.0310	1 in 3225	99.9690
40–49	0.0820	1 in 1220	99.9180
50–59	0.2700	1 in 370	99.7300
60–69	0.5900	1 in 169	99.4100
> 70 community	2.4000	1 in 42	97.6000
> 70 overall	5.5000	1 in 18	94.5000

Source: Adapted from Axfors C, Ioannidis JPA. Infection fatality rate of COVID-19 in community-dwelling elderly populations. Eur J Epidemiol. In press 2022;37(3):235–249. https://doi.org/10.1007/s10654-022-00853-w

IFR, infection fatality rate.

TABLE 2: Deaths prevented, and number needed to vaccinate to prevent a death based on death rates and case fatality rates from UKHSA data for England during Delta wave.

Age	Deaths prevented (in England) based on differences in death rates per 100 000	Number needed to vaccinate per death prevented based on differences in death rates per 100 000
< 18	-0.1	Negative
18–29	70	93 000
30–39	240	27 000
40–49	640	10 000
50–59	2740	2600
60–69	4580	1300
70–79	9100	520
80+	11 900	230
Total	29 270	-

Source: Adapted from HART. How many injections to prevent one covid death? (homepage on the Internet). No date. Available from: https://www.hartgroup.org/number-needed-to-vaccinate/

UKHSA, United Kingdom Health Security Agency.

small in absolute terms and did not reach statistical significance in the trial, suggesting that it may just be coincidence, but without further studies it was not possible to rule out this being a genuinely causal relationship (especially without access to the raw data), in which case it could have the effect of causing a surge in cardiac arrests once the vaccine was rolled out to tens of millions of people across the globe.

In terms of efficacy, headlines around the world made very bold claims of 95% effectiveness, the interchangeable use of 'efficacy' and 'effectiveness' glossing over the big difference between controlled trial and real-world conditions.[8] It would be understandable for the lay public and doctors to interpret this that if 100 people are vaccinated then 95% of people would be protected from getting the infection. Even the Centers of Disease Control (CDC) director Rochelle Walensky recently admitted in an interview that it was initial news from CNN that made her optimistic that the vaccine would significantly stop transmission and infection, but this was later to be proved far from true for the COVID-19 vaccines.[9] The original trial revealed that a person was 95% 'less likely' to catch the autumn 2020 variant of COVID-19. This is known in medical speak as relative risk reduction, but to know the true value of any treatment one needs to understand for that person, by how much is their individual risk reduced by the intervention – that is, the *absolute individual risk reduction*.

Importantly, it turns out that the trial results suggest that the vaccine was only preventing a person from having a symptomatic positive test, and the absolute risk reduction for this was 0.84% (0.88% reduced to 0.04%). In other words, if 10 000 people had been vaccinated and 10 000 had not, for every 10 000 people vaccinated in trial 4 would have tested positive with symptoms compared to 88 who were unvaccinated. Even in the unvaccinated group, 9912 of the 10 000 (over 99%) would not have tested positive during the trial period. Another way of expressing this is that you would need to vaccinate 119 people to prevent one such symptomatic positive test (assumed to be indicative of an infection, which, in itself, is potentially misleading but beyond the scope of this article).[10]

This absolute risk reduction figure (0.84%) is extremely important for doctors and patients to know but how many of them were told this when they received the shot? Transparent communication of risk and benefit of any intervention is a core principle of ethical evidence-based medical practice and informed consent.[11]

The Academy of Medical Royal Colleges made this clear in a paper published in the *BMJ* in 2015.[12] A co-author at the time was also the then chair of the General Medical Council. In fact, in a 2009 World Health Organization (WHO) bulletin Gerd Gigerenzer, the director of the Max Planck institute stated, 'It's an ethical imperative that every doctor and patient understand the difference between relative and absolute risks to protect patients against unnecessary anxiety and manipulation'.[13]

Contrary to popular belief, what the trial did not show was any statistically significant reduction in serious illness or COVID-19 mortality from the vaccine over the 6-month period of the trial, but the actual numbers of deaths (attributed to COVID-19) are still important to note. There were only two deaths from COVID-19 in the placebo group and one death from COVID-19 in the vaccine group. Looking at all-cause mortality over a longer period, there were actually slightly more deaths[14] in the vaccine group (19 deaths) than in the placebo group (17 deaths). Also of note was the extremely low rate of COVID-19 illness classed as severe in the placebo group (nine severe cases out of 21 686 subjects, 0.04%), reflecting a very low risk of severe illness even in regions chosen for the trial because of perceived high prevalence of infection.

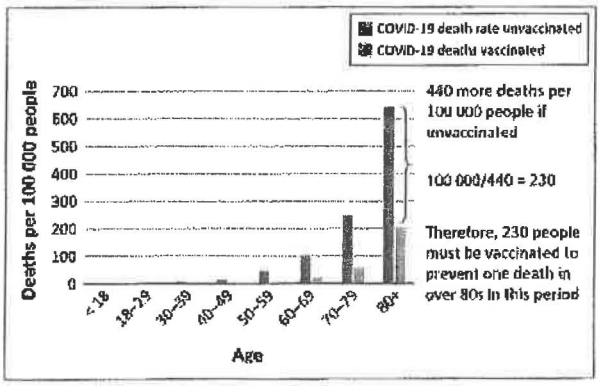
Finally, the trials in children did not even show a reduction in symptomatic infections but instead used the surrogate measure of antibody levels in the blood to define efficacy, even though the relationship between Wuhan-spike vaccine-induced antibody levels and protection from infection is tenuous, at best. The Food and Drug Administration's (FDAs) own website states that:

> [R]esults from currently authorised SARS-COV-2 antibody tests should not be used to evaluate a person's level of immunity or protection from COVID-19 at any time, and especially after the person received a COVID-19 vaccination.[15]

Now that we know what the published trial did and did not show in terms of the vaccine efficacy, we can attempt to extrapolate what the effect of the vaccine would be in reducing mortality or any other adverse outcome from the virus. If there is a 1 in 119 chance the vaccine protects you from getting symptomatic infection from ancestral variants, then to find the protection against death, this figure ($n = 119$) must be multiplied by the number of infections that lead to a single death for each age group. This would give (for up to two months after the inoculation) the absolute risk reduction (for death) from the vaccine. For example, if my risk at age 44 from dying from Delta (should I get infected with it) is 1 in 3000, then the absolute risk reduction from the vaccine protecting me from death is 1 over 3000 multiplied by 119, that is, 1 per 357000.

Of course, even for those people who do become infected the vaccination may provide some protection against death. From observational data it is possible to calculate the number who would need to be vaccinated to prevent a COVID-19 death. For example, comparing the population death rates[16] during the Delta wave gives 230 for people over 80s needing to be vaccinated to prevent a single death in that period with that number rising to 520 for people in their 70s and 10000 for people in their 40s (see Table 2 and Figure 1[17]). However, these figures will be distorted by inaccuracies in the measure of the size of the unvaccinated population. As also pointed out in a recent editorial by John Ioannidis in *BMJ* evidence-based medicine the inferred efficacy of the vaccine from non-randomised studies may be 'spurious', with bias being generated by 'pre-existing immunity, vaccination misclassification, exposure differences, testing, disease risk factor confounding, hospital admission decision, treatment use differences and death attribution'.[18]

These numbers are for the whole population of England and do not necessarily apply to the healthy; more than 95% of deaths were in people with pre-existing conditions.[19] It is also important to note that the vaccinated and unvaccinated populations are different in other ways, which could bias the death data. For example, the unvaccinated are more likely to be from a lower socioeconomic demographic, which puts them at a greater risk of severe illness or death should they be infected.



Source: Fraiman J, Erviti J, Jones M, et al. Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. Vaccine. 2022 Aug 30:S0264-410X(22)01028-3. https://doi.org/10.1016/j.vaccine.2022.08.036

Note: Difference between proportion of unvaccinated and vaccinated population dying with COVID-19 from 27 Aug to 16 Dec 2021.

UKHSA, United Kingdom Health Security Agency.

FIGURE 1: Calculation of number needed to be vaccinated from COVID-19 death rates in vaccinated and unvaccinated from UKHSA data for England during the Delta wave. The difference between the deaths that occurred in the vaccinated and that would have occurred if they had the same rate as the unvaccinated was used to calculate the number of people who would need to be vaccinated to prevent a single death.

Professor Carl Heneghan, the director of the Centre of Evidence Based Medicine in Oxford, has explained his own clinical experience of healthy user bias. Some of his own patients who ended up in intensive care unit (ICU) with COVID-19 (classified as unvaccinated) did not take the vaccine because they were already suffering from terminal illness.

Given these limitations, the above figures are likely an overestimate of the individual benefit of vaccination; the open and frank discussion of such uncertainties is an essential component of shared decision-making.

What should be part of the shared decision-making informed consent discussion when any member of the public is considering taking the shot is something along these lines: Depending on your age, several hundreds or thousands of people like you would need to be injected in order to prevent one person from dying from the Delta variant of COVID-19 over a period of around three months. For the over 80s, this figure is at least 230, but it rises the younger you are, reaching at least 2600 for people in their 50s, 10000 for those in their 40s, and 93 000 for those between 18 and 29 years. For omicron, which has been shown to be 30% – 50% less lethal, meaning significantly more people would need to be vaccinated to prevent one death. How long any protection actually lasts for is unknown; boosters are currently being recommended after as short a period as 4 months in some countries.

But how many people have had a conversation that even approaches an explanation similar to that? This is before we get into the known, unknown and as yet to be fully quantified harms.

Although many have proposed that omicron is intrinsically less lethal (supported by observed molecular differences between omicron and the Wuhan-type virus) immunity built up by prior exposure protecting against severe illness is likely to be relevant to some extent as well. The critical point to note that, whether it is a viral or immune-related phenomenon, the milder nature of omicron is evident in the unvaccinated and therefore the reduction in mortality should not be attributed to vaccines. ≤

What are the harms?

Concerns have already been raised about the under-reporting of adverse events in the clinical trials for the COVID-19 vaccines. Investigative medical reporter Maryanne Demasi analysed the various ways that the pivotal mRNA trials failed to account for serious harms.[20] Not only were trial participants limited to the type of

adverse event they could report on their digital apps, but some participants who were hospitalised after inoculation were withdrawn from the trial and not reported in the final results. After two months into the pivotal trials, the FDA allowed vaccine companies to offer the vaccine to subjects in the placebo group, essentially torpedoing any chance of properly recording adverse events from that point on, forcing a reliance of pharmacovigilance data.

Such data have shown that one of the most common mRNA COVID-19 vaccine-induced harms is myocarditis. A study across several Nordic countries showed an increased risk from mRNA vaccination over background, especially in young males.[21] Authorities have repeatedly maintained that myocarditis is more common after COVID-19 infection than after vaccination.[22] However, trial data demonstrating that vaccination reduces the risk of myocarditis in subsequent infection is elusive, and in fact the risks may be additive. Incidence of myocarditis rocketed from spring 2021 when vaccines were rolled out to the younger cohorts having remained within normal levels for the full year prior, despite COVID-19,[23] with the most up-to-date evidence, a paper from Israel[24] found that the infection itself, prior to roll-out of the vaccine, conferred no increase in the risks of either myocarditis or pericarditis from COVID-19, strongly suggesting that the increases observed in earlier studies were because of the mRNA vaccines, with or without COVID-19 infections as an additional risk in the vaccinated.[24]

Indeed, this reflects my own clinical experience of advising and managing several patients in the community who presented with a clear suggestion from the history of myocarditis post mRNA vaccination but aren't necessarily unwell enough to require hospital admission. A very fit lady in her 50s developed fatigue and shortness of breath on exertion a few weeks after her second Pfizer injection. An echocardiogram revealed severe impairment of her left ventricular function. Another lady in her 30s experienced similar symptoms with distressing palpitations within a few days of her second shot; mild left ventricular impairment was also present on echo and a subsequent cardiac MRI scan revealed several areas of *late gadolinium enhancement*, a feature seen on the scan, which is consistent with damaged heart tissue, and given that heart cells cannot be replaced this is likely to have a long-term impact.

Although vaccine-induced myocarditis is not often fatal in young adults, MRI scans reveal that, of the ones admitted to hospital, approximately 80% have some degree of myocardial damage.[25,26] It is like suffering a small heart attack and sustaining some – likely permanent – heart muscle injury. It is uncertain how this will play out in the longer-term, including if, and to what degree, it will increase the risk of poor quality of life or potentially more serious heart rhythm disturbances in the future.

A number of reports have produced concerning rates of myocarditis, depending on age, ranging from 1 in 6000 in Israel[27] to 1 in 2700 in a Hong Kong study in male children and adolescents aged 12–17 years.[28] Most of the epidemiology studies that have been carried out have measured myocarditis cases that have been diagnosed in a hospital setting, and do not claim to be a comprehensive measure of more mild cases (from which long-term harm cannot be ruled out). In addition, under-reporting of adverse events is the scourge of pharmacovigilance data.[29]

The United Kingdom relies on the Medicines and Health Regulatory Agency's (MHRAs) 'Yellow Card' reporting system,[30] which is far from adequate to cope with a rapid roll-out of a brand new product. It only detected the clotting problems that resulted in the withdrawal of the AstraZeneca product in April 2021 for younger people after 9.7 million doses had been given in the United Kingdom[31]; in contrast, Denmark detected the problem after only 150 000 doses had been administered.[32]

In the United Kingdom, since the vaccine roll-out there have been almost 500 000 adverse event reports recorded (via the Yellow Card system) in association with the mRNA COVID-19 vaccinations involving over 150 000 individuals. In terms of the number of reports per person (i.e. having received at least one dose), the MHRA figures show around 1 in 120 suffering a likely adverse event that is beyond mild.[30] However, the MHRA are unclear about the rate and furthermore do not separate out the serious adverse events. Nevertheless, this level of reporting is unprecedented in the modern medical era and equals the total number of reports received in the first 40 years of the Yellow Card reporting system (for all medicines – not just vaccines) up to 2020.[33] In comparison, for the measles, mumps and rubella (MMR) vaccine, the number of reports per person vaccinated was around 1 in 4000, more than thirty times less frequent than the 1 in 120 Yellow Card reports for COVID-19 vaccine recipients.[34] Norway does separate out the reported serious adverse reactions and has shown a rate of approximately 1 in 1000 after two doses of BioNTech / Pfizer mRNA product that result in hospitalisation or are life changing.[35]

Another, and more useful, source of information (because of the level of detail for each report made available to the public) is the United States (US) Vaccine Adverse Effect Reporting System (VAERS). As with the UK's system, the level of reports – including serious ones – associated with COVID-19 vaccines is completely unprecedented. For example, over 24 000 deaths have now been recorded in VAERS as of 02 March 2022; 29% of these occurred within 48 h of injection, and half within two weeks. The average reporting rate prior to 2020 was less than 300 deaths per annum. One explanation often given for this is that the COVID-19 vaccine roll-out is unprecedented in scope; however, this is not valid, since (for the last decade at any rate) the United States has administered 150 million – 200 million vaccinations annually. Another criticism of VAERS is that 'anyone can make an entry', yet, in fact, an analysis of a sample of 250 early deaths suggested that the vast majority are hospital or physician

entries,[36] and knowingly filing a false VAERS report is a violation of Federal law punishable by fine and imprisonment.[37]

Given that VAERS was set up to generate early signals of potential harm for new vaccines, and was instrumental in doing so for several products, it seems perverse to only now criticise it as unreliable when there seem to have been no changes in the way it operates.

It has been estimated that serious adverse effects that are officially reported are actually a gross underestimate, and this should be borne in mind when the above comments in relation to VAERS reports are considered. For example, a paper by David Kessler (a former FDA Commissioner) cites data suggesting that as few as 1% of serious adverse events are reported to the FDA.[38] Similarly in relation to the Yellow Card scheme in the United Kingdom, it has been estimated that only 10% of serious adverse effects are reported.[39,40] A recent pre-print publication co-authored by some of the most trusted medical scientists in the world in relation to data transparency adds validity to pharmacovigilance data. Accessing data from the FDA and health Canada websites and combining results from journal articles that published the Pfizer and Moderna trials, the authors concluded that the absolute risk of a serious adverse event from the mRNA vaccines (a rate of one in 800) significantly exceeded the risk of COVID-19 hospitalisation in randomised controlled trials.[17]

What VAERS and other reporting systems (including the yet to be accessed and independently evaluated raw data from randomised controlled trials) will miss are potential medium to longer term harms that neither patients nor doctors will automatically attribute to the drug. For example, if the mRNA vaccine increases the risk of a coronary event within a few months (in what was a likely contributory factor in my father's sudden cardiac death), then this would increase event rates well beyond the first few weeks of the jab yet linking it back to the vaccine, and thus reporting it is highly unlikely to occur later on.

It is instructive to note that according to ambulance service data, in 2021 (the year of the vaccine roll-out), there were approximately an extra 20000 (~20% increase) out-of-hospital cardiac arrest calls compared to 2019, and approximately 14000 more than in 2020. Data obtained under Freedom of Information laws from one of the largest ambulance trusts in England suggest that there was no increase from November 2020 to March 2021, and thereafter the rise has been seen disproportionately in the young.[41] This is a huge signal that surely needs investigating with some urgency.[42]

Similarly, a recent paper in *Nature* revealed a 25% increase in both acute coronary syndrome and cardiac arrest calls in the 16- to 39-year-old age groups significantly associated with administration with the first and second doses of the mRNA vaccines but no association with COVID-19 infection.[43] The authors state that:

> [T]he findings raise concerns regarding vaccine-induced undetected severe cardiovascular side effects and underscore the already established causal relationship between vaccines and myocarditis, a frequent cause of unexpected cardiac arrest in young individuals. (p. 1)

The disturbing findings in this paper have resulted in calls for a retraction. In the past, scientists with a different view of how data should be analysed would have published a paper with differing assumptions and interpretation for discussion. Now they try to censor.

Many other concerns have been raised about potential harms from the vaccines in the mid- to long-term. Although some of these concerns remain hypothetical, it may be a grave mistake to focus only on what can be measured and not on the wider picture, especially for the young.

What could be the mechanism of harm?

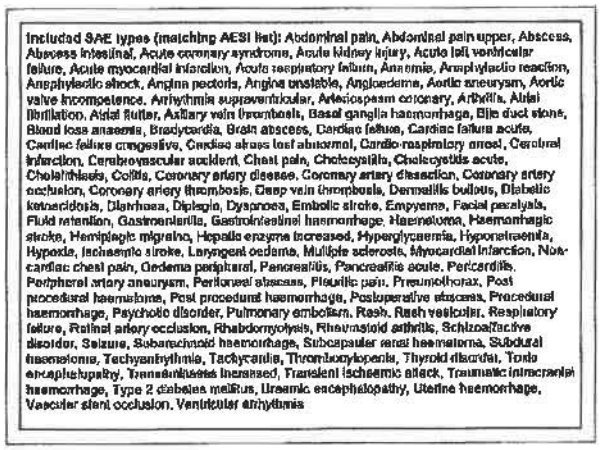
For 'conventional vaccines', an inert part of the bacteria or virus is used to 'educate' the immune system. The immune stimulus is limited, localised and short-lived. For the COVID-19 vaccines, spike protein has been shown to be produced continuously (and in unpredictable amounts) for at least four months after vaccination[44] and is distributed throughout the body after intramuscular injection.[45] For the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines, the spike protein was chosen, possibly because it enables cell entry. However, this protein is not inert, but rather it is the source of much of the pathology associated with severe COVID-19, including endothelial damage,[46] clotting abnormalities[47] and lung damage. It is instructive to note that prior to roll-out of the mRNA products, the WHO endorsed a priority list of potential serious adverse events of special interest that may occur as a direct result of COVID-19 vaccines. The list was based upon the specific vaccine platform, adverse events associated with prior vaccines in general, theoretical associations based upon animal models and COVID-19-specific immunopathogenesis[48] (see Figure 2).

Is the vaccine doing more harm than good?

The most objective determinant of whether the benefits of the vaccines outweigh the harms is by analysing its effects on 'all-cause mortality'. This gets round the thorny issue as to what should be classified as a COVID-19 death, and also takes full account of any negative effects of the vaccine. It would be surprising – to say the least – if during an apparently deadly pandemic, an effective vaccine could not clearly and unequivocally be shown to reduce all-cause mortality.

Pfizer's pivotal mRNA trial in adults did not show any statistically significant reduction in all-cause mortality, and in absolute terms there were actually slightly more deaths in the treatment arm versus in the placebo.

Work by Fenton et al. showed an unusual spike in mortality in each age group of the unvaccinated population, which


Included SAE types (matching AESI list): Abdominal pain, Abdominal pain upper, Abscess, Abscess intestinal, Acute coronary syndrome, Acute kidney injury, Acute left ventricular failure, Acute myocardial infarction, Acute respiratory failure, Anaemia, Anaphylactic reaction, Anaphylactic shock, Angina pectoris, Angina unstable, Angioedema, Aortic aneurysm, Aortic valve incompetence, Arrhythmia supraventricular, Arteriospasm coronary, Arthritis, Atrial fibrillation, Atrial flutter, Axillary vein thrombosis, Basal ganglia haemorrhage, Bile duct stone, Blood loss anaemia, Bradycardia, Brain abscess, Cardiac failure, Cardiac failure acute, Cardiac failure congestive, Cardiac stress test abnormal, Cardio-respiratory arrest, Cerebral infarction, Cerebrovascular accident, Chest pain, Cholecystitis, Cholecystitis acute, Cholelithiasis, Colitis, Coronary artery disease, Coronary artery dissection, Coronary artery occlusion, Coronary artery thrombosis, Deep vein thrombosis, Dermatitis bullous, Diabetic ketoacidosis, Diarrhoea, Diplegia, Dyspnoea, Embolic stroke, Empyema, Facial paralysis, Fluid retention, Gastroenteritis, Gastrointestinal haemorrhage, Haematoma, Haemorrhagic stroke, Hemiplegic migraine, Hepatic enzyme increased, Hyperglycaemia, Hyponatraemia, Hypoxia, Ischaemic stroke, Laryngeal oedema, Multiple sclerosis, Myocardial infarction, Non-cardiac chest pain, Oedema peripheral, Pancreatitis, Pancreatitis acute, Pericarditis, Peripheral artery aneurysm, Peritoneal abscess, Pleuritic pain, Pneumothorax, Post procedural haematoma, Post procedural haemorrhage, Postoperative abscess, Procedural haemorrhage, Psychotic disorder, Pulmonary embolism, Rash, Rash vesicular, Respiratory failure, Retinal artery occlusion, Rhabdomyolysis, Rheumatoid arthritis, Schizoaffective disorder, Seizure, Subarachnoid haemorrhage, Subscapular renal haematoma, Subdural haematoma, Tachyarrhythmia, Tachycardia, Thrombocytopenia, Thyroid disorder, Toxic encephalopathy, Transaminases increased, Transient ischaemic attack, Traumatic intracranial haemorrhage, Type 2 diabetes mellitus, Uraemic encephalopathy, Uterine haemorrhage, Vascular stent occlusion, Ventricular arrhythmia

Source: Fraiman J, Erviti J, Jones M, et al. Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults. Vaccine. 2022 Aug 30:S0264-410X(22)01028-3. https://doi.org/10.1016/j.vaccine.2022.08.036.

SAE, serious adverse events; AESI, adverse events of special interest.

FIGURE 2: World Health Organization endorsed a list of adverse events of special interest associated with COVID-19 vaccinations.

coincides with the vaccine roll-out for each age group.[18] The rapid shrinking in the size of this population means a small-time lag could theoretically produce this effect artifactually. Alternative explanations must include the (more likely) possibility that a rise in mortality after vaccination was misattributed to the unvaccinated population: in other words, those counted as 'unvaccinated deaths' would in fact be those who had died within 14 days of being vaccinated (a freedom of information [FOI] request has now confirmed that authorities in Sweden were indeed categorising deaths within 14 days of dosing as unvaccinated, creating a misleading picture of efficacy vs death).

One has to raise the possibility that the excess cardiac arrests and continuing pressures on hospitals in 2021/2022 from non-COVID-19 admissions may all be signalling a non-COVID-19 health crisis exacerbated by interventions, which would of course also include lockdowns and/or vaccines.

Given these observations, and reappraisal of the randomised controlled trial data of mRNA products, it seems difficult to argue that the vaccine roll-out has been net beneficial in all age groups. While a case can be made that the vaccines may have saved some lives in the elderly or otherwise vulnerable groups, that case seems tenuous at best in other sections of the population, and when the possible short-, medium- and unknown longer-term harms are considered (especially for multiple injections, robust safety data for which simply does not exist), the roll-out into the entire population seems, at best, a reckless gamble. It's important to acknowledge that the risks of adverse events from the vaccine remain constant, whereas the benefits reduce over time, as new variants are (1) less virulent and (2) not targeted by an outdated product. Having appraised the data, it remains a real possibility that my father's sudden cardiac death was related to the vaccine. A pause and reappraisal of vaccination Policies for COVID-19 is long overdue.

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Author's contribution

A.M. is the sole author of this article.

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Data availability

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Disclaimer

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Curing the pandemic of misinformation on COVID-19 mRNA vaccines through real evidence-based medicine - Part 2

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Background: Authorities and sections of the medical profession have supported unethical, coercive, and misinformed policies such as vaccine mandates and vaccine passports, undermining the principles of ethical evidence-based medical practice and informed consent. These regrettable actions are a symptom of the 'medical information mess': The tip of a mortality iceberg where prescribed medications are estimated to be the third most common cause of death globally after heart disease and cancer.

Aim: To identify the major root causes of these public health failures.

Methods: A narrative review of both current and historical driving factors that underpin the pandemic of medical misinformation.

Results: Underlying causes for this failure include regulatory capture – guardians that are supposed to protect the public are in fact funded by the corporations that stand to gain from the sale of those medications. A failure of public health messaging has also resulted in wanton waste of resources and a missed opportunity to help individuals lead healthier lives with relatively simple – and low cost – lifestyle changes.

Conclusion: There is a strong scientific, ethical and moral case to be made that the current COVID vaccine administration must stop until all the raw data has been subjected to fully independent scrutiny. Looking to the future the medical and public health professions must recognise these failings and eschew the tainted dollar of the medical-industrial complex. It will take a lot of time and effort to rebuild trust in these institutions, but the health – of both humanity and the medical profession – depends on it.

Contribution: This article highlights the importance of addressing metabolic health to reduce chronic disease and that insulin resistance is also a major risk factor for poor outcomes from COVID-19.

Keywords: COVID-19; mRNA vaccine; cardiac arrests; real evidence-based medicine; shared decision making.

A pandemic of misinformation

What has become clear with regard to the coronavirus disease 2019 (COVID-19) vaccines is that we have a pandemic of misinformed doctors and a misinformed and unwittingly harmed public. Coercively mandating these COVID-19 vaccinations (most certainly not an evidence-based policy) has been a particularly egregious mis-step, especially in the light of clear indicators suggesting that the use of these pharmaceutical interventions – especially in younger age groups – should have been suspended. Such policies continue to undermine the principles of ethical evidence-based medical practice and informed consent, to the detriment of optimising patient outcomes.

In his 2017 paper, 'How to survive the medical misinformation mess', Professor John Ioannidis and colleagues highlight that:

> [M]ost clinical trial results may be misleading or not useful for patients. Most guidelines (which many clinicians rely on to guide treatment decisions) do not fully acknowledge the poor quality of data on which they are based. Most medical stories in mass media do not meet criteria for accuracy, and many stories exaggerate benefit and minimise the harms.[1] (p. 1)

A senior doctor in regular contact with the United Kingdom's (UKs) Chief Medical Officer Professor Chris Whitty recently expressed concerns to me that he felt most of his colleagues in

leadership positions influencing health policy may not be critically appraising the evidence and instead are relying on media stories on COVID-19 and the vaccine. This is consistent with the admission of Rochelle Walensky, the former chair of the Centers of Disease Control (CDC), whose optimism in the efficacy of Pfizer's COVID-19 vaccine came from reading a CNN news story, which was an almost verbatim reproduction of Pfizer's own press release.[2]

Has the UKs Chief Medical Officer Professor Chris Whitty critically appraised the evidence? Recently, he publicly shared a letter[3] outlining the importance of healthcare staff to become vaccinated against COVID-19, which was neither comprehensive nor consistent with the totality of the evidence: 'The COVID-19 vaccines are safe and effective'. It would have been more accurate to state that 'the vaccine is not completely safe and not anywhere close to being as effective as we'd hoped for. Not even in the same ball park when compared to the efficacy and safety of traditional vaccines'.

Professor Chirs Witty stated:

> Our professional responsibility is to get the covid vaccines as recommended to protect our patients'.[3]

He should have said as far as omicron is concerned, 'the vaccine offers little to no protection against infection. Data on the delta variant also revealed that once infected there is no significant difference in transmission rates between the vaccinated and unvaccinated individuals.

Professor Whitty's statements are especially surprising given that the CEO of Pfizer has stated that in realtion to omicron 'We know that the two doses of a vaccine offer very limited pretection, if any'.[5]

Could it be that Professor Whitty is also a victim of the medical misinformation mess?

There are four key drivers and seven sins that are at the root of the medical misinformation mess:

- Drivers:
  - Much published medical research is not reliable or is of uncertain reliability, offers no benefit to patients or is not useful for decision makers;
  - Most healthcare professionals are not aware of this problem;
  - Even if they are aware of this problem, most healthcare professionals lack the skills necessary to evaluate the reliability and usefulness of medical evidence; and
  - Patients and families frequently lack relevant, accurate medical evidence and skilled guidance at the time of medical decision making.[1]
- Sins:
  - Biased funding of research (that's research that's funded because it's likely to be profitable, not beneficial for patients)
  - Biased reporting in medical journals
  - Biased reporting in the media
  - Biased patient pamphlets
  - Commercial conflicts of interest
  - Defensive medicine
  - An inability of doctors to understand and communicate health statistics.[6]

Ioannidis and colleagues highlight that:

> 'Ignorance of this problem, even at the highest levels of academic and clinical leadership, is profound'[1]

Compounded over several decades, these upstream and downstream risk factors for misinformation have had a devastating effect in the healthcare environment we find ourselves in today. Over-prescription of drugs is considered such a public health threat that two leading medical journals in the past 10 years (the *BMJ* and *JAMA Internal Medicine*) have launched campaigns to reduce the harms of too much medical intervention. According to the cofounder of the Cochrane Collaboration, Peter Gotzsche, prescribed medications are the third most common cause of death globally after heart disease and cancer.[7] This is not surprising when one understands that most published research is misleading specifically where benefits from drug trials are exaggerated, and harms downplayed (Box 1[8]).

If a doctor is making clinical decisions on biased information, it will lead (at best) to suboptimal outcomes and (more concerningly) harm to patients.

Shortcomings of the medical profession

According to Professor Carl Heneghan and urgent care General Practitioner, the director of the University of Oxford's Centre of Evidence-Based Medicine: 'with every intervention you do as a doctor you must ask yourself two questions: how much difference does it make? How do I know this?'[9]

Building on the Academy of Medical Royal Colleges Choosing Wisely campaign,[10] it is instructive to note that the

BOX 1: Major limitations in the interpretation, external validity and usefulness of drug industry-sponsored clinical trials.

1. Trials are conducted of a study drug against a treatment known to be inferior
2. Use multiple endpoints in the trial and select for publication those that give favourable results
3. Do multicentre trials and select for publication results from centres that are favourable
4. Conduct subgroup analyses and select for publication those that are favourable
5. Present results that exaggerate the benefit – for example, use of relative risks as opposed to absolute risks
6. Conduct trials on subjects that are unrepresentative of the patient population
7. Conflate primary and secondary endpoints in the published report
8. Conceal unblinded patients and include them in efficacy analyses for publication
9. Exclude placebo responders in the wash-out phase of the trial
10. Delay publication of negative trial results until positive trial results are published
11. Conceal negative trial results whilst publishing only positive trial results
12. Conceal serious adverse events
13. Fail to distinguish clinical from statistical significance

Source: Adapted from Jureidini J, McHenry L. The illusion of evidence based medicine. Adelaide: Wakefield Press; 2020

General Medical Council in 2020 issued guidance on the duty of doctors to engage in Shared Decision Making with patients, underpinned by informed consent.[11]

There are six components essential to informed decision making: (1) description of the nature of the decision; (2) discussion of alternatives; (3) discussion of risks and benefits (in absolute terms); (4) discussion of related uncertainties; (5) assessment of the patient's understanding; and (6) elicitation of the patient's preference.

If the administration of the vaccine did not adhere to these principles (which is likely widespread, consistent with historical evidence[12]), then it is also a significant breach of General Medical Council duties of a doctor to 'give patients the information they want or need in a way that they can understand'.[13]

It is instructive to note that the greater the financial interests in a given field, the less likely the research findings are to be true.[14] As has been already demonstrated in Part 1[15] of this article, mandating a novel emergency use authorisation vaccine to non-vulnerable people has little to no effect on preventing infection and serious illness, therefore does not have any scientific validity, and therefore breaches the principles of informed consent. It does, however, dramatically enhance the profits of the manufacturer. By expanding the uptake of the mRNA vaccine to the majority of the population that are very low risk of serious complications from COVID-19 but are more likely to suffer serious and/or life-threatening adverse events such as myocarditis or sudden cardiac death, Pfizer has generated tens of billion dollars in revenues to date, making it one it one of the most lucrative products in history. If policymakers had focussed more on protecting the vulnerable – and doctors had been given the opportunity to practice shared decision making with patients using transparent communication of risk and benefit – patient outcomes would likely have been significantly improved,[16] but the drug companies' profits would likely have been a tiny fraction of what they actually generated. As former Editor of the *New England Journal of Medicine* Dr Marcia Angell has previously pointed out 'the real battle in healthcare is one of truth versus money'.[17]

Institutional corruption and erosion of public trust

Institutional corruption is defined as an institution's deviation from a baseline of integrity.[18] There is a long-documented history (both through studies and lawsuits) of the strategies in which drug companies hide, ignore or misrepresent evidence about new drugs. Distortion of medical literature and misrepresentation of data by companies keen to expand the marketplace for their product may result in overprescribing with predictable consequences of millions of patients suffering from avoidable adverse reactions.

Prior to 2020 there already existed gross shortcomings in the medical–industrial complex – there has been too much pharmaceutical industry influence on clinical decision making. This has not gone unnoticed, resulting in a growing crisis of trust in medical research: a report by the Academy of Medical Sciences in 2017 revealed that 82% of GPs and 63% of the public did not believe the results of pharmaceutical industry-sponsored research to be unbiased.[19] Similarly, only 37% of the public trust medical research compared to 65% who trust the experience of their friends and family.[20]

This growing lack of trust – most recently exacerbated by coercion, vaccine passports and little mainstream media coverage of an unprecedented scale of reported vaccine harms in the population – has been most recently exemplified by 8 million people in the UK refusing to take the COVID-19 booster shot. In addition, with all the attention on COVID-19 (which poses almost zero risk to children in its current omicron form), diverts attention away from, and even worse raises the suspicion of, more efficacious and safe interventions such as the measles, mumps, rubella (MMR) vaccine. Indeed, in the UK MMR vaccination rates have hit their lowest for 10 years.

Failure of regulation and research misconduct

Authorities want the public to 'trust the science', but vaccine manufacturers have successfully negotiated deals with several major governments globally that indemnify them against any financial liability in the event of vaccine-related harm. Interestingly, India, the world's largest democracy, refused to grant Pfizer indemnity from harms for its vaccine. An Indian government source told Reuters that:

> [T]he whole problem with Pfizer is the indemnity bond. Why should we sign it? If something happens, a patient dies, we will not be able to question them [*Pfizer*]. If somebody challenges in a court of law, the central government will be responsible for everything, not the company.[21] (p. 1)

Pfizer walked away from the Indian market rather than undertake a local safety and immunogenicity study.[22]

It is important to first understand that drug companies have a fiduciary obligation to deliver profits to their shareholders, not any legal responsibility to provide you with the best treatment. At a talk at the Centre of Evidence-Based Medicine in Oxford in 2014, Peter Wilmshurst said the real scandal is that many of those with a responsibility to patients and scientific integrity (doctors, academic institutions and medical journals) often collude with industry for financial gain.[23] It is this very industry that has been found guilty of the most egregious corporate crimes: between 2003 and 2016 the top 11 pharmaceutical companies paid $28.8 billion in fines just within the United States (US),[24] much of it for criminal activity such as the illegal marketing of drugs, manipulation of results and hiding data on harms. As pointed out in the *BMJ*, since then no systemic changes have been made to mitigate these harms.[9]

In an international survey of respondents from higher education institutions, 14% admitted to knowing a colleague who fabricated, falsified and modified data, and 34% of scientists report questionable research practices that included selective reporting of clinical outcomes in published research and concealing conflicts of interest.[25] An egregious documented case of research misconduct involved a prominent Dutch physician whose work influenced the European Society of Cardiology guidelines on the use of beta blocker drugs in non-cardiac surgery. He was dismissed from Erasmus University for 'violations in academic integrity', including using 'fictitious data' in research. It's estimated that these guidelines increased patient mortality by 27% resulting in 800000 excess deaths across Europe over an 8-year period.[26]

In evidence submitted to the UK parliamentary science and technology review into research integrity committee in 2017 (Chaired by Sir Norman Lamb), Dr Peter Wilmshurst lists a number of risk factors that drive research misconduct in British institutions (see Box 2[27]). His solution, which I agree with, would be to ensure that serious forms of research misconduct are made into criminal offences with meaningful sanctions and that allegations of such activity should be investigated by an independent body with legal powers.[27]

BOX 2: Written evidence from Dr Peter Wilmshurst to UK Parliamentary Science and Technology Research Integrity Committee (June 2018).

Academic institutions bear responsibility for the pressure to publish for career advancement that can result in research misconduct.

A record of prominent publication is likely to attract future funding, which institutions demand, and good publicity, which institutions desire.

Other pressures for misconduct come from the association of academic institution with industry, such as when investigators or their institutions hold patents or shares, or they receive payments from industry, so that there is financial pressure to publish research that will be profitable for the company and to suppress 'negative' findings.

Some publications are simply organised criminal activities, which may be at the behest of sponsors, when prominent academics are paid large sums of money to publish false data by industry, or a sponsor may be one of the victims, when payments for conducting research are made to 'investigators', who simply fabricate data.

Medical journals have financial pressures to publish positive findings of research on drugs and medical devices, because their manufacturers buy reprints of the papers for distribution to doctors and they pay for advertisements linked to articles favourable to their product.

Academic institutions and journals depend on the public belief in the integrity of science, so they are unwilling to admit the seriousness and frequency of research misconduct.

To protect their reputations academic institutions conceal research misconduct, destroy evidence and silence whistle-blowers.

Journals are reluctant to admit that they published flawed research, so they commonly refuse to publish failures to replicate.

Fear of a libel action contributes to the failure to expose research misconduct.

Investigation of research misconduct may be difficult because there may be international collaboration between investigators, many of whom do not see the full data, and the resulting publications may be in journals that are published in countries where none of the investigators work.

The bodies that investigate research misconduct in the UK (such as the GMC and UKRIO) are hampered by a desire to play down the problem, by lack of proper forensic skills when investigating, by inconsistent interpretation of rules and by inadequate powers to compel the cooperation of academic institutions and journals.

Because lenient sanctions are imposed, institutions believe that the misconduct is not very serious, and potential research fraudsters are not deterred.

Source: Wilmshurst P. Written evidence (homepage on the Internet). 2017 [cited 2022 Jun 5]. Available from: http://data.parliament.uk/writtenevidence/committeeevidence.svc/evidencedocument/science-and-technology-committee/research-integrity/written/68813.html

GMC, General Medical Council; UKRIO, United Kingdom Research Integrity Office.

One researcher at a prestigious UK institution contacted me to inform me that in his cardiology department a group of academics were deliberately suppressing research that revealed that the mRNA vaccine was shown to significantly increase coronary risk as determined by cardiac imaging as compared to the unvaccinated. The chair of the group expressed concerns that publishing the data may result in loss of funding from the pharmaceutical industry.[28] After I had alluded to this on GB News, the whistle-blower informed me that non-disclosure agreement letters were sent to all members of the team involved in this particular area of research.

Evidence-based medicine and COVID-19 vaccine roll-out

Neither the drug regulators nor the vaccine manufacturers have yet to share all the raw data from the pivotal trials for the COVID-19 vaccines.[29] The raw data from clinical trials comprise thousands of pages that have yet to be released for independent scrutiny. This is important because historically when independent researchers have on occasion gained access to this data then it can completely overturn the conclusions of the published trials: A case in point is Tamiflu.[30] Getting access to clinical case reports for Tamiflu ultimately revealed that the drug was no more effective than paracetamol for influenza and also came with small but significant harms. The UK government had spent half a billion dollars stockpiling a drug that in effect proved to be useless despite claims by the manufacturers (Roche, Basil, Switzerland) that it shortened the duration and severity of the illness. The independent researchers who were able to analyse the data concluded that all industry-sponsored research should be considered marketing until proven otherwise.

It is against this backdrop that transparency advocates sued the Food and Drug Administration (FDA) to gain access to the data upon which the Pfizer (BNT162b2) vaccine was granted emergency use authorisation.[31] The FDA wanted a US Federal court judge to allow the agency 55 years to release this data.[32] Why would the FDA – 'which is responsible for the oversight of more than $2.7 trillion in consumption of food, medical products, and tobacco'[31] – do this? Secrecy should never surround any public health intervention. The lawyer acting on behalf of the plaintiff Aaron Siri reported that:

> [T]he government also sought to delay full release of the data it relied upon to license this product until almost every American alive today is dead. That form of governance is destructive to liberty and antithetical to the openness required in a democratic society.[31]

Instead, the judge ordered the FDA to release the data over a period of eight months after all commercially sensitive information has been redacted.

A major risk factor for failure to protect the public from such harms is lack of independence of the regulator. The FDA's

Centre for Drug Evaluation Research (CDER) receives 65% of its funding from the pharmaceutical industry (mainly in the form of user fees).[34] For example, as part of the approval process for its COVID-19 vaccine, Pfizer made a wire transfer to the FDA of $2875842 million in May 2021[35] under the *Prescription Drug User Fee Act* of 1992.[36] Full FDA approval for Pfizer's COVID-19 injection duly followed in August 2021[37] despite recent evidence emerging that the original RCT data suggested a greater risk of serious adverse events from the vaccine than from hospitalisation because of COVID-19.

Separate analyses have revealed the overwhelming majority of new drugs that have been approved by the FDA in the past few decades have later been shown to be just copies of old ones, which is not surprising when one understands that drug companies spend 19 times more on marketing than they do on researching new molecular entities, which all contributes to considerable waste. Between 2000 and 2008 of the 667 drugs approved by the FDA, only 11% were found to be truly innovative. In the US it's estimated that 30% – 50% of healthcare activity brings no benefit to patients. Extraordinarily, a survey of FDA scientists revealed 70% of them did not feel the FDA had the resources to perform effectively in its mission in 'protecting public health … and helping the public get accurate science-based information to use medicines and foods to improve their health'.[38]

An analysis of every new drug product approved in France between 2002 and 2011 revealed only 8% offered some advantages and double that amount – at 15.6% – were found to be more harmful than beneficial with the majority of other new drugs being essentially copies of old ones contributing to a colossal waste of public money.[39] Similar conclusions have been drawn in Canada and Holland. In my opinion the evidence is overwhelming that the overall net effect of the pharmaceutical industry in the last few decades on society and population health has been a hugely negative one.

COVID-19 vaccination in lower risk individuals

Irrespective of the merits of inoculating higher risk groups where a small but significant benefit may exist against the original Wuhan strain, vaccinating lower risk children in the name of preventing asymptomatic transmission has no strong scientific validity and therefore exposes them to possible harm.

In the UK the Office for National Statistics has revealed an as yet unexplained significant increase in deaths over the 5-year average in 15- to 19-year-old children since May 2021. Given what we now know of potential harms especially in relation to myocarditis, myocardial infarction and sudden cardiac death (even in 16- to 39-year-olds) has the COVID-19 vaccine been excluded as a possible cause?[40]

In September 2021, the Joint Committee on Vaccination and Immunisation (JCVI) made a controversial recommendation that the Pfizer/BioNTech vaccine is marginally beneficial for 12- to 15-year-old children.[41] The Medicines and Healthcare products Regulatory Agency (MHRA, the UK's equivalent of the FDA) had previously stated that:

> [T]hey have carefully reviewed clinical trial data for Pfizer/BioNtech vaccine in over 2000 children aged 12–15 years of age and have concluded that the benefits of this vaccine outweigh any risk and that it is effective and acceptably safe in this age group … No new side effects were identified and the safety data in children was comparable to that seen in young adults. As in the young adult age group, the majority of adverse events were mild to moderate, relating to reactogenicity (e.g. sore arm and tiredness).[41] (p. 1)

Is this in keeping with the totality of the evidence?

Award winning investigative science journalist Maryanne Demasi published the harrowing story of one of those trial participants, 12-year-old Maddie De Garay. After experiencing severe abdominal pain followed by seizures she was admitted to hospital and is now left permanently disabled, wheelchair bound and fed through a nasogastric tube. In Pfizer's trial they reported her adverse effect as mild: stomach upset.[42]

It is important to emphasise that the risk of death from COVID-19 in a 12- to 15-year-old is close to zero at 1 in 76 000. In keeping with the principles of ethical evidence-based medical practice through shared decision making, parents need to be told that there is no high-quality data in children that the vaccine will prevent infection, transmission, serious illness or death but may come with serious side effects of myocarditis – particularly in young males where it occurs in up to 1 in 2700[43] – and serious disability as a general principle of transparent communication of risk and informed consent: without understanding the numbers involved the public is vulnerable to their hopes and anxieties being exploited by political and commercial interests.

Could financial interests be biasing the recommendations?

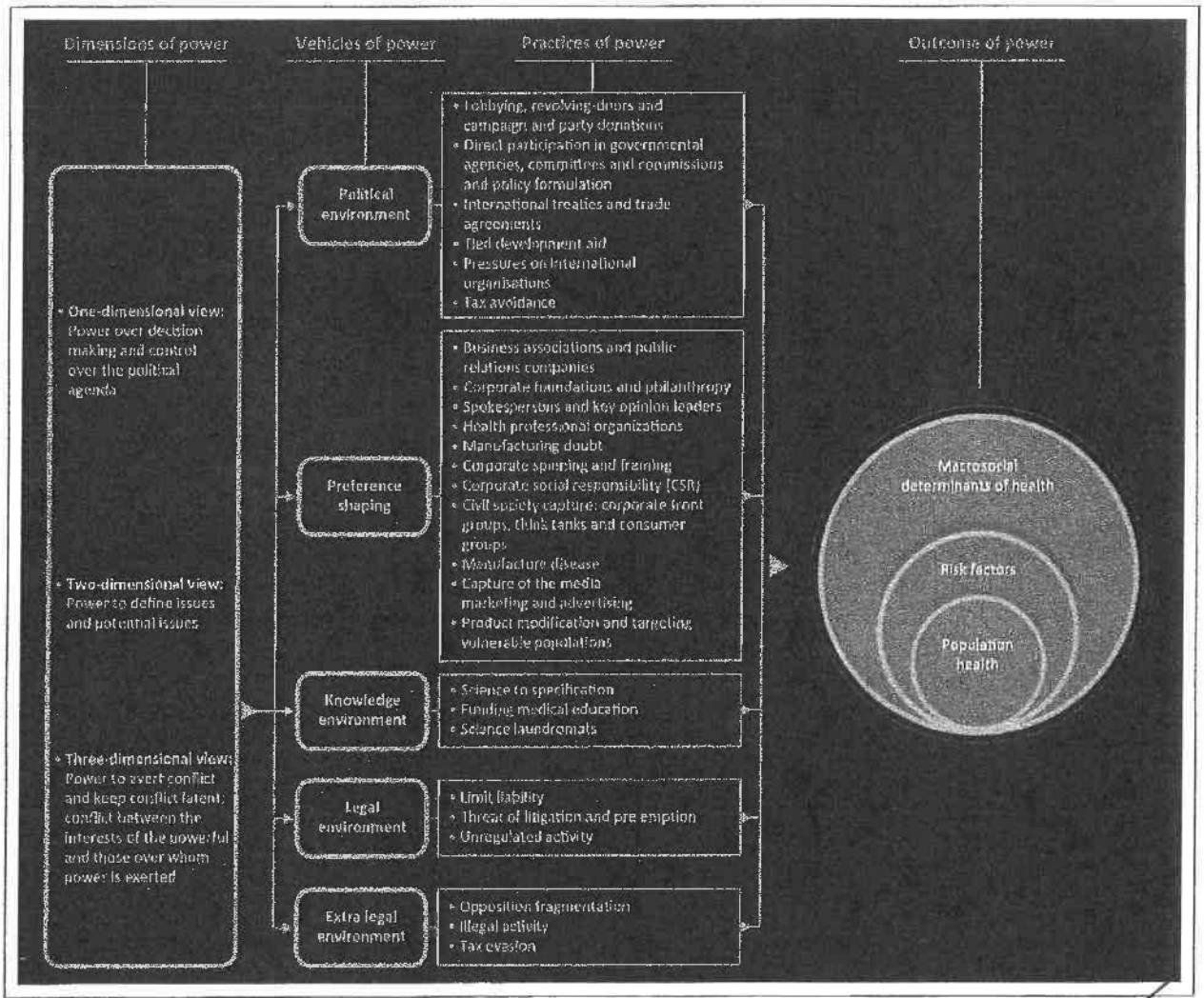
On its website the MHRA declares that the majority of its funding comes from the pharmaceutical industry and £3 million (UK pounds) from the Bill and Melinda Gates Foundation (BMGF). Are policymakers and the public aware that the foundation's corporate stock endowment is heavily invested in food (including McDonald's and Coca-Cola) and pharmaceutical companies, directly and indirectly? As pointed out in a 2009 *Lancet* paper, the funders' priorities are often driven by personal interests, not the health priority interests of the recipient country.[44] 'The BMGF's portfolio of pharmaceutical companies calls for attention given Mr Gates' personal belief in the role of patents as motors for innovation in medicines and medical technology'.[45]

Obesity researcher Dr Zoe Harcombe has also investigated the financial ties that could potentially be biasing the view of the joint committee for vaccines and immunisation and discovered that the subcommittee members work for organisations that receive in total $1bn from the BMGF.[46] It is

also worth noting that Professor Wei Shen Lim, chairman of the JCVI vaccine subcommittee, has direct responsibility for material levels of funding received by his department from Pfizer.[42] This is not in any way suggesting that the JCVI have acted in an improper way, but when confidence in an organisation such as the JCVI is imperative it's essential that there should be no perceptions of conflicts of interest. The systems of selection of panellists, the scrutiny of evidence and the methodology and openness of their recommendations need to be beyond reproach.

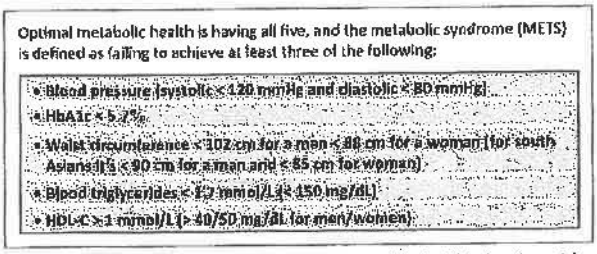
The most proximate cause of detrimental health outcomes: Corporate power and the commercial determinants of health

The commercial determinants of health are best defined by 'strategies and approaches adopted by the private sector to promote products and choices that are detrimental to health'.[38] Corporations exert their power by a combination of factors including intellectual exploitation. This includes the ability to define the dominant narrative: set the rules and procedures by which society is governed; determine the rights, living and working conditions of ordinary people; and take ownership of knowledge and ideas[39] (see Figure 1[45]). It appears that in the case of the mRNA vaccine, Pfizer has at least to some degree taken advantage of this corporate framework strategy by shaping the knowledge environment (Pfizer was responsible for the design and conduct of the trial, data collection, data analysis, data interpretation and the writing of the manuscript), the political environment (lobbying), preference shaping (corporate foundations and philanthropy, spokespersons and key opinion leaders, capture of the media), the legal environment (limit liability) and the extra-legal environment (opposition fragmentation by de-platforming critics of the current dominant narrative that the vaccine is safe and effective).[43] Consequently, it has made tens of billions of dollars in revenue from a product that in comparison with time-tested traditional vaccines and most other drugs has extremely poor efficacy and unprecedented reports of serious harms.



Source: Madureira Lima J, Galea S. Corporate practices and health: A framework and mechanisms. Global Health. 2018;14(1):21

FIGURE 1: Diagram of dimensions, vehicles, practices and outcomes of power.



Source: Araujo J, Cai J, Stevens J. Prevalence of optimal metabolic health in American adults: National Health and Nutrition Examination Survey 2009–2016. Metab Syndr Relat Disord. 2019;17(1):46–52. https://doi.org/10.1089/met.2018.0105

HDL-C, high density lipoprotein cholesterol.

FIGURE 2: Markers of metabolic health.

Biased reporting in the media and censorship of legitimate scientific debate

Corporations are able to shape preferences and frame the dominant narratives on the determinants of health, through unchecked invisible power. One pathway is through the ownership of mass media. The global media market is dominated by seven corporations and chains that own 80% of the newspapers in the US.[50] The grants paid to global media companies by the BMGF are notable – for example, The Guardian Media Group has been in receipt of over $12m in grants from the BMGF over the last 12 years. Control over advertising in print and broadcast media also has an influence over editorial decisions. Most health journalists (including a number I have spoken to) are generally unaware that the information they obtain for stories has been deliberately shaped by the private interests of manufacturers and 'research' universities.

The BBC, though seemingly not directly influenced by industry interests, has traditionally been seen by some as the UK's most trusted media source. Its coverage of issues surrounding COVID-19 has in my view (possibly through additional government pressure) been extremely poor and – specifically on issues surrounding the vaccine – grossly negligent. During a recent report on tennis player Novak Djokovic explaining his decision to not take the vaccine until he has more information on its benefits and harms, a reporter asked the question 'how much more information does he need?'. The reporter failed to mention the fact that Djokovic has had COVID-19 and that evidence suggests that natural immunity offers *significant* protection against reinfection and severe disease, and that systemic side effects are almost threefold more likely in those with natural immunity who subsequently get vaccinated. Furthermore, the BBC falsely framed a guest on popular podcast host Joe Rogan, Dr Robert Malone, as a 'known anti-vaxxer, who is against vaccinating kids', failing to mention that Dr Malone is a co-inventor of the very technology that led to the vaccine, has spent 20 years in vaccine development at US government level and was one the first to actually receive two shots of the Moderna jab. The BBC also strangely failed to cover perhaps one of the most significant stories of the pandemic published in one of the most respected and influential medical journals in the world: An investigation by the *BMJ* revealed evidence of poor practices at a contract research company involved in Pfizer's pivotal COVID-19 vaccine trial. A regional director employed at one of the trial sites in Texas, US, documented evidence that Pfizer falsified data, unblinded patients, employed inadequately controlled vaccinators and was slow to follow up on adverse events. The very same day that she emailed her complaint to the FDA she was fired from her position.[51] She subsequently commenced litigation under whistle-blower legislation for fraud against Pfizer on behalf of the American Government (and the people of the US). Pfizer's motion to dismiss the case (which apparently did not sway the judge) was based on the fact that the FDA had not acted on her (or any other) complaints, hence the allegations were not material to the Government.

In the US, Senator Ron Johnson, who conducted hearings with healthcare professionals who were presenting data on clear, substantial and very common adverse effects from the mRNA jabs, which deserved widespread public attention, said 'the mainstream media are co-conspirators in this political dirty trick. Will they be held accountable for their role in this deception'?[52]

Social media platforms continue to be guilty of spreading misinformation. Their business model that focusses on increasing engagement at any cost makes society increasingly lose access to the truth and worsens our capacity for empathy as individuals, sowing even greater division and hostility. The so-called 'fact checkers' have censored anything that challenges the prevailing mainstream narrative (the establishment is trustworthy, and the vaccines are completely safe). They even labelled the *BMJ*'s investigation into potential fraud in Pfizer's pivotal trial as misinformation and stopped users sharing the story on their platform. A letter from the journal's current and former editor in chief to Mark Zuckerberg calls into question the integrity of Facebook's fact checkers:

> [R]ather than investing a proportion of Meta's substantial profits to help ensure the accuracy of medical information shared through social media, you apparently delegated responsibility to people incompetent in carrying out this crucial task.[53] (p. 1)

It has also come to light that Facebook has partnered with drug company Merck in deciding what content should be censored on its platform in relation to COVID-19 and the vaccine.[54] Is Facebook aware that Merck paid one of the largest fines in US history for being found guilty of fraud in relation to their pain killer Vioxx?[55] Not only did an investigation reveal that the drug did not reduce gastric bleeds (their original key selling point) in comparison with ibuprofen, but it significantly increased the risk of heart attacks and strokes, estimated to have caused excess deaths of between 40 000 and 60000 Americans over a 5-year period.[56]

Improving metabolic health

Failure of public health messaging and policies to help individuals to improve their lifestyles during the pandemic represents a missed opportunity to mitigate harms from respiratory diseases such as COVID-19. After age, the biggest risk factor for worse COVID-19 outcomes has been obesity and

conditions related to excess body fat. More than 90% of the deaths from COVID-19 occurred in countries where more than 50% of the population is overweight or obese. The United Kingdom's biobank data during the first wave revealed a more than fourfold higher risk in hospitalisation from COVID-19 depending on lifestyle factors. For example, a non-smoking adult in their mid-fifties with a normal body mass index (BMI) and obtaining adequate physical activity levels had a 1 in 1521 chance of being admitted to hospital after contracting COVID-19, whereas an obese, smoking, sedentary person's risk was 1 in 327.[57]

Postulated pathophysiological mechanisms of risk and complications from infection include an array of markers that have insulin resistance and chronic inflammation at the root.

Even a single high blood glucose reading in non-diabetics (a marker of insulin resistance) admitted to hospital has been shown to be associated with worse outcomes.[58] It has also recently emerged in the UK that of the 175 256 deaths associated with COVID-19 (2020–2021 inclusive) less than 10% (17 371) had COVID-19 as the only cause on the death certificate suggesting that the risk to those individuals with optimal metabolic health from COVID-19 (Figure 2[59]) was significantly smaller, as per the results of the aforementioned UK biobank study.[60]

The government and medical authorities should have made it a priority to emphasise the importance of eliminating ultra-processed foods and low-quality carbohydrates to reduce risk. They could have made the public aware that reversal of metabolic syndrome has been shown to occur in up to 50% of patients – independent of weight loss – within four weeks of dietary changes alone.[61]

The coronavirus disease 2019 was a momentary crisis that exploited a slow pandemic of poor metabolic health (see Figure 2[59]), which is also the predominant root cause behind the major chronic diseases that have been putting healthcare systems around the world under increasing strain for decades. It is estimated that healthier lifestyles would (in absolute terms) *potentially* eliminate 40% of cancers and 75% of cardiovascular disease and type 2 diabetes.[63]

Optimising metabolic health would not just improve immune resilience but also reduce the burden of heart disease, type 2 diabetes, cancer and dementia. Learning lessons from tobacco control, policy changes that target the availability, acceptability and affordability of ultra-processed food and drink and low-quality carbohydrates would significantly reduce the burden of obesity, related metabolic diseases and likely optimise immune resilience in populations within a few years (see Box 3[62]).

The solutions

There was never any evidence justifying any COVID-19 vaccine mandates, passports or any of the other coercive measures adopted by various governments worldwide. Every patient who was offered any COVID-19 vaccine should have been made aware of what their risk from COVID-19 is according to age and risk factors. In keeping with ethical medical practice, doctors should have informed patients of their absolute risk reduction for infection from previous more lethal variant being approximately 0.84% or 1 in 119 (based on non-transparent data) and that this level of protection only lasts for a few months. They should also have provided more precise and robust data on what the actual absolute individual risk reduction of COVID-19 death from the vaccine is, what the true rates of serious adverse events (such as permanent disability, hospitalisation or death) are.

BOX 3: Policies to curb obesity and lifestyle-related disease.

1. Taxation of all ultra-processed foods and drinks needs to be enforced with the money gained going directly to subsidise whole and minimally processed foods such as fruit and vegetables
2. All medical students and doctors need to have adequate training in nutrition and lifestyle medicine
3. Every doctor should be measuring the metabolic health of their patients and making lifestyle prescriptions specifically linked to diet, physical activity and stress reduction to improve those health markers as their first-line intervention before the use of medication
4. Compulsory nutrition education and cooking skills introduced into all school curriculums
5. All hospital chief executives need to be made accountable for allowing the sale of ultra-processed food on hospital grounds, as it continues to harm the health of staff and patients and legitimises the acceptability of such food consumption to the wider public
6. A ban on advertising of all ultra-processed food and drink on television and online demand services
7. A public education campaign is needed to help consumers understand what ultra-processed food is and the harm it causes
8. A complete ban and dissociation of ultra-processed food and drink sponsorship of sports teams and sporting events
9. Local authorities should encourage active travel and protect and increase green spaces in urban areas to make the healthy option the easy option
10. Medical staff, including doctors, nurses and dietitians, should themselves be assessed on their metabolic health and encouraged and helped to improve it, not just to set an example to patients but to optimise their own health and performance.

Source: Malhotra A. The 21-day immunity plan. United Kingdom: Yellow Kite; 2021.

BOX 4: Defining real evidence-based medicine and actions to deliver it.

1. Is the application of individual clinical expertise with best available evidence and taking into consideration patient preferences and values in order to improve patient outcomes (relieve suffering and pain, treat illness and address risks to health)
2. Makes the ethical care of the patient it's top priority
3. Demands individualised evidence in a format that clinicians and patients can understand
4. Is characterised by expert judgement rather than mechanical rule following
5. Shares decisions with patients through meaningful conversations
6. Builds on a strong clinician–patient relationship and the human aspect of care
7. Applies these principles at community level for evidence-based public health

Actions to deliver real evidence-based medicine

1. Although the pharmaceutical industry plays an important role in developing new drugs, they should play no role in testing them
2. All results of all trials that involve humans must be made publicly available
3. Regulators such as the FDA and MHRA must be publicly funded, and not receive any money from the pharmaceutical industry
4. Independent researchers must increasingly shape the production, synthesis and dissemination of high-quality clinical and public health evidence
5. Medical education should not be funded or sponsored by the pharmaceutical industry
6. Patients must demand better evidence, better presented (using absolute and not relative risk), better explained and applied in a more personalised way

Source: Adapted from Greenhalgh T, Howick J, Maskrey N. Evidence based medicine Renaissance Group. Evidence based medicine: A movement in crisis? *BMJ*. 2014;348:g3725. https://doi.org/10.1136/bmj.g3725

It is only when doctors and patients have all this information that they can then be empowered to have frank decision making conversations on whether any treatment – including this vaccine – is right for them.

The profession must explain that optimising metabolic health will give patients the best chance for ensuring they are not just resilient to infection but reducing their risk of chronic disease including heart disease, cancer and dementia.

The time has come to stop misleading evidence flowing downstream into media reporting and clinical decision making and resulting in unethical and unscientific policy decisions. It's time for real evidence-based medicine (Box 4[44]).

There is also a strong scientific, ethical and moral case to be made that the current mRNA vaccine administration must stop until Pfizer releases all the raw data for independent scrutiny.[30] This will allow a more accurate understanding of which groups are more likely to potentially benefit from the vaccine versus those who are more likely to be harmed.

Given all the recent well-documented aforementioned shortcomings in medical research integrity (including that possibly half the published medical literature 'may simply be untrue'), the editor of the *Lancet* Richard Horton wrote in 2015 that science has taken a turn towards darkness and asked who was going to take the first step in cleaning up the system.[65] The unprecedented roll-out of an emergency use authorisation vaccine without access to the raw data, with increasing evidence of significant harms, compounded by mandates that appear to serve no purpose other than to bolster profits of the drug industry, have highlighted modern medicine's worst failings on an epic scale, with additional catastrophic harms to trust in public health.

We must use this as an opportunity to transform the system to produce better doctors, better decision making, healthier patients and restore trust in medicine and public health. Until all the raw data on the mRNA COVID-19 vaccines have been independently analysed, any claims purporting that they confer a net benefit to humankind cannot be considered to be evidence-based.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Author's contribution

A.M. is the sole author of this article.

Ethical considerations

This article followed all ethical standards for research without direct contact with human or animal subjects.

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Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Disclaimer

The views and opinions expressed in this article are those of the author and do not necessarily reflect the official policy or position of any affiliated agency of the author.

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"HE13"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF HEALTH	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: LIMPOPO DEPARTMENT OF HEALTH	Twelfth Respondent

SJS

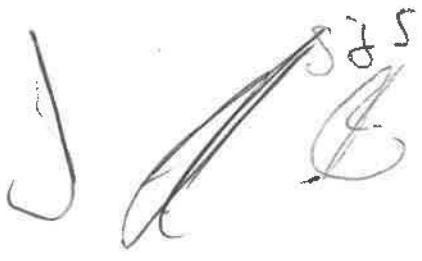
MPUMALANGA DEPARTMENT OF HEALTH	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: MPUMALANGA DEPARTMENT OF HEALTH	Fourteenth Respondent
NORTHERN CAPE DEPARTMENT OF HEALTH	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTHERN CAPE DEPARTMENT OF HEALTH	Sixteenth Respondent
NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

CONFIRMATORY AND SUPPORTING AFFIDAVIT

I, the undersigned

DR STEPHEN SCHMIDT

do hereby make oath and state that:-



1. I am an adult male specialist physician and gastroenterologist, and an expert drug trialist, domiciled at 77 Linkside, Mosselbay, 6500.

2. The facts in this affidavit are, to the best of my knowledge, both true and correct, and, unless the contrary appears from the context of this document, they fall within my personal knowledge.

3. I am a specialist physician and gastroenterologist, and an expert drug trialist. I have been involved in drug trials for over thirty (30) years and have completed trials for the following manufacturing companies: Pfizer, Astra Zeneca, Janssen Cilag, Novavax, Gilead, Johnson and Johnson, Glaxo Smith, Adcock-Ingram, and the US Defence Force. I hold an MBChB and MMed(Int) from the University of Stellenbosch. From 1990 to 2022 I was part of, or was the responsible principal investigator in, fifty-seven (57) clinical drug trials. My experience as a training trialist and eventual Principal Investigator taught me every skill needed to conduct clinical trials, including the complete administrative management of the trial site, logistics, pharmacy control, dispensing and drug accountability, blood and tissue sampling and shipping, writing of- and updating 72 standard operative procedures detailing every action at the trial site, assessing and understanding novel drug protocols, continuous training of staff and refresher courses in Good Clinical Practice every 2 years, attending international trial commencement meetings, receiving clinical trial monitors and auditors, assessing and management of adverse events of any type, acting as first responder to safety signals observed at the site. I acted as national investigator in several studies and was audited by sponsors' auditors, CRO auditors, the Medical Control Council, SAHPRA and the FDA. Neither of my trial sites ever received a negative audit report. My conduct as

a Principal Investigator was based on the ethical principles of national and international institutions. I conducted my trial work in South Africa following the strict ethical guidelines of SA-GCP (South African Good Clinical Practice), the DOH research guidelines and the Constitution of South Africa. My full curriculum vitae is annexed as "**SS1**".

4. I have read the founding affidavit deposed to by Dr Herman Edeling. In his affidavit, Dr Edeling makes three references to me, my expertise and my conclusions. I confirm the content and correctness of those references. Specifically, I confirm that:

   4.1. The Pfizer trial design was flawed from commencement. The problem is that the trial compared the vaccine arm (injected with the vaccine candidate, BNT162b2) to a saline placebo. The trial should have compared the vaccine intervention to, at the very least, other interventions against Covid-19 and/or natural immunity – not a saline placebo. But, as set out in the Pfizer trial protocol, they didn't do this. Instead, trial subjects who had been treated with medicines intended to prevent infection, and those with previous exposure to Covid-19 (and who therefore had natural immunity) were excluded.

   4.2. There are multiple reasons why the vaccine arm should have been compared to other interventions against Covid-19 and/or natural immunity instead of a saline placebo:

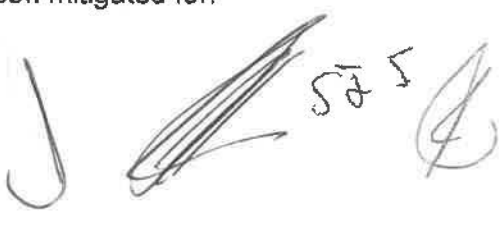
      4.2.1. First, it is the only way to preserve equipoise. Equipoise is a concept in clinical research that refers to a state of genuine uncertainty about the

relative effectiveness and safety of two or more interventions being compared in a clinical trial. In other words, equipoise is a state of genuine uncertainty that exists in the minds of researchers as to which of the interventions being compared is better, or whether there is no difference between them.

4.2.2. This state of uncertainty is important because it helps to ensure that the clinical trial is conducted in an ethical manner. If researchers have a clear preference for one intervention over another, or believe that one intervention is clearly superior, then it may not be ethical to subject some patients to the inferior intervention.

4.2.3. By maintaining equipoise, researchers can ensure that patients are randomized to different interventions in a fair and unbiased manner, and that the results of the trial will provide reliable information about the relative effectiveness and safety of the interventions being compared.

4.2.4. The problem is this: when equipoise is not maintained because the researchers believe that one product will be more efficacious/safe than the other, it can bias not only the collection of trial data but the analysis thereof. In the Pfizer trial, equipoise did not exist. The mere fact that the vaccine arm was trialled against a saline placebo meant that those conducting the trial commenced the trial with the bias that the vaccine would be more effective than the saline placebo. Had they used alternative Covid-19 treatments or natural immunity, they would not have had that certainty, and the bias would have been mitigated for.



4.2.5. Second, testing the vaccine arm against the saline placebo artificially inflated the efficacy profile. Obviously, a vaccine candidate appears highly effective when compared to nothing (saline placebo). The efficacy profiles would likely have been substantially lower if compared to other interventions or natural immunity.

4.2.6. Third, it is unethical in the midst of a global pandemic to give some patients a saline placebo if there is a known effective treatment available. In my view, it was unethical to withhold this standard of care from the control group. It seems as though this ethical violation was countenanced in pursuit of Pfizer's own ends – to artificially inflate the efficacy profiles.

4.2.7. Fourth, the saline placebo may not have accurately reflected the natural course of the disease or the effects of the experimental treatment. Comparing the experimental vaccine treatment to a natural immunity or another type of medication was more likely to provide a realistic and informative comparison.

4.3.I also confirm Dr Edeling's reasoning in his affidavit as it pertains to the unblinding and the cross-over.

4.3.1. In any phase three clinical randomised controlled trial (RCT), which is what the Pfizer trial purported to be, there must be an inoculated group

of trial subjects and an equivalent placebo group. Those groups must subsist until the end of the trial. It is the long-term comparison of the efficacy and safety profiles between the vaccinated trial arm and the placebo trial arm which allows for a proper assessment as to whether the product (in this case, Comirnaty) has acceptable efficacy and safety profiles. Without this data it is impossible to assess long term efficacy or safety.

4.3.2. Usually, vaccine trials are run for a period of ten to fifteen years. This time, because of the exigencies of the situation, the trial period was severely truncated to three years, due to terminate sometime in 2023. The vaccine arm and placebo arm should have been maintained until the culmination of the trial in order to secure decent efficacy and safety data sets.

4.3.3. But Pfizer sabotaged the entire comparative data collection process, thereby invalidating their trial.

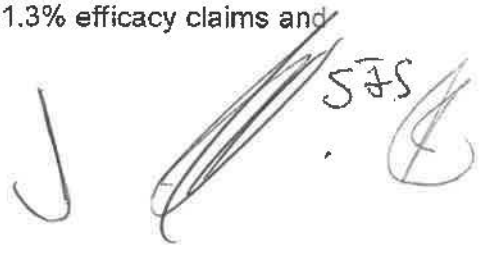
4.3.4. After only 2 months, the trial groups were unblinded. "Unblinding" is a term used in the context of clinical trials to refer to the process of revealing the group assignment of a participant in a study – in other words, telling trial subjects whether they were part of the vaccine arm, or the placebo arm of the study. Following the unblinding, those in the placebo group were offered the vaccine.

4.3.5. As set out in Dr Edeling's affidavit, 88.8% of the trial subjects in the placebo group elected to take the vaccine and crossed over.

4.3.6. An 88.8% crossover is a calamity. It effectively annihilates any prosect of collecting reliable long-term efficacy and safety data about the vaccines. In all my years of conducting clinical trials, I have never seen an unblinding and cross-over of virtually the entire control group. In my view, the only plausible explanation is that Pfizer wanted to destroy the control group and the long-term collection of safety and efficacy data. Whether their motivation for this was to conceal what they knew would be problematic outcomes, I cannot say.

4.4. Lastly I confirm that a serious issue of concern in the Pfizer trial related to the conveniently and selectively chosen study population itself, and the blanket vaccine efficacy and safety claims made in the published summary of the trial data. In trials that test for efficacy, it is only possible to make efficacy claims for the population demographics and other circumstances that applied in the trial. For example, if you're trialing medicine X, and you test it in adults in the trial, you cannot then claim efficacy or safety for children. The reasons are self-evident.

4.5. In this trial, adolescents below the age of 16 years were excluded from the initial trial, pregnant women and women who were breastfeeding were excluded, and those who were sick with underlying health conditions were also excluded. The candidate vaccine intervention was only trialed on healthy individuals over the age of 16. The supposed 95%/91.3% efficacy claims and



the so-called favourbale safety profiles (which I dispute for all the reasons set out in Dr Edeling's affidavit) should have been limited to the population demographics in which the medicine was trialed (healthy individuals over the age of 16) – but instead it was marketed by Pfizer, regulatory authorities and governments as being safe and effective for all cohorts, including those in which it was never tested. Not only is this unethical but it is severely scientifically flawed.

Schmidt

DR STEPHEN SCHMIDT

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me at Mossel Bay on this the 18th day of March 2023, the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

COMMISSIONER OF OATHS

Name:

Address:

Position:

JOHAN CILLIERS
COMMISSIONER OF OATHS
Practising Attorney in the Republic of South Africa
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SJS

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Pr Nr: 1900366

CURRICULUM VITAE

Dr Stephen John Schmidt

PERSONAL DETAIL

Title	Dr
Initials	SJ
Full Name	Stephen John
Surname	Schmidt
Date of Birth	13 September 1959
Nationality	South African
HPCSA Nr	MP0289450
Malpractice Insurance	Medical Protection Society Member Nr: 03/27947
Professional Body Membership	HPCS, SAGES, SAVIMS
Physical address	77 Rodger Street, Mossel Bay 6500, Western Cape, South Africa
Postal Address	77 Rodger Street, Mossel Bay 6500, Western Cape, South Africa
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Mobile Number	+27 82 7729228
e-mail	stephen@endocare.co.za
Website	www.endocare.co.za

SJS

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QUALIFICATIONS

Academic and Professional Qualifications	Year
MBChB. University of Stellenbosch	1984
MMed (Int). University of Stellenbosch	1995
Registered Gastroenterologist. University of Stellenbosch	1999

WORK EXPERIENCE AND CURRENT POSITION

Internship: Kimberley Hospital	1985
South African Defense Force: Rank Captain	1986 - 1988
Medical Officer Emergency Unit: Somerset Hospital	1989 - 1990
Registrar in training: Internal Medicine: Tygerberg Hospital and University of Stellenbosch	1990 - 1994
Consulting in training Department of Gastroenterology: Tygerberg Hospital and University of Stellenbosch	1995 - 1999
Consultant in General medicine and Gastroenterology: Tygerberg Hospital and University of Stellenbosch	1997 - 1999
Founder and principal Investigator: Quatro Clinical Trial Institute	2000 - 2009
Specialist Physician and Principal Investigator in private practice	2000 - 2022
Managing Director and Principal Investigator Endocare Clinics	2009 – 2022

CURRENT POSITION

CEO Endocare Clinics Pty Ltd: Integrative Health Initiatives and alternate Therapeutics

Icanfunction Health: Consulting Physician and member of management team

e-mail: stephen@endocare.co.za website: www.endocare.co.za mobile:0827729228

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TEACHING AND COURSES

Lecturer undergraduate medicine: Medical School University of Stellenbosch	1991- 1999
Continuing Medical education (GUT CLUB) to general practitioners	2000 - 2020
Pharmacy course: Dispensing License	2000-2002
International Training course Small Bowel endoscopy: GIVEN	2002
Certificate Course in Metabolic Diseases: Nutritional Network: Prof Tim Noakes	2019

SKILLS

CLINICAL

During training as a specialist physician, I rotated through the intensive care units and departments of Cardiology, Nephrology, Pulmonology, Neurology, Endocrinology, Psychiatry, Internal Medicine, Occupational Medicine.

In the period from 1995 to 2022 I specialized in practice as a Gastroenterologist and specialist Physician with special interest and expertise in stomach diseases, hepatology, small bowel diseases and colon diseases. I developed a special interest in metabolic syndrome, Diabetes and fatty liver disease applying innovative and novel concepts in life-style management to reverse chronic disease. I performed > 15000 endoscopies of the upper digestive tract, the colon and was an expert in assessing the small bowel with capsule endoscopy.

RESEARCH

I am a expert drug trialist. I started my training in 1990 at the University of Stellenbosch Medical School and Tygerberg Hospital. My mentors were the late Prof's Frans Maritz and Steven Hough, both Endocrinologist and Lipidologists. I trained as a trialist by performing all aspects of trial work.

1990 – 1999: Junior study coordinator, senior study coordinator, administrative clerk, data capturer, therapeutic pharmacist, intensive care pharmacist and sub-investigator.

I started Quatro Clinical trial Institute in 2000 and performed the duties of Principal Investigator from 2000 – 2009. In 2009 I founded Endocare Clinics as the Principal Investigator with a staff of 10 employees. From 1990 to 2022 I was part of or was the responsible principal investigator in 57 clinical drug trials. My experience as a training trialist and eventual Principal Investigator taught me every skill needed to conduct clinical trials. This entails the complete administrative management of the trial site, logistics, pharmacy control, dispensing and drug accountability, blood and tissue sampling and shipping, writing of- and updating 72 standard operative procedures detailing every action at the trial site, assessing and understanding novel drug protocols, continuous training to staff and refresher courses in

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Good Clinical Practice every 2 years, attending international trial commencement meetings, receiving clinical trial monitors and auditors, assessing and management of adverse events of any type, acting as first responder to safety signals observed at the site. I acted as national investigator in several studies and I was audited by sponsors auditors, CRO auditors, the Medical Control Council, SAHPRA and the FDA. Neither of my trial sites ever received a negative audit report.

My conduct as a Principal Investigator was based on national and international ethical bodies and principles. I conducted my trial work in South Africa following the strict ethical guidelines of SA-GCP, the DOH research guidelines and the Constitution of South Africa.

PARTICIPATION IN CLINICAL TRIALS:

GASTROENTEROLOGY

- An open label access trial to document the humanitarian use of oral R1 08512 1 to 4 mg in subjects with chronic constipation.
- A double- blind placebo- controlled dose-finding trial to evaluate the efficacy and safety of R149524 in diabetic subjects with symptoms of gastroparesis.
- An open label access trial to document the humanitarian use of oral R 08512 1 to 4 mg in subjects with chronic constipation.
- Maintenance treatment of patients with healed oesophagitis, comparing the remission rates during 6 months with esomeprazole 20 mg q.i.d. – a randomized, double- blind, multi centre study (METROPOLE)
- On demand versus continuous treatment of endoscopy negative subjects with gastroesophageal reflux disease (GERD) with esomeprazole 20mg O>D> over a 6-months long term treatment phase. An open, randomized, multi-center study (NEED)
- Efficacy of esomeprazole 40 mg once daily versus placebo and esomeprazole 20 mg daily versus placebo in treatment for relief of upper gastrointestinal symptoms associated with continuous use of NSAIDS including COX-2 selective NSAIDS (SPACE)
- Efficacy of esomeprazole 40 mg daily versus placebo and esomeprazole 20 mg daily versus placebo in prevention of upper gastrointestinal symptoms associated with continuous use of NSADS including COX-2 selective NSAIDS (SPACE 2)
- A comparative efficacy and safety study of esomeprazole delayed-release capsules (40 mg qd and 20 mg qd) versus placebo for the prevention of gastric ulcers associated with daily NSAID use in patients at risk (PLUTO)

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- A randomized, double-blind, multi-center Phase III study to evaluate safety of esomeprazole 40 mg give IV or orally o.d. for 1 week to subjects with erosive reflux oesophagitis, followed by 3 weeks open oral treatment with esomeprazole 40 mg o.d.

- Healing rates after the administration of 10 mg BY359 o.d. versus 5 mg b.i.d. over 28 days in patients suffering from gastroesophageal reflux disease.

- A Double-Blind, Placebo-Controlled, Randomized, Multinational study to investigate the Safety and Efficacy of 2 mg TID of Cilansetron Over 26 Weeks in Diarrhea-Predominant Irritable Bowel Syndrome Subjects

- An Open-Label, Multi-center study to investigate the safety of 2 mg TID of Cilansetron over one year in Diarrhea-Predominant Irritable Bowel Syndrome Subjects (Protocol nr : S241.3.008)

- Change of health-related quality of life (HRQoL) in patients suffering from endoscopically confirmed reflux oesophagitis after treatment with Pantoprazole 40 mg o.d. over 4 weeks

- PPI Comparator Study to compare the efficacy of healing and maintenance treatment with esomeprazole and pantoprazole in subjects with reflux oesophagitis – a multi-center, randomized, double-blind study (EXPO)

- A Clinical study investigating the effects of treatment with tegaserod in female patients with constipation-predominant irritable bowel syndrome (PHASE 4)

- A Clinical study investigating the effects of treatment with tegaserod in female patients with constipation-predominant irritable bowel syndrome (PHASE 3)

- A Clinical proof of concept study of the efficacy of oral xxxxxxx versus Azathioprine in Crohn's disease

- A Clinical study using a novel anti-TNF treatment in Crohn's disease.

- An eight-week, randomized, double blind Placebo-controlled, dose-ranging study to evaluate efficacy and safety of xxx in subjects with irritable bowel syndrome.

- A Study to assess the safety and maintenance of response of XXXXX versus placebo in patients with active Crohn's disease.

- Patients with mild to moderate ulcerative Colitis.

- The prevention of Ascites Recurrence due to cirrhosis of the liver

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CARDIOLOGY

- A Randomized, double blind study to investigate the safety and clinical efficacy of MK- 383 in patients with unstable angina/non-q-wave myocardial infarction. Protocol 011/097. 1994 – 1995, Principal Investigator
- The continuous infusion versus bolus administration of Alteplase (COBALT) study. Protocol ID 135.70. 1995 – 1996. Principal Investigator
- The Prism Plus Study. 1995 – 1996 Principal Investigator
- Safety assessment of single-bolus administration of TNK0-tissue-plasminogen adtivator in acute myocardial infarction. He assent-1trial. 1996. Principal investigator
- A randomized, double-blind, placebo-controlled trial comparing two drugs in subject with acute ST Elevation Myocardial Infarction (STEMI) treated with Fibrinolytic therapy Principal Investigator

DERMATOLOGY

- A Multi Centre, Double blind, Parallel-group study comparing Mupirocin Ointment 2% and Bactroban ® Ointment (mupirocin Ointment 2%) in the treatment of Impetigo. Principal Investigator
- A Multi-center, double-blind, Parallel-group, Placebo-controlled Study to compare the efficacy and safety of Mupirocin Ointment 2% and Bactroban ® Ointment (Mupirocin Ointment, 2%) in the treatment of Impetigo (MUP-0204) Principal Investigator
- A Randomized, observer-blind, multi-center, non-inferiority, comparative phase III study of the safety and efficacy of topical xxx ointment applied twice a day, for five days, versus topical xxx ointment applied three times daily for 7 days in the treatment of adult and pediatric subjects with Impetigo. Principal Investigator

NEUROLOGY

- A randomized, double-blind, parallel group, dose-response study to evaluate the efficacy and safety of two doses of topiramate compared to placebo and propranolol in the prophylaxis of migraine. Protocol Pri/TopInt47. Principal Investigator
-

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545

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ONGOING RESEARCH / CLINICAL TRIALS:

- Ulcerative Colitis Study: To evaluate Clinical efficacy and safety of induction and maintenance Therapy of BMS 936557
- Preventative RSV disease in infants: Study to determine Immunogenicity and Safety of a RSV vaccine.

Schmidt

Dr SJ Schmidt **Date**

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Exhibit 10.45

Execution Version

THE SYMBOL "[***]" DENOTES PLACES WHERE CERTAIN IDENTIFIED INFORMATION HAS BEEN EXCLUDED FROM THE EXHIBIT BECAUSE IT IS BOTH (i) NOT MATERIAL, AND (ii) WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED

COLLABORATION AGREEMENT

by and between

PFIZER INC.

and

BIONTECH SE

March 17, 2020

TABLE OF CONTENTS

COLLABORATION AGREEMENT

This Collaboration Agreement (the "Agreement") is entered into as of March 17, 2020 (the "Effective Date"), by and between Pfizer Inc., a corporation organized and existing under the laws of Delaware and having a principal place of business at 235 East 42nd Street, New York, New York, 10017 United States ("Pfizer") and BioNTech SE, a corporation organized and existing under the laws of Germany and having a place of business at An der Goldgrube 12, D-55131 Mainz, Germany ("BioNTech"). Pfizer and BioNTech may each be referred to herein individually as a "Party" and collectively as the "Parties".

WHEREAS, BioNTech owns or otherwise Controls (as defined below) certain patents, patent applications, technology, know-how, scientific and technical information and other proprietary rights and information relating to the identification, research and development of Candidates (as defined below) in the Field (as defined below) for delivery via Delivery Technology (as defined below);

WHEREAS, Pfizer has extensive experience and expertise in the development and commercialization of pharmaceutical and biopharmaceutical products;

WHEREAS, in view of the current COVID-19 crisis, Pfizer and BioNTech wish to engage in expedited collaborative research and development pursuant to the Research and Development Plan (as defined below) to identify and develop Candidates for inclusion in the Product, seek expedited regulatory approval for such Product, and launch such Product in all countries of the Territory (as defined below) as quickly as reasonably possible; and

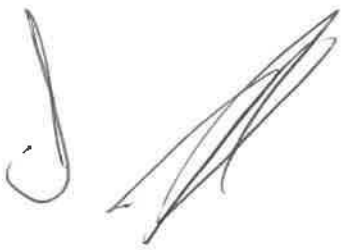
WHEREAS, Pfizer and BioNTech wish that Pfizer Commercializes the Product in all countries of the Territory, subject to BioNTech having the right to exclusively commercialize the Product in the BioNTech Commercialization Territory.

NOW THEREFORE, in consideration of the mutual promises and covenants set forth below and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties hereby agree as follows:

1. DEFINITIONS

As used in this Agreement, the following terms will have the meanings set forth below:

1.1. "Affiliate" means any entity directly or indirectly controlled by, controlling, or under common control with, a Person, but only for so long as such control will continue. For purposes of this definition, "control" (including, with correlative meanings, "controlled by", "controlling" and "under common control with") means (a) possession, direct or indirect, of the power to direct or cause direction of the management or policies of an entity (whether through ownership of securities or other ownership interests, by contract or otherwise), or (b) beneficial ownership of more than 50% of the voting securities or other ownership or general partnership interest (whether directly or pursuant to any option, warrant or other similar arrangement) or other comparable equity interests of an entity; *provided, however*, that where an entity owns a majority of the voting power necessary to elect a majority of the board of directors or other governing board of another entity, but is restricted from electing such majority by contract or otherwise, such entity will not be considered to be in control of such other entity until such time as such restrictions are no longer in effect. Notwithstanding the foregoing, for the purposes of this Agreement, AT Impf GmbH, having its place of business at Rosenheimer Platz 6, 81669 Munich, Germany, and any entity that directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with AT Impf GmbH (other than BioNTech SE or any entity that is directly or indirectly controlled by BioNTech SE) (collectively, the "Impf Group") shall not be considered Affiliates of BioNTech.



1.2. "Anti-Corruption Laws" means all applicable anti-bribery and anti-corruption laws and regulations, including the U.S. Foreign Corrupt Practices Act of 1977, the U.K. Bribery Act 2010, and the local laws and regulations of any countries in which Candidates or Products, payments or services will be provided or procured under or pursuant to this Agreement.

1.3. "Applicable Data Protection Law" means all applicable personal data protection laws, rules and regulations, including the EU General Data Protection Regulation ("GDPR").

1.4. "Bankruptcy Code" means Section 101(35A) of Title 11 of the United States Code, as amended, or such other legislation, Law or code with effect in another jurisdiction to which BioNTech or its Affiliates is subject having equivalent or reasonably similar purpose or provisions to the foregoing.

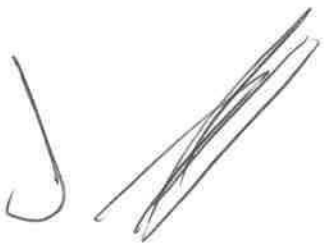
1.5. "Binding Obligation" means, with respect to a Party (a) any oral or written agreement or arrangement that binds or affects such Party's operations or property, including any assignment, license agreement, loan agreement, guaranty, or financing agreement, (b) the provisions of such Party's charter, bylaws or other organizational documents or (c) any order, writ, injunction, decree or judgment of any court or Governmental Authority entered against such Party or by which any of such Party's operations or property are bound.

1.6. "BioNTech Commercialization Territory" means (a) Germany and Turkey, until such time, on a country by country basis, a BioNTech Territory Exit Option is exercised by BioNTech in respect of one or both of those countries; (b) those countries, on a country by country basis, which become Pfizer Exit Countries (if any); and (c) those countries within the Developing Countries Territory for so long as BioNTech or its Affiliate or designee pursuant to the relevant Third Party Funder agreement undertakes Commercialization of the Product in such countries.

1.7. "BioNTech Improvement" means any Research and Development Program Technology, regardless of inventorship, that is a modification or improvement made to the RNA Technology or RNA Process Technology and (a) would also be applicable to one or more candidates or products in addition to or other than the Candidates or Products (b) is not predominantly directed to the Pfizer Technology and (c) could have reasonably been developed without the aid, use or application of Pfizer Materials, Pfizer Improvements or Pfizer's Confidential Information or any improvements or enhancements thereto.

1.8. "BioNTech Know-How" means [***].

1.9. "BioNTech Materials" means any tangible materials (but not information about or contained in such materials) owned or Controlled by BioNTech that relate to or embody the BioNTech Know-How or BioNTech Patent Rights.



1.10. "BioNTech Patent Right" means any Patent Right (other than Pfizer Patent Rights or Patent Rights jointly owned by BioNTech and Pfizer pursuant to Section 10.2) in any form and whether pending or issued that (a) is Controlled by BioNTech or any of its Affiliates as of the Effective Date or comes into the Control of BioNTech or any of its Affiliates during the Term (other than, in either case, through the grant of a license by Pfizer) and (b) claims any BioNTech Know-How.

1.11. "BioNTech Technology" means the BioNTech Patent Rights, BioNTech Materials, BioNTech Know-How. For avoidance of doubt, BioNTech Technology includes all Intellectual Property Rights Controlled by BioNTech pursuant to the Fosun Agreement.

1.12. "BioNTech Territory Exit Option" is defined in Schedule 4.1.

1.13. "BioNTech Third Party Agreement" means any agreement between BioNTech (or any of its Affiliates) and any Third Party (such Third Party, a "Third Party Licensor") that (a) relates to any of the BioNTech Technology or Research and Development Program Technology, or (b) otherwise grants a license or otherwise transfers any right to practice under any Patent Rights or Know-How, in each case that relate to the Candidates or Products or activities under this Agreement. For clarity, all Current Licenses shall be deemed BioNTech Third Party Agreements hereunder and all Current Licensors shall be deemed Third Party Licensors hereunder.

1.14. "Biologics License Application" or "BLA" means an application requesting permission from the FDA to introduce, or deliver for introduction, a biological product into interstate commerce, or any similar application or submission for marketing authorization of a product filed with a Regulatory Authority to obtain Regulatory Approval for such product in a country or group of countries.

1.15. "Biosimilar Notice" means a copy of any application submitted by a Third Party to the FDA under 42 U.S.C. § 262(k) of the Public Health Service Act (or, in the case of a country of the Territory outside the United States, any similar law) for Regulatory Approval of a biopharmaceutical product, which application identifies a Product as the Reference Product with respect to such product, and other information that describes the process or processes used to manufacture the biopharmaceutical product.

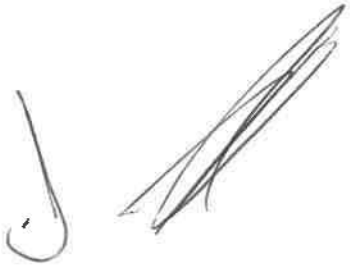
1.16. "Business Day" means a day other than a Saturday, Sunday or bank or other public holiday in New York, New York, USA or Mainz, Germany.

1.17. "Candidate" means an immunogenic composition in the Field that comprises Unmodified RNA Technology, Modified RNA Technology or Replicon Technology that (a) is Developed pursuant to the Research and Development Plan, (b) is Controlled by BioNTech as of the Effective Date or from time to time during the Term or (c) subject to Section 4.1, is Exploited by any of the Parties or their Affiliates pursuant to this Agreement, the Commercialization Terms and the Commercialization Agreement. Those Candidates Controlled by BioNTech and existing as of the Effective Date are set forth in Schedule 1.17.

1.18. "Calendar Quarter" means the respective periods of three consecutive calendar months ending on March 31, June 30, September 30 and December 31.

1.19. "Calendar Year" means any twelve (12) month period beginning on January 1 and ending on the next subsequent December 31.

1.20. "Capex Costs" means any capital expenditure costs associated with (a) the Research and Development Program or (b) the build-out, establishment, construction, expansion or investment in any Manufacturing facilities.



1.21. "Change of Control" means, with respect to a Party (a) the acquisition of beneficial ownership, directly or indirectly, by any Person (other than such Party or an Affiliate of such Party, and other than by virtue of obtaining irrevocable proxies) of securities or other voting interest of such Party representing of the combined voting power of such Party's then outstanding securities or other voting interests, (b) any merger, reorganization, consolidation or business combination involving such Party with a Third Party that results in the holders of beneficial ownership (other than by virtue of obtaining irrevocable proxies) of the voting securities or other voting interests of such Party (or, if applicable, the ultimate parent of such Party) immediately prior to such merger, reorganization, consolidation or business combination ceasing to hold beneficial ownership of at least 50% of the combined voting power of the surviving entity immediately after such merger, reorganization, consolidation or business combination, (c) any sale, lease, exchange, contribution or other transfer (in one transaction or a series of related transactions) of all or substantially all of the assets of such Party to which this Agreement relates, other than a sale or disposition of such assets to an Affiliate of such Party or (d) the approval of any plan or proposal for the liquidation or dissolution of such Party (other than in circumstances where such Party is deemed a Debtor pursuant to Section 13.7).

1.22. "Clinical Trial" means a human clinical study conducted on sufficient numbers of human subjects that is designed to (a) establish that a pharmaceutical product is reasonably safe for continued testing, (b) investigate the safety and efficacy of the pharmaceutical product for its intended use, and to define warnings, precautions and adverse reactions that may be associated with the pharmaceutical product in the dosage range to be prescribed or (c) support Regulatory Approval of such pharmaceutical product or label expansion of such pharmaceutical product. Without limiting the foregoing, Clinical Trial includes any Phase I Clinical Trial, Phase II Clinical Trial, Phase III Clinical Trial or other expedited clinical trial conducted by or on behalf of one or both Parties in connection with this Agreement.

1.23. "Combination Product" means a product comprising a Candidate or Product in combination with one or more other therapeutically active ingredients (which includes any prophylactic activity) that are co-formulated as part of the same dosage form or packaged and administered to patient together. For the avoidance of doubt, adjuvants, including molecular adjuvants, are not considered therapeutically active ingredients for the purposes of this definition regardless of whether or not such adjuvant is packaged together with a Candidate or Product but in a separate container.

1.24. "Commercialization Agreement" means the definitive agreement pursuant to which (i) Pfizer shall be licensed to Commercialize the Product on the Commercialization Terms and (ii) BioNTech shall retain and have rights to Commercialize the Product in the BioNTech Commercialization Territory; such agreement to be entered into between the Parties in accordance with the provisions of Section 4 and Schedule 4.1.

1.25. "Commercialize" or "Commercializing" means to market, promote, distribute, offer for sale, sell, have sold, import, have imported, export, have exported or otherwise commercialize a compound or product. When used as a noun, "Commercialization" and "Commercialized" means any and all activities involved in Commercializing.

1.26. "Commercially Reasonable Efforts" means, with respect to the efforts to be expended by a Party with respect to any objective, those reasonable, good faith efforts to accomplish such objective as such Party would normally use to accomplish a similar objective under similar circumstances, in particular taking into account the then-current urgency of the COVID-19 crisis. With respect to any efforts relating to the Development, Regulatory Approval or Commercialization of a Candidate or Product by a Party, generally or with respect to any particular country in the Territory, a Party will be deemed to have exercised Commercially Reasonable Efforts if such Party has exercised those efforts normally used by such Party having regard to the circumstances, in the relevant country, with respect to a compound or protein, product

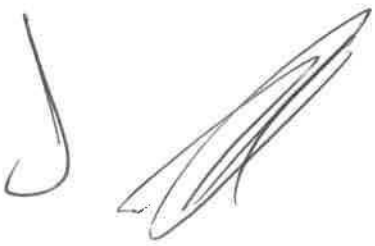
or product candidate, as applicable (a) of similar modality Controlled by such Party, (b) to which such Party has similar rights, (c) which is of similar market potential in such country, and (d) which is at a similar stage in its development or product life cycle, as any Candidate or Product, in each case, taking into account all Relevant Factors in effect at the time such efforts are to be expended. Further, to the extent that the performance of a Party's obligations hereunder is adversely affected by the other Party's failure to perform its obligations hereunder, the impact of such performance failure will be taken into account in determining whether such Party has used its Commercially Reasonable Efforts to perform any such affected obligations.

1.27. "Compassionate Use Purposes" means, with respect to the Product, providing Product under compassionate or emergency use or expanded access programs, including pursuant to an emergency use authorization granted by a Governmental Authority or Regulatory Authority, or in jurisdictions or to vulnerable populations experiencing emergency pandemic, or crisis epidemic, coronavirus conditions.

1.28. "Competitive Product" means a pharmaceutical product that incorporates an immunogenic composition comprising RNA in the Field that is intended to be, has been, or is being Exploited by a Third Party. For avoidance of doubt, Competitive Product does not include Product (a) Commercialized by or on behalf of BioNTech in the BioNTech Commercialization Territory pursuant to this Agreement or the Commercialization Agreement, as applicable; or (b) Commercialized outside of the Territory in accordance with the terms of the Fosun Agreement.

1.29. "Compliance" means the adherence by the Parties in all material respects to all applicable Laws and Party Specific Regulations, in each case with respect to the activities to be conducted under this Agreement.

1.30. "Confidential Information" means, with respect to each Party, all Know-How or other information, including proprietary information and materials (whether or not patentable) regarding or embodying such Party's or its Representatives' technology, products, business information or objectives, that is communicated by or on behalf of the Disclosing Party to the Receiving Party or its permitted recipients, on or after the Effective Date, but only to the extent that: (a) such Know-How or other information in written form is marked in writing as "confidential" at the time of disclosure, (b) such Know-How or other information disclosed orally or in non-tangible form is identified by the Disclosing Party as "confidential" at the time of disclosure or within 30 days thereafter, or (c) such Know-How or other information (regardless of the form of disclosure) is disclosed in circumstances of confidence or would be understood by the Parties, exercising reasonable business judgment, to be confidential. Confidential Information does not include any Know-How or other information to the extent the Receiving Party can demonstrate by competent proof that such Know-How or other information (a) was already known by the Receiving Party (other than under an obligation of confidentiality to the Disclosing Party) at the time of disclosure by or on behalf of the Disclosing Party, (b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party, (c) became generally available to the public or otherwise part of the public domain after its disclosure to the Receiving Party, other than through any act or omission of the Receiving Party in breach of its obligations under this Agreement, (d) was disclosed to the Receiving Party, other than under an obligation of confidentiality, by a Third Party who had no obligation to the Disclosing Party not to disclose such information to the Receiving Party or (e) was independently discovered or developed by or on behalf of the Receiving Party without the use of any Confidential Information belonging to the Disclosing Party. The terms and conditions of this Agreement will be considered Confidential Information of both Parties. Joint Know-How shall be deemed Confidential Information of either Party and either Party shall be deemed the Receiving Party in respect of Joint Know-How.



1.31. "Control" or "Controlled" means with respect to any Intellectual Property Right or material (including any Patent Right, Know-How or other data, information or material), the ability (whether by sole, joint or other ownership interest, license or otherwise, other than pursuant to this Agreement) to, without violating the terms of any agreement with a Third Party, grant a license or sublicense or provide access or other right in as provided in this Agreement, to or under such Intellectual Property Right or material.

1.32. "Conversion Costs" means [***].

1.33. "Copyright" means any copyright which pertains to the promotional materials and literature utilized by Pfizer in connection with the Commercialization of Products in the Territory.

1.34. "Cover", "Covered" or "Covering" means, with respect to (a) a given Candidate or Product and Patent Right, that a valid claim of such Patent Right would, absent a license thereunder or ownership thereof, be infringed by the making, sale, offer for sale or importation of such Candidate or Product and (b) a given Candidate or Product and Know-How, that such Know-How would, absent a license thereunder or ownership thereof, be misappropriated or misused by the use or making of such Candidate or Product.

1.35. "Current Good Manufacturing Practices" or "cGMP" means all applicable standards and applicable Laws relating to manufacturing practices for products (including ingredients, testing, storage, handling, intermediates) promulgated by the U.S. Food and Drug Administration and any other governmental authority (including, European Union or member state level and Japan), including, but not limited to, standards in the form of applicable laws, guidelines, advisory opinions and compliance policy guides, and current interpretations of the applicable authority or agency thereof (as applicable to pharmaceutical and biological products and ingredients), as the same may be updated, supplemented or amended from time to time, in each case of those jurisdictions in which the products are Manufactured.

1.36. "Current Licenses" means any agreement (a) that BioNTech or its Affiliates has entered into prior to the Effective Date with a Third Party and (b) pursuant to which BioNTech or its Affiliates are (i) granted rights to any BioNTech Technology as of the Effective Date or (ii) granted a license or otherwise transferred any right to practice under any Patent Rights or Know-How, in each case that relate to the Candidates or Products or activities under this Agreement. BioNTech's Current Licenses are disclosed on Schedule 1.36.

1.37. "Current Licensor" means any Third Party that is a party to a Current License.

1.38. "Delivery Technology" means the BioNTech Know-How applicable to formulating nucleic acids to enable the delivery of such nucleic acids to target cells *in vivo*. For clarity, Delivery Technology does not include [***].

1.39. "Develop", "Developed" or "Developing" means to discover, research or otherwise develop or improve a process, compound or product, including planning and conducting non-clinical and clinical research and development activities prior to Regulatory Approval or any research or development conducted after receipt of Regulatory Approval, including those required by any Regulatory Authority to maintain any Regulatory Approval. When used as a noun, "Development" means any and all activities involved in Developing.

1.40. "Developing Countries Territory" means, to the extent BioNTech or any of its Affiliates receive Third Party funding from [***] to fund Development or Manufacturing of the Candidates or Products pursuant to this Agreement, those countries listed in Schedule 1.40 which are also defined in the relevant funding documents as "Developing Countries"; *provided* that if prior to the execution of such funding documents, the price of any medicinal product (including the Product) in any country within Schedule 1.40 is made relevant as a reference price for the sale of the Product in any country outside of the countries listed within Schedule 1.40, then such country shall be automatically removed as a country within Schedule 1.40, unless otherwise mutually agreed in writing by the Parties.

1.41. "Development Budget" means the budget to be agreed and updated by the JSC for all activities, costs and expenses that are to be funded as Shared Development Costs, and which initial budget for the first [***] of this Agreement is to be agreed between the Parties in accordance with Section 2.2.

1.42. "EMA" means the European Medicines Agency or any successor agency thereto.

1.43. "Expedited Trial Pathway" means a Clinical Trial protocol or pathway recognized or authorized by any Regulatory Authority for the emergency or expedited approval of medicines for human use, as opposed to a traditional Clinical Trial.

1.44. "Exploit" means to Develop, Manufacture, Commercialize, use or otherwise exploit. Cognates of the word "Exploit" will have correlative meanings.

1.45. "FD&C Act" means the United States Federal Food, Drug, and Cosmetic Act, as amended, and the rules and regulations promulgated thereunder.

1.46. "FDA" means the United States Food and Drug Administration or any successor agency thereto.

1.47. "Field" means immunogenic compositions comprising RNA encoding a SARS-CoV-2 polypeptide or fragment thereof, including naturally occurring or engineered variants thereof, for prophylaxis against COVID-19 in humans.

1.48. "Flu Collaboration License" means the separate research collaboration and license agreement between, inter alia, the Parties for the development and commercialization of immunogenic compositions comprising RNA that encodes at least one Antigen for prophylaxis against influenza in humans dated July 20, 2018, as amended.

1.49. "Fosun" means Shanghai Fosun Pharmaceutical Industrial Development, Co. Ltd, a company incorporated in China, and having a place of business at No. 1289 Yishan Road, Shanghai, China.

1.50. "Fosun Agreement" means the Development and License Agreement concluded between BioNTech and Fosun on March 13, 2020.

1.51. "Funding Event" means (a) the BioNTech Deferred Development Costs have been repaid in full (other than solely through the payment of the Regulatory Approval Milestone in the event that the then-current Development Budget contemplates the expenditure of additional funds for the continued Development of the Product); (b) a Change of Control of BioNTech; or (c) the date notice is served by either Party to terminate this Agreement in accordance with Section 13.

1.52. "Future License" means an agreement approved by the Parties (a) that BioNTech or its Affiliates enters into on or after the Effective Date with a Third Party or (b) that Pfizer or its Affiliates enters into on or after the Effective Date; which in the case of (a) and (b) grants a license (sublicensable in accordance with the licenses granted hereunder) to that Third Party's ("Future Licensor") Patent Rights for the Commercialization of the Candidates or Products by BioNTech and Pfizer in the Field, and which license is applicable to the Candidates or Products and is necessary to avoid, overcome or settle any potential or actual infringement of those Third Party Patent Rights.

1.53. "GAAP" means United States generally accepted accounting principles, consistently applied.

1.54. "GEIA" means the German Employee Invention Act.

1.55. "GEIA Technology" means all BioNTech Technology and Research and Development Program Technology invented by employees of BioNTech or its Affiliates (solely or jointly with employees of Third Parties) under the jurisdiction of GEIA.

1.56. "Government" or "Governmental Authority" is to be broadly interpreted and includes (a) any national, federal, state, local, regional or foreign government, or level, branch, or subdivision thereof; (b) any multinational or public international organization or authority; (c) any ministry, department, bureau, division, authority, agency, commission, or body entitled to exercise any administrative, executive, judicial, legislative, police, regulatory, or taxing authority or power; (d) any court, tribunal, or governmental arbitrator or arbitral body; (e) any government-owned or controlled institution or entity; (f) any enterprise or instrumentality performing a governmental function; and (g) any political party.

1.57. "Government Official", to be broadly interpreted, means (a) any elected or appointed government official (e.g., a member of a ministry of health), (b) any employee or person acting for or on behalf of a government official, Governmental Authority, or other enterprise performing a governmental function, (c) any political party, candidate for public office, officer, employee, or person acting for or on behalf of a political party or candidate for public office, (d) any member of a military or a royal or ruling family, and (e) any employee or person acting for or on behalf of a public international organization (e.g., the United Nations). For clarity, healthcare providers employed by Government-owned or -controlled hospitals, or a person serving on a healthcare committee that advises a Government, will be considered Government Officials.

1.58. "Gross Profit" means [***].

1.59. "GxP" means, collectively, all relevant good practice quality guidelines and regulations, encompassing such internationally recognized standards as Good Manufacturing Practice (GMP), Good Clinical Practice (GCP), Good Laboratory Practice (GLP), Good Distribution Practice (GDP), and Good Review Practice (GRP).

1.60. "HCP" or "Healthcare Professional" includes any physician, nurse, pharmacist, or other person who may administer, prescribe, purchase or recommend pharmaceutical products or other healthcare products.

1.61. "Human Material" means any biological samples of one or more Subjects collected, provided or utilized by BioNTech during the Research and Development Plan pursuant to this Agreement.

1.62. "ICF" means an informed consent form that was approved by a qualified Institutional Review Board or Independent Ethics Committee ("IRB / IEC") in accordance with all applicable Laws and recognized international standards for the protection of human research subjects.

1.63. "IFRS" means International Financing Reporting Standards, as in effect from time to time, together with its pronouncements thereon from time to time, consistently applied.

1.64. "IND" means an Investigational New Drug Application submitted under the FD&C Act, or an analogous application or submission with any analogous agency or Regulatory Authority outside of the United States for the purposes of obtaining permission to conduct Clinical Trials.

1.65. "Intellectual Property Rights" means any and all (a) Patent Rights, (b) proprietary rights in Know-How, including trade secret rights, (c) proprietary rights associated with works of authorship and software, including copyrights, moral rights, and copyrightable works, and all applications, registrations, and renewals relating thereto, and derivative works thereof, (d) other forms of proprietary or intellectual property rights however denominated throughout the world, other than trademarks, service marks, trade names, domain names and other indicators of origin.

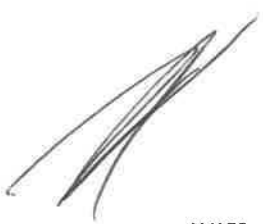
1.66. "Joint Steering Committee" or "JSC" means the steering committee described in Section 7.3.1.

1.67. "Joint Know-How" means any Research and Development Program Know-How, whether or not patentable, made or created jointly by (a) BioNTech or any of its Representatives and (b) Pfizer or any of its Representatives, which does not constitute BioNTech Know-How, Product Know-How or Pfizer Know-How.

1.68. "Joint Patent Rights" means Research and Development Program Patent Rights that claim or disclose any invention included in Joint Know-How.

1.69. "Joint Technology" means the Joint Know-How and the Joint Patent Rights.

1.70. "Know-How" means any proprietary invention, discovery, development, data, information, process, method, technique, technology, result, cell line, cell, antibody or other protein, compound, probe, nucleic acid, (including RNAi) or other sequences or other know-how, whether or not patentable, and any physical embodiments of any of the foregoing or any information contained in any of the foregoing.



1.71. "Law" means any law, statute, rule, regulation, order, judgment or ordinance of any Governmental Authority, including all applicable Anti-Corruption Laws, accounting and recordkeeping laws, and laws relating to interactions with HCPs and Government Officials. For the avoidance of doubt, any specific references to any applicable Law or any portion thereof shall be deemed to include all then-current amendments thereto or any replacement or successor law, statute, standard, ordinance, code, rule, regulation, resolution, promulgation, order, writ, judgment, injunction, decree, stipulation, ruling or determination thereto.

1.72. "MA Holder" means, on a country by country basis within the Territory, the Party (or its Affiliate or designee under its control) that holds the Regulatory Approval required for the Commercialization of the Product in such country.

1.73. "Major EU Market Country" means any of France, Germany, Italy, Spain or the United Kingdom.

1.74. "Major Market Country" means the Major EU Market Countries, the United States and Japan.

1.75. "Manufacture" or "Manufacturing" means to make, produce, manufacture, process, fill, finish, package, label, perform quality assurance testing, release, ship or store, and for the purposes of further Manufacturing, distribute, import or export, a compound or product or any component thereof. When used as a noun, "Manufacture", "Manufactured" or "Manufacturing" means any and all activities involved in Manufacturing a compound or protein, device or product or any component thereof.

1.76. "Manufacturing Costs" means [***].

1.77. "Manufacturing Plan" means the plan for establishing Manufacturing and the Manufacturing facilities, as well as the Manufacturing obligations of each Party, in respect of the Candidates and Products, as such plan may be updated and modified from time to time with the unanimous consent of the JSC, and which initial plan for the first [***] of this Agreement is to be agreed between the Parties in accordance with Section 2.2.

1.78. "Manufacturing Variances" means [***].

1.79. "Materials" means the Pfizer Materials or the BioNTech Materials, as the context requires.

1.80. "Modified RNA" means an mRNA that has been modified by the incorporation of one or more modified nucleosides, excluding the 5' CAP.

1.81. "Modified RNA Technology" means the BioNTech Know-How applicable to Modified RNA. For clarity, Modified RNA Technology does not include [***].

1.82. "Mutation" means [***].

1.83. "Net Sales" means with respect to a Product [***].

[***]

[***]

1.84. "Patent Rights" means any and all (a) issued patents, (b) pending patent applications, including all provisional applications, non-provisional applications, substitutions, continuations, continuations-in-part, divisions and renewals, applications sharing a priority claim and all patents granted thereon, (c) patents-of-addition, reissues, reexaminations and extensions or restorations by existing or future extension or restoration mechanisms, including patent term adjustments, patent term extensions, supplementary protection certificates or the equivalent thereof, (d) inventor's certificates, (e) other forms of government-issued rights substantially similar to any of the foregoing and (f) United States and foreign counterparts of any of the foregoing.

1.85. "Party Specific Regulations" means all non-monetary judgments, decrees, orders or similar decisions issued by any Governmental Authority specific to a Party, and all consent decrees, corporate integrity agreements, or other agreements or undertakings of any kind by a Party with any Governmental Authority, in each case as the same may be in effect from time to time and applicable to a Party's activities contemplated by this Agreement.

1.86. "Person" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, incorporated association, joint venture or similar entity or organization, including a government or political subdivision or department or agency of a government.

1.87. "Personal Data" means any information relating to an identified or identifiable natural person as further specified in Art. 4 no. 1 of the GDPR.

1.88. "Pfizer Commercialization Territory" means the Territory, except for countries within the BioNTech Commercialization Territory from time to time.

1.89. "Pfizer Exit Countries" means, on a country by country basis, those countries out of the United Arab Emirates and South-East Asia where Pfizer elects, pursuant to the Commercialization Terms or Commercialization Agreement, not to Commercialize the Product pursuant to any Pfizer Exit Option.

1.90. "Pfizer Improvements" means any Research and Development Program Technology, regardless of inventorship, that is a modification or improvement to the Pfizer Technology and (a) would also be applicable to one or more candidates or products in addition to or other than the Candidates or Products, (b) is not predominantly directed to the Candidates or Products or the RNA Technology or RNA Process Technology and (c) could have reasonably been developed without the aid, use or application of BioNTech Materials, BioNTech Know-How or BioNTech's Confidential Information or any improvements or enhancements thereto.

1.91. "Pfizer Know-How" means [***]

[***]

1.92. "Pfizer Patent Right" means any Patent Right (other than Patent Rights jointly owned by BioNTech and Pfizer pursuant to Section 10.2) in any form and whether pending or issued that (a) is Controlled by Pfizer or any of its Affiliates on the Effective Date or that comes into the Control of Pfizer or any of its Affiliates during the Term (other than, in either case, through the grant of a license by BioNTech), and (b) claims any Pfizer Know-How.

1.93. "Pfizer Quarter" means each of the four (4) thirteen (13) week periods (a) with respect to the United States, commencing on January 1 of any Pfizer Year and (b) with respect to any country in the Territory other than the United States, commencing on December 1 of any Pfizer Year. Wherever non-country specific timelines are specified in this Agreement in reference to a Pfizer Quarter, such reference shall be deemed to be made to the Pfizer Year applicable in the United States.

1.94. "Pfizer Technology" means the Pfizer Patent Rights, Pfizer Materials and Pfizer Know-How.

1.95. "Pfizer Year" means the twelve (12) month fiscal periods observed by Pfizer (a) commencing on January 1 with respect to the USA; and (b) commencing on December 1 with respect to any country in the Territory other than the USA.

1.96. "Phase I Clinical Trial" means a Clinical Trial that generally provides for the first introduction into humans of a pharmaceutical product with the primary purpose of determining safety, metabolism and pharmacokinetic properties and clinical pharmacology of such product, in a manner that is generally consistent with 21 CFR § 312.21(a), as amended (or its successor regulation), provided, however, a Phase I Clinical Trial does not include any study generally characterized by the FDA as an "exploratory IND study" in CDER's Guidance for Industry, Investigators, and Reviewers Exploratory IND Studies, January 2006, irrespective of whether or not such study is actually performed in the United States or under an IND. A so-called Phase I/II Clinical Trial shall be deemed to be a Phase I Clinical Trial unless such trial, when completed, allows Pfizer to proceed directly to a Phase III Clinical Trial.

1.97. "Phase II Clinical Trial" means a Clinical Trial, the principal purpose of which is to make a preliminary determination as to whether a pharmaceutical product is safe for it intended use and to obtain sufficient information about such product's efficacy, in a manner that is generally consistent with 21 CFR § 312.21(b), as amended (or its successor regulation), to permit the design of further Clinical Trials.

1.98. "Phase III Clinical Trial" means a pivotal Clinical Trial with a defined dose or a set of defined doses of a pharmaceutical product designed to ascertain efficacy and safety of such product, in a manner that is generally consistent with 21 CFR § 312.21(c), as amended (or its successor regulation), for the purpose of enabling the preparation and submission of an NDA.

1.99. "Price Approval" means, in any country where a Governmental Authority authorizes reimbursement for, or approves or determines pricing for, pharmaceutical products, receipt (or, if required to make such authorization, approval or determination effective, publication) of such reimbursement authorization or pricing approval or determination (as the case may be).

1.100. "Product" means any pharmaceutical product in a formulation suitable for administration to humans that [***].

1.101. "Product Know-How" means any Research and Development Program Know-How that is predominantly directed to the composition of matter, treatment with, or the delivery of, Manufacture, form, formulation, or use of a Candidate or Product in the Field and is not generally applicable to compositions or products in addition to or other than a Candidate or Product.

1.102. "Product Materials" means all raw materials (including, without limitation, active pharmaceutical ingredients and excipients, vectors, plasmids and mRNA), labeling or packaging materials and components needed for the Manufacture and supply of a given Candidate or Product.

1.103. "Product Patent Rights" means any Patent Right that claims any invention included in Product Know-How.

1.104. "Product Technology" means the Product Know-How and Product Patent Rights.

1.105. "Public Health Service Act" or "PHS Act" means the United States Public Health Service Act (42 U.S.C. 201 *et seq*), as amended from time to time (including any rules and regulations promulgated thereunder) or any subsequent or superseding law, statute or regulation.

1.106. "RNA" means ribonucleic acid.

1.107. "RNA Process Technology" means the BioNTech Know-How used to Manufacture Candidates or Products.

1.108. "RNA Technology" means Replicon Technology, Unmodified RNA Technology, Modified RNA Technology and Delivery Technology that is, in each case, used by BioNTech in the Research and Development Program

1.109. "Regulatory Approval" means all technical, medical and scientific licenses, registrations, authorizations and approvals (including approvals of INDs, NDAs, BLAs, supplements and amendments, pre- and post- approvals and labeling approvals) of any Regulatory Authority, necessary or useful for the use, Development, Manufacture, and Commercialization of a pharmaceutical or biopharmaceutical product in a regulatory jurisdiction, including commercially reasonable Price Approvals and commercially reasonable Third Party reimbursement approvals.

1.110. "Regulatory Authority" means, with respect to a country in the Territory, any national (e.g., the FDA), supra-national (e.g., the European Commission, the Council of the European Union, or the European Medicines Agency), regional, state or local regulatory agency, department, bureau, commission, council or other Governmental Authority involved in the granting of a Regulatory Approval or, to the extent required in such country, Price Approval, for pharmaceutical products in such country.

1.111. "Relevant Factors" means all relevant factors that may affect the Development, Regulatory Approval or Commercialization of a Candidate or Product, including (as applicable): [***]

[***]

1.112. "Replicon" means an RNA molecule(s) that comprises a gene encoding a polymerase that can, when the RNA molecule(s) is introduced into a cell, replicate the same or a different RNA molecule(s), that also comprises a gene or a sequence encoding at least one non-human polypeptide that is capable of eliciting an immune response (an "Antigen") and does not comprise the full set of genes required to make an infectious virus and is capable, when introduced into a cell, of expressing detectable levels of the encoded Antigen.

1.113. "Replicon Product" means any Product comprising Replicon Technology.

1.114. "Replicon Technology" means the BioNTech Know-How applicable to Replicons. For clarity, Replicon Technology does not include Modified RNA Technology, Unmodified RNA Technology or Delivery Technology.

1.115. "Representatives" means (a) with respect to Pfizer, Pfizer, its Affiliates, its Sublicensees and subcontractors, and each of their respective officers, directors, employees, consultants, contractors and agents and (b) with respect to BioNTech, BioNTech, its Affiliates, its Sublicensees and subcontractors, and each of their respective officers, directors, employees, consultants, contractors and agents.

1.116. "Research and Development Plan" means the research and development plan to define the Development activities pursuant to the collaboration anticipated under this Agreement, which plan is initially to be agreed between the Parties in accordance with Section 2.2 for the first [***] of activities under this Agreement, and as may be amended from time to time pursuant to Section 6.1.

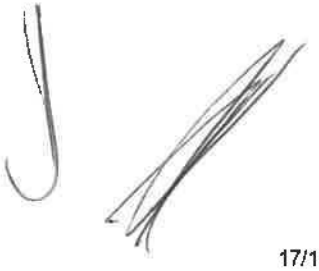
1.117. "Research and Development Program" means the program of collaboration between the Parties to Develop and Manufacture Candidates and Products in the Field, including the activities described in the Research and Development Plan.

1.118. "Research and Development Program Know-How" means any and all Know-How, Candidates and Products, whether or not patentable, made or created solely by or on behalf of either Party or its Representatives in the conduct of activities under the Research and Development Plan or made jointly by or on behalf of (a) BioNTech or its Representatives and (b) Pfizer or its Representatives in the conduct of activities under the Research and Development Plan.

1.119. "Research and Development Program Patent Rights" means any and all Patent Rights claiming or disclosing any invention included in Research and Development Program Know-How.

1.120. "Research and Development Program Technology" means the Research and Development Program Patent Rights and Research and Development Program Know-How.

1.121. "Residual Knowledge" means knowledge, techniques, experience and Know-How that (a) are, or are based on, any Confidential Information of the Disclosing Party and (b) are retained in the unaided memory of any authorized Representative of the Receiving Party after having access to such Confidential Information. An individual's memory will be considered to be unaided if the individual has not intentionally memorized the Confidential Information for the purpose of retaining and subsequently using or disclosing it.



1.122. "Shared Development Cost" means [***].

1.123. "Signing Date" means April 9, 2020.

1.124. "South-East Asia" means [***].

1.125. "Subject" means the individual donor of the Human Material or of the original tissues from which the Human Material was derived.

1.126. "Sublicensee" means any Person to whom a Party grants or has granted, directly or indirectly, a license or sublicense of any of the same Intellectual Property Rights licensed to such Party by the other Party under this Agreement in accordance with Section 3.6. For the avoidance of doubt, distributors used by a Party to Commercialize Product in a country or region shall not be regarded a Sublicensees.

1.127. "Tax" means all corporation tax, advance corporation tax, income tax, capital gains tax, value added tax, customs and other import duties, inheritance tax, purchase tax, capital duties, social insurance contributions, foreign taxation and duties and all penalties, charges and interest relating to any of the foregoing or resulting from a failure to comply with the provisions of any enactment relating to any of the foregoing.

1.128. "Territory" means worldwide, except for the People's Republic of China (including Hong Kong SAR and Macau SAR) and Taiwan.

1.129. "Third Party" means any Person other than Pfizer, BioNTech or their respective Affiliates.

1.130. "Third Party License Payment" shall mean a payment due to a Third Party Licensor or Future Licensor pursuant to a Current License or Future License, as applicable, that is [***]. For the avoidance of doubt, [***]

[***].

1.131. "Trademark" means any trademark, trade name, service mark, service name, brand, domain name, trade dress, logo, slogan or other indicia of origin or ownership, including the goodwill and activities associated with each of the foregoing.

1.132. "Transfer Price" shall mean [***] of the Manufacturing Cost of such Candidate or Product, subject to any different percentage between [***] as determined by the JCC, to be applied for Products to be supplied to the Developing Countries Territory or to take account of any supply requirements of any Governmental Authority within the Territory or pursuant to the terms and conditions of any funding agreement with a Third Party Funder.

1.133. "Unmodified RNA" means an mRNA that [***].

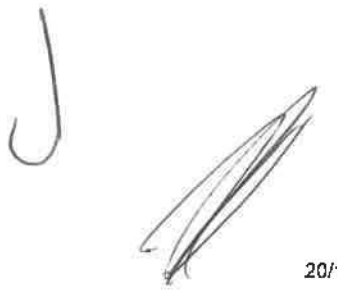
1.134. "Unmodified RNA Technology" means the BioNTech Know-How applicable to Unmodified RNA. For clarity, Unmodified RNA Technology does not include Replicon Technology, Modified RNA Technology or Delivery Technology.

1.135. "UPC Agreement" means the treaty Agreement on the Unified Patent Court signed 19 February 2013, as may be amended or superseded from time.

1.136. The following terms are defined in the section of this Agreement listed opposite each term:

Defined Term	Section in Agreement
Acquirer	14.2.2
Acquisition Program	14.1.1
Additional Patent Jurisdictions	10.3.1.1
Affected Party	14.1
Agreement	Preamble
Alliance Managers	7.1
Audited Party	5.10
Auditing Party	5.10
BARDA	5.5.1
BioNTech	Preamble
BioNTech Deferred Development Costs	5.4.2
BioNTech Enforcement Patent Rights	10.4.2
BioNTech Indemnified Party	15.2
BioNTech JSC Members	7.3.1
BioNTech Prosecution Patent Rights	10.3.1.1
Capex Funding	5.5.1

Defined Term	Section in Agreement
Change of Control Party	11.7
Commercialization Terms	4.1
Consequential Damages	15.1
Competitive Product Infringement	10.4.3
Continuing Party	10.3.2
Cure Plan	3.7.3
Debtor	13.7.1
Declining Party	10.3.2
Disputed Matter	7.3.5
Disclosing Party	11.1
Enforcement Action	10.4.1
Effective Date	Preamble
Equity Investment	5.2
Force Majeure	16.3
FTO Action	10.7.1
Global Trade Control Laws	16.10
Impf Group	1.1
Incremental Withholding Tax	5.7.1
Indemnified Party	15.4.1
Indemnifying Party	15.4.1
Infringement Claim	10.8
IRB / IEC	1.62
JSC Chair	7.3.2
Key Patent Jurisdictions	10.3.1.1
Lead Development Party	9.1.1
Lead Party	5.5.1
Liabilities	15.2
Licensed Activities	10.7.1
Litigation Conditions	15.4.2
Marketing Authorization Applications	9.2.2
Notice of Dispute	16.11.1
Party or Parties	Preamble
Patent Committee	10.1
Patent Term Extension	10.3.4
Pfizer	Preamble
Pfizer Indemnified Party	15.3
Pfizer JSC Members	7.3.1
Pfizer Materials	7.4.1
Pharmacovigilance Agreement	9.2.7
Prosecution Proceedings	10.3.5
Policies	12.3.20
Program Director and Program Directors	7.2
Reference Product Sponsor	10.4.6.2
Receiving Party	11.1
Regulatory Approval Milestone	5.3
Restricted Market	16.10.1
Restricted Parties	16.10.2
Restricted Party List	16.10.2
Review Period	11.5.2
ROW	9.1.1



Defined Term	Section in Agreement
Term	13.2
Third Party Claim	15.4.1
Third Party Funder	5.5.1
Third Party Licensor	1.12
Upfront Payment	5.1
VAT	5.7.2
Withholding Tax	5.7.1

2. SCOPE OF COLLABORATION

2.1. Scope of Collaboration. Subject to the terms and conditions of this Agreement, the Parties shall (a) cooperate in good faith to conduct their respective activities under the Agreement; and (b) establish one or more committees as described in Article 7 of this Agreement to oversee and coordinate the Development, Manufacture and Commercialization of Candidates and Products in the Territory.

2.2. Initial Research and Development Plan and Manufacturing Plan. Commencing on the Signing Date each Party shall, acting reasonably and in good faith, negotiate and seek to agree binding versions of the Research and Development Plan, Development Budget and the Manufacturing Plan, which shall be agreed by [***]. The Research and Development Plan to be agreed shall reflect the requirements described in Sections 6.1 and 6.2.

3. LICENSES.

3.1. Research Licenses.

3.1.1. **Research License from BioNTech to Pfizer**. Subject to the terms and conditions of this Agreement, effective as of the Effective Date, BioNTech on behalf of itself and its Affiliates hereby grants (and will procure that its Affiliates grant) to Pfizer a sole license under the BioNTech Technology to use, have used, Develop, have Developed, Manufacture, and have Manufactured [***] Candidates and Products within the Territory [***].

3.1.2. **Research License from Pfizer to BioNTech**. Subject to the terms and conditions of this Agreement, effective as of the Effective Date, Pfizer on behalf of itself and its Affiliates hereby grants (and will procure that its Affiliates grant) to BioNTech a sole license under the Pfizer Technology to use, have used, Develop, have Developed, Manufacture, and have Manufactured [***] (a) Candidates and Products and within the Territory [***], and (b) Candidates or products identical to any Product within the Field for their Development (but not Manufacture) outside the Territory by or on behalf of BioNTech (including by Fosun or its Affiliates) pursuant to the Fosun Agreement. With respect to (b) above, such license shall (i) exclude and prohibit the disclosure and license by BioNTech of Pfizer Technology used for Manufacture or formulation of the Candidate or Products, other than to the extent necessary for Fosun or its Affiliates to undertake fill/finish of a product identical to any Product in China or to comply with information requirements of the China National Medical Products Administration relating to such product required under applicable Law; and (ii) automatically terminate on the termination or expiration of the Fosun Agreement and will, unless earlier terminated, survive the termination or expiration of this Agreement in those circumstances described in Section 13.

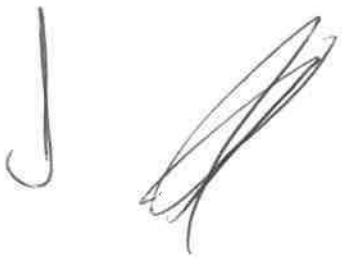
3.1.3. **Scope of Research Licenses**. Each of the licenses granted under Section 3.1.1 and 3.1.2 is (a) a sole license, such that the applicable licensor Party shall not grant a Third Party (unless it is necessary for the Third Party undertaking a fee-for-service Development or Manufacturing activity on its behalf pursuant to this Agreement) a license under the same Intellectual Property Rights for any Exploitation within the Field and within the Territory in respect of any product, whether or not it is a Candidate or Product; (b) royalty-free; (c) sub-licensable in accordance with and subject to Section 3.6; (d) non-assignable, in whole or part, other than where a Party's benefit under this Agreement may be assigned pursuant to Section 16.1; and (e) granted subject to the provisions of this Agreement, and for the duration of the Term or until termination or expiry of this Agreement if earlier, unless otherwise specified herein.

3.2. Licenses for Commercial Manufacturing.

3.2.1. **License from BioNTech to Pfizer.** Subject to the terms and conditions of this Agreement, effective as of the Effective Date, BioNTech on behalf of itself and its Affiliates hereby grants (and will procure that its Affiliates grant) to Pfizer a non-exclusive license under the BioNTech Technology to Manufacture and have Manufactured Candidates and Products for use within the Territory and, subject to Section 3.4, Commercialization within the Territory in any indication.

3.2.2. **License from Pfizer to BioNTech.** Subject to the terms and conditions of this Agreement, effective as of the Effective Date, Pfizer on behalf of itself and its Affiliates hereby grants (and will procure that its Affiliates grant) to BioNTech a non-exclusive license under the Pfizer Technology to Manufacture and have Manufactured (a) Candidates and Products for Commercialization within the Territory in accordance with Section 3.4 in any indication and (b) Candidates and products identical to any Product within the Field for their use and Commercialization outside the Territory by BioNTech or Fosun and its Affiliates pursuant to the Fosun Agreement. With respect to (b) above, such license shall (i) exclude and prohibit the disclosure and license by BioNTech of Pfizer Technology used for Manufacture or formulation of the Candidate or Product, other than to the extent necessary for Fosun or its Affiliates to (x) undertake fill/finish of a product identical to any Product in China or (y) comply with information requirements of the China National Medical Products Administration relating to such product required under applicable Law; and (ii) shall automatically terminate on the termination or expiration of the Fosun Agreement and will, unless earlier terminated, survive the termination or expiration of this Agreement in those circumstances described in Section 13.

3.2.3. **Scope of Commercial Manufacturing Licenses**. Each of the licenses granted under Section 3.2.1 and 3.2.2 is (a) royalty-free; (b) sub-licensable in accordance with and subject to Section 3.6; (c) non-assignable, in whole or part, other than where a Party's benefit under this Agreement may be assigned pursuant to Section 16.1; and (d) granted subject to the provisions of this Agreement, and for the duration of the Term or until termination or expiry of this Agreement if earlier, unless otherwise specified herein.



3.3. Regulatory Dossier Licenses.

3.3.1. **License from BioNTech to Pfizer**. Effective as of the Effective Date, in respect of the Drug Master Files, Regulatory Approvals and Regulatory Documentation (as defined in the Fosun Agreement), BioNTech hereby grants to Pfizer a sole license to rely upon and make reference to such Drug Master Files, Regulatory Approvals and Regulatory Documentation (and the data referenced therein), to use the same in respect of any application for, and maintaining, any Regulatory Approvals (as defined in this Agreement) filed by Pfizer pursuant to this Agreement in respect of Candidates or Products. The license granted under this Section 3.3.1 is (a) royalty-free; (b) sub-licensable in accordance with and subject to Section 3.6; (c) non-assignable, in whole or part, other than where a Party's benefit under this Agreement may be assigned pursuant to Section 16.1; and (d) granted subject to the provisions of this Agreement, and for the duration of the Term or until termination or expiry of this Agreement if earlier, unless otherwise specified herein. BioNTech shall procure disclosure of such Drug Master Files, Regulatory Approvals and Regulatory Documentation upon Pfizer's request. Without limiting any of the foregoing, but subject to Section 3.10, BioNTech shall be permitted to use such Drug Master Files, Regulatory Approvals and Regulatory Documentation (to the extent not comprising Pfizer's Technology or Pfizer's Confidential Information) with respect to any application for or maintenance of any Regulatory Approvals outside the Field.

3.4. Commercialization Licenses.

3.4.1. **License from BioNTech to Pfizer**. Subject to the terms and conditions of this Agreement, and the terms of Schedule 4.1 until the Parties execute the Commercialization Agreement, BioNTech on behalf of itself and its Affiliates hereby grants (and will procure that its Affiliates grant) to Pfizer an exclusive (even as to BioNTech) license under the BioNTech Technology to Commercialize and have Commercialized Products within the Pfizer Commercialization Territory in any indication. The foregoing license shall be subject to the terms of the Commercialization Agreement once executed.

3.4.2. **License from Pfizer to BioNTech**. Subject to the terms and conditions of this Agreement, and the terms of Schedule 4.1 until the Parties execute the Commercialization Agreement, Pfizer on behalf of itself and its Affiliates hereby grants (and will procure that its Affiliates grant) to BioNTech a license under the Pfizer Technology to Commercialize and have Commercialized (a) Products within the BioNTech Commercialization Territory in any indication, which license shall be granted on a sole basis; and (b) products identical to any Product within the Field but outside the Territory by BioNTech or by Fosun or its Affiliates pursuant to the Fosun Agreement. With respect to (b) above, such license shall (i) be sole; (ii) royalty-bearing; (iii) exclude and prohibit the disclosure and license by BioNTech of Pfizer Technology used for Manufacture or formulation of any Candidate or Product, other than to the extent necessary for Fosun or its Affiliates to (x) undertake fill/finish of a product identical to any Product in China or (y) comply with information requirements of the China National Medical Products Administration relating to such product required under applicable Law; and (iv) shall automatically terminate on the termination or expiration of the Fosun Agreement and will, unless earlier terminated, survive the termination or expiration of this Agreement in those circumstances described in Section 13.

3.4.3. **Scope of Commercialization Licenses**. Each of the licenses granted under Section 3.4.1 and 3.4.2 is (a) sub-licensable in accordance with and subject to Section 3.6; (b) non-assignable, in whole or part, other than where a Party's benefit under this Agreement may be assigned pursuant to Section 16.1; and (c) granted subject to the provisions of this Agreement, the Commercialization Agreement upon its execution, Schedule 4.1 and for the duration of the Term or until termination or expiry of this Agreement if earlier, unless otherwise specified herein. Furthermore, [***].

3.4.4. **Financial Provisions for Commercialization.** The license under:

3.4.4.1. Section 3.4.1 and 3.4.2(a) is royalty-free but each is subject to the Gross Profit share set out in the Commercialization Terms; and

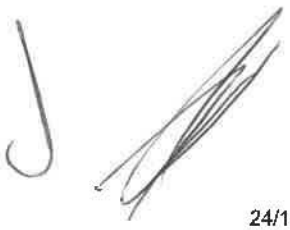
3.4.4.2. Section 3.4.2(b) shall be royalty bearing at a rate of (i) [***] percent of net sales of the product(s) sold pursuant to the Fosun Agreement where such product(s) is Covered by any Pfizer Patent Right or any Joint Patent Rights (ii) if, or when, (i) does not apply, then [***] percent of net sales of the product(s) sold pursuant to the Fosun Agreement where such product(s) is Covered by any Pfizer Know-How or any Joint Know-How with net sales having the same definition, *mutatis mutandis*, to Net Sales under this Agreement, with sales and royalty reporting every Pfizer Quarter, payments on a Pfizer Quarter basis, and Pfizer having audit rights comparable with those under this Agreement); *provided, however*, that (a) during the period in which a generic or biosimilar equivalent to such product(s) is Commercialized in any part of the territory that is the subject of the Fosun Agreement, the royalty under (i) above shall be reduced by [***]; or (b) if the gross profit share earned by BioNTech in connection with sale of products under the Fosun Agreement is lower than the royalty amount to be paid to Pfizer hereunder in respect of those same sales, then no royalty shall be payable hereunder for those sales. The foregoing royalty obligations shall commence on the first commercial sale of the product(s) sold pursuant to the Fosun Agreement, and extend (a) with respect to the royalty under (i) for so long as such product(s) is Covered by any such Patent Rights (until such Patent Right expires, is surrendered, or is otherwise irrevocably revoked or declared invalid), and (b) with respect to the royalty under (ii), the [***] anniversary of the date of the first commercial sale of such product(s) in the territory that is the subject of the Fosun Agreement; and in each case, such provision shall survive the termination or expiry of this Agreement.

3.5. Additional Licenses.

3.5.1. **To Pfizer.** Without limiting any other license or sublicense granted under this Agreement or the Commercialization Agreement and subject to the terms and conditions of this Agreement, BioNTech on behalf of itself and its Affiliates, effective as of the Effective Date, hereby grants (and will procure that its Affiliates grant) to Pfizer a non-exclusive, royalty-free, fully paid-up, sublicensable license under all BioNTech Improvements and Product Technology that were solely or jointly made or invented by Pfizer Representatives to use, have used, Develop, have Developed, Manufacture, have Manufactured, Commercialize, have Commercialized and otherwise Exploit any products or processes outside the Field. In addition to the obligations set forth in Section 3.10 for the avoidance of doubt, the license granted in this Section 3.5.1 shall not include or imply a right of Pfizer to use any of BioNTech's Confidential Information (that is not a BioNTech Improvement or Product Technology) outside the Field.

3.5.2. **To BioNTech.**

3.5.2.1. Without limiting any other license or sublicense granted under this Agreement or the Commercialization Agreement and subject to the terms and conditions of this Agreement, Pfizer, effective as of the Effective



Date, hereby grants to BioNTech a non-exclusive, royalty-free, fully paid-up, sublicensable license under all Pfizer Improvements that were solely or jointly invented by BioNTech Representatives to use, have used, Develop, have Developed, Manufacture, have Manufactured, Commercialize, have Commercialized and otherwise Exploit any products or processes outside the Field.

3.5.2.2. Without limiting any other license or sublicense granted under this Agreement or the Commercialization Agreement and subject to the terms and conditions of this Agreement, Pfizer, effective as of the Effective Date, hereby grants to BioNTech a non-exclusive, royalty-free, fully paid-up, sublicensable license under Pfizer's interest in the Research and Development Program Technology to use, have used, Develop, have Developed, Manufacture, have Manufactured, Commercialize, have Commercialized and otherwise Exploit any products or processes outside the Field.

3.5.2.3. For the avoidance of doubt, the licenses granted in this Section 3.5.2 shall not include or imply a right of BioNTech to use any Pfizer Confidential Information (that is not a Pfizer Improvement or Research and Development Program Technology) outside the Field, but remain subject to the obligations set forth in Section 3.10.

3.6. Sublicensees. Either Party shall have the right to grant sublicenses and, as applicable, sub-sublicenses under and subject to the rights granted to it under this Section 3 to (a) its Affiliates; (b) permitted Third Party subcontractors which such Party uses to undertake services for, or to perform its obligations under, this Agreement, the Commercialization Terms and the Commercialization Agreement; (c) Sublicensees in respect of Manufacturing, provided that, other than where a sublicense is required by a Governmental Authority or pursuant to a Third Party Funder agreement, the sublicensing Party shall (i) discuss the proposed use of a Third Party with the other Party, and take into account any reasonable views, objections or comments with respect to the proposed Third Party; (ii) impose industry standard obligations of confidentiality and non-use on the Third Party with respect to the other Party's Confidential Information, and limit the disclosure of that other Party's Confidential Information so far as is reasonably necessary; and (iii) not, where Pfizer is the sublicensing Party, subcontract Manufacturing of the Product [***] without BioNTech's prior consent (such consent not to be unreasonably withheld); and (d) distributors of the Product in the Territory; and (e) in the case of BioNTech, and subject to the restrictions in Sections 3.1, 3.2, and 3.4 and the terms of Section 11, Fosun and any of Fosun's Affiliates pursuant to the Fosun Agreement for Commercialization in the Field outside the Territory. In respect of any and all such sublicenses (or sub-sublicenses):

3.6.1. the sublicensing Party shall be responsible for failure by its Sublicensees to comply with the terms and conditions of this Agreement;

3.6.2. the rights sublicensed under the sublicense may not be further sublicensed by the Sublicensee;

3.6.3. the sublicensing Party shall notify the other Party in writing of any sublicenses granted to Third Parties (other than Fosun);

3.6.4. in the event of a sublicense in respect of the Commercialization of Product, shall provide a copy of the relevant sublicense agreement to the other Party upon request which may be redacted to delete provisions not applicable to the calculation of Gross Profits; and

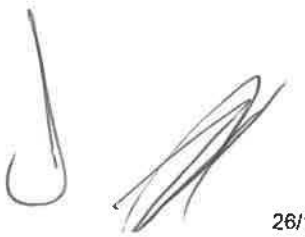
3.6.5. unless otherwise agreed between the Parties on a case-by-case basis, all sublicenses shall automatically terminate (and the sublicensing Party shall ensure that all sublicenses automatically terminate) upon termination (for whatever reason) or expiry of a license granted hereunder, but only to the extent necessary to terminate the sublicense in so far as it corresponds to any terminated or expired licenses granted in this Agreement.

3.7. BioNTech Current Licenses.

3.7.1. **Maintenance of Current Licenses.** BioNTech will maintain in full effect and will perform all of its obligations in a timely manner under each of the Current Licenses. Absent Pfizer's prior written consent (which may be provided, conditioned or withheld in Pfizer's sole discretion), BioNTech will not terminate, modify or amend any Current License in any manner that would adversely affect any of the rights granted or that may be granted to Pfizer under this Agreement or that would impose any obligations upon Pfizer hereunder (including any increase in Third Party License Payments) that are in addition to those obligations that would exist under this Agreement based on the Current Licenses as they exist on the Effective Date or adversely affect BioNTech's ability to perform its obligations under this Agreement. Further, BioNTech will not take any action or omit to take any action that would cause it to be in breach of any Current License or that would give rise to a right of any Current Licensor to terminate the applicable Current License.

3.7.2. **Communications and Performance.** Notwithstanding anything to the contrary in this Agreement, BioNTech will use Commercially Reasonable Efforts to facilitate any communications between Pfizer and any Current Licensor required for Pfizer to exercise the rights granted to it pursuant to Section 3 and will use Commercially Reasonable Efforts to cause each applicable Current Licensor to perform all of its obligations under the applicable Current License.

3.7.3. **Breach of Current License by BioNTech.** If BioNTech receives notification of any actual or potential breach or otherwise becomes aware of its breach of any Current License (and if uncured, such breach could give rise to the termination of the applicable Current License), then BioNTech will immediately notify Pfizer of such breach. To the extent that any act or omission on the part of Pfizer is the cause of such breach of a Current License, Pfizer will take all actions and provide BioNTech with all cooperation necessary to cure such breach, in each case as reasonably requested by BioNTech and at Pfizer's sole cost and expense. To the extent that Pfizer is not the cause of such breach of a Current License, BioNTech will have the first opportunity to cure such breach in accordance with a plan to be mutually agreed upon by the Parties in writing, acting reasonably (each, a "Cure Plan"). If (a) BioNTech, at any time, is not using diligent efforts to cure such breach pursuant to the applicable Cure Plan or (b) BioNTech is unable to cure such breach in accordance with the applicable Cure Plan or it becomes reasonably apparent that BioNTech will not be able to cure such breach pursuant to the applicable Cure Plan, then Pfizer may, at its election and in its sole discretion and without prejudice to its other remedies against BioNTech, act reasonably to cure such breach and BioNTech will take all actions and provide Pfizer with all cooperation to cure such breach, in each case as directed by Pfizer. Further, if Pfizer is not the cause of such breach of a Current License, then BioNTech will, at Pfizer's sole election, (i) reimburse Pfizer for all out-of-pocket costs and expenses incurred by or on behalf of Pfizer or any of its Representatives in connection with curing such breach; or (ii) permit Pfizer, under the Commercialization Agreement, to offset any such costs and expenses incurred by or on behalf of Pfizer or any of Pfizer's Representatives in connection with curing such breach against Pfizer's future payment obligations to BioNTech (or any of its successor or assigns) under this Agreement.



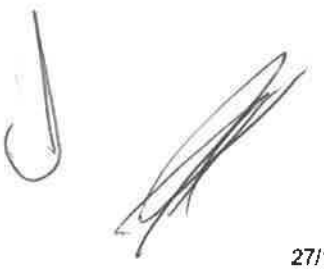
3.7.4. **Termination of any Current License**. In the event that any Current License is terminated by the applicable Current Licensor and this Agreement, as of the effective date of such termination, has not otherwise been terminated, Pfizer, to the extent permitted by such Current License (or if not permitted or addressed in such Current License, to the extent permitted by the applicable Current Licensor), will have the right without prejudice to its other remedies against BioNTech, at Pfizer's election, to convert the sublicenses granted under this Agreement by BioNTech to Pfizer under such Current License to a direct license from the applicable Current Licensor to Pfizer on the terms and conditions contained in such Current License (with Pfizer assuming the applicable obligations of BioNTech thereunder) or such other terms and conditions as may be negotiated by Pfizer and the applicable Current Licensor. In the event Pfizer enters into any such direct license with a Current Licensor, BioNTech will, at Pfizer's sole election and without prejudice to its other remedies hereunder:

3.7.4.1. in respect of royalties payable by Pfizer under such direct license to the Current Licensor, to the extent such royalties are due in connection with the sale of Candidates or Products hereunder, reimburse to Pfizer the difference between (a) the amount that would have been payable by BioNTech to the Current Licensor under the Current License if the Current License had not been terminated and (b) the amount that would have to be reimbursed by Pfizer to BioNTech in accordance with the terms of the Commercialization Agreement; or

3.7.4.2. permit Pfizer to offset any such reimbursement amounts (to the extent not reimbursed pursuant to clause (a) above), against Pfizer's future payment obligations to BioNTech (or any of its successor or assigns) under the Commercialization Agreement.

3.7.5. **Consents and Waivers.** BioNTech represents, warrants and covenants to Pfizer that, to the extent any terms and conditions of this Agreement do not (or will not at any time during the Term) conform to any requirements relating to the grant of sublicenses under any Current License, it has obtained the irrevocable consent (or, if applicable, the waiver of any resultant conflict) from the applicable Current Licensor that is necessary to permit the activities contemplated under this Agreement, including, such that BioNTech may grant the applicable sublicenses granted or to be granted hereunder and perform all of its obligations hereunder and Pfizer may exercise all of its rights and perform all of its obligations hereunder, in each case, without breaching the applicable Current License. In the event that any provision in any Current License which conflicts with this Agreement or adversely impacts the activities contemplated under this Agreement comes to the attention of either BioNTech or Pfizer or which otherwise, at any time during the Term, would cause the representation, warranty and covenant set forth in the preceding sentence to be untrue, BioNTech, in consultation with Pfizer, will obtain any and all additional required consents or waivers from the applicable Current Licensor(s) which may be necessary to align the conflicting provision(s) of the applicable Current License with this Agreement and to permit the activities contemplated by this Agreement.

3.7.6. **Exceptions to the Fosun Agreements.** If BioNTech (as opposed to Pfizer) has breached the Fosun Agreement [***]. In addition, in respect of the Fosun Agreement (i) [***]; and (ii) [***].



3.7.7. **Reduction in Royalties**. BioNTech shall use reasonable efforts to obtain any reductions or waivers in royalties or other payments due under the Current Licenses that could constitute Third Party License Payments due to the pandemic status of COVID-19 or with respect to countries or populations experiencing emergency pandemic or crisis epidemic, coronavirus conditions, including taking into account any restrictions on pricing for the Product based on applicable Law and funding agreements with Third Party Funders. For the avoidance of doubt, BioNTech does not guarantee that any such reductions or waivers can be obtained from such licensors.

3.8. Third Party Agreements. Each Party will be solely responsible for all obligations (including royalty and payment obligations) that relate to Candidates, Products, BioNTech Technology or Pfizer Technology under its or its Affiliates' own agreements with Third Parties that are in effect on or prior to the Effective Date, including the Current Licenses for which BioNTech has sole responsibility.

3.9. No Implied Rights. Except as expressly provided in this Agreement, neither Party will be deemed to have granted the other Party (by implication, estoppel or otherwise) any right, title, license or other interest in or with respect to any Patent Rights, Know-How or other Intellectual Property Rights or information Controlled by such Party.

3.10. Exclusivity.

3.10.1. **Mutual Exclusivity.** Except if otherwise permitted by the unanimous consent of the JSC, during the Term, neither Party shall, and shall procure that its Affiliates shall not, itself or with or on behalf of a Third Party, Develop, have Developed, Manufacture, have Manufactured, Commercialize, have Commercialized or otherwise Exploit or have Exploited any [***] in the Field within the Territory, except that each Party may continue any existing agreement with a Third Party for non-clinical research within the Field with academic institutions and consortia. For avoidance of doubt, the foregoing exclusivity obligation shall not apply to (a) [***]; (b) [***]; (c) [***]; or (d) [***].

3.10.2. **Exclusivity of the Licenses.** Without prejudice to the licenses granted by BioNTech pursuant to this Section 3 or pursuant to the Commercialization Agreement, BioNTech shall not, and shall procure that its Affiliates shall not, grant any license, permission, waiver, covenant not to sue, or other right to use or Exploit any of the BioNTech Technology within the Field and within the Territory that would conflict with or erode any of Pfizer's rights hereunder.

3.10.3. **Exclusivity in the Product.** Except pursuant to this Agreement or the Commercialization Terms or Commercialization Agreement, neither Party shall, and shall procure that its respective Affiliates shall not, itself or with or on behalf of a Third Party, Develop, have Developed, Manufacture, have Manufactured, Commercialize, have Commercialized or otherwise Exploit (a) any Candidate Controlled by BioNTech as of the Effective Date within the Field; or (b) any Candidate that, as a consequence of the Development under this Agreement, becomes Controlled by BioNTech after the Effective Date, for any field; or (c) any Product for any field or application; in each case (a), (b) and (c) other than for non-clinical research purposes, or within the Field pursuant to the Fosun Agreement.

4. COMMERCIALIZATION

4.1. Commercialization Agreement. With respect to Commercialization, the Parties have agreed to the terms set forth in Schedule 4.1 ("Commercialization Terms") and will, for [***] following the Signing Date (or any other time period agreed by the Parties in writing), negotiate and execute a definitive Commercialization Agreement reflecting such Commercialization Terms. Such agreement shall be negotiated in good faith and acting reasonably, and shall set forth the rights and responsibilities of the Parties in connection with the Commercialization of the Products and which shall be consistent with the Commercialization Terms. If the Commercialization Agreement is not executed within the [***] period the Parties will prioritize and engage in additional discussions to conclude and execute the Commercialization Agreement as soon as possible.

4.2. Commercialization Rights Pending Agreement. If a definitive Commercialization Agreement is not executed before the Product is first ready to be Commercialized in the Territory, each Party may still commence and continue with the Commercialization of the Product in its respective Commercialization territory, but shall do so subject to the provisions of the Commercialization Terms until the Commercialization Agreement is executed.

5. PAYMENTS AND FUNDING.

5.1. Upfront Payment. Pfizer shall make a one-time, non-refundable (without limiting Pfizer's right to claim for damages under this Agreement) payment of Seventy-two Million Dollars ($72,000,000) to BioNTech ("Upfront Payment") within thirty (30) days of receipt of BioNTech' s invoice (such invoice to be delivered on or following the Signing Date), but not before the Research and Development Plan, Development Budget and Manufacturing Plan are agreed between the Parties in accordance with Section2.2, which payment shall be dedicated to activities to be performed under the Research and Development Plan.

5.2. Equity Investment. Pfizer and BioNTech shall enter into an "Investment Agreement" contemporaneously with this Agreement pursuant to which Pfizer agrees to subscribe for shares in BioNTech in consideration for an investment amount of One Hundred and Thirteen Million Dollars ($113,000,000) based on a price per share of $47.53, subject to the conditions as prescribed in such Investment Agreement ("Equity Investment").

5.3. Regulatory Milestone Payment. Within [***] of the date upon which either BioNTech or Pfizer first obtains all Regulatory Approvals required for the Commercialization of the Product in a Major Market Country in the Territory, Pfizer shall pay BioNTech a one-time, non-refundable (without limiting Pfizer's right to claim for damages under this Agreement) milestone payment of [***] Dollars (US$[***]) ("Regulatory Approval Milestone"), which shall be automatically applied to repayment of, and offset against, the BioNTech Deferred Development Costs, and to the extent that at such time the BioNTech Deferred Development Costs are less than the value of the Regulatory Approval Milestone any difference shall be paid to BioNTech.

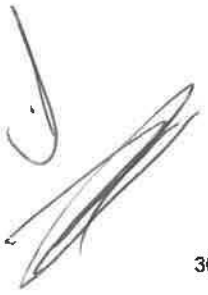
5.4. Sharing of Development Costs.

5.4.1. **Shared Development Costs.** Except as otherwise provided herein, each Party shall bear fifty percent (50%) of all Shared Development Costs.

5.4.2. **BioNTech Deferred Development Costs**. Without prejudice to Section 5.4.1, BioNTech's share of the Shared Development Costs incurred in accordance with the binding parts of the Development Budget, Research and Development Plan and the Manufacturing Plan, and this Agreement, and which are not funded by a Third Party Funder, shall be funded initially by way of an interest free repayable loan from Pfizer unless and until there is a Funding Event ("BioNTech Deferred Development Costs"). Following a Funding Event, BioNTech shall thereafter fund its share of the Shared Development Costs in accordance with Section 5.4.4. The BioNTech Deferred Development Costs shall be funded by Pfizer but shall be subject to the reporting and reconciliation provisions of Section 5.4.4. The BioNTech Deferred Development Costs shall be repayable through (a) the Regulatory Approval Milestone, if paid pursuant to Section 5.3; (b) a proportion of the Commercialization Sales Milestone Payments (as defined and described in Schedule 4.1); (c) Pfizer's retention of the Enhanced Profit Share element of Gross Profits pursuant to the Commercialization Terms set out in the Commercialization Terms and (d) an immediate lump sum paid by BioNTech upon (i) Change of Control of BioNTech pursuant to Section 14.1.3.3, provided that the most recent published annual group net income, published prior to the date of such Change of Control, of the Third Party acquiring BioNTech is [***] Dollars or (ii) termination of this Agreement for BioNTech's breach or its bankruptcy or insolvency. If this Agreement is terminated by Pfizer pursuant to its right under Section 13.4, the BioNTech Deferred Development Costs shall cease to be repayable by BioNTech.

5.4.3. **Budgeting of Shared Development Costs.** The Parties shall agree on, and regularly update (if required), the Development Budget through the JSC. As soon as either Party determines that it is likely to overspend on the binding part of the Development Budget that is allocated to that Party by more than [***], it shall inform the JSC accordingly, and shall only be entitled to incur such overrun costs as Shared Development Costs pursuant to Section 5.4.1 and 5.4.2 upon the JSC's mutual consent.

5.4.4. **Reporting and Reconciliation.** Wherever possible and practicable, prior to any Funding Event any external Shared Development Costs incurred in accordance with the binding parts of the Development Budget shall initially be invoiced to and borne by Pfizer, but shall be subject to reimbursement in accordance with this Section 5.4.4. All other Shared Development Costs incurred in accordance with the binding parts of the Development Budget shall initially be borne by the Party incurring such costs and shall thereafter be subject to reimbursement in accordance with this Section 5.4.4. Each Party shall report to the other Party, within [***] after the end of each Pfizer US Quarter, the Shared Development Costs incurred by such Party during such Pfizer Quarter. Such report shall specify in reasonable detail all amounts included in such Shared Development Costs during such Pfizer Quarter (broken down by activity), and out-of-pocket costs shall be allocated to the extent possible to a specific activity in the applicable binding part of the Research and Development Plan. Each such report shall enable the receiving Party to compare the reported Shared Development Costs against the applicable binding part of the Development Budget previously approved by the JSC, on both a quarterly basis and a cumulative basis for each activity. The Parties shall seek to resolve any questions related to such accounting statements within [***] following receipt by each Party of the other Party's report hereunder. Following such resolution, BioNTech shall prepare a reconciliation report for the Shared Development Costs for such Pfizer Quarter (including as against the binding parts of the Development Budget) and shall either (a) deliver an invoice to Pfizer for any amounts due to



BioNTech as a result of reconciliation or (b) notify Pfizer that it should issue an invoice to BioNTech for any amounts due to Pfizer as a result of reconciliation. Any such invoice from BioNTech to Pfizer shall be payable within [***] from receipt by Pfizer. Prior to any Funding Event, any such invoice from Pfizer to BioNTech shall not be payable upon receipt, but shall be accounted as BioNTech Deferred Development Costs and shall be payable in accordance with the mechanism described in Section 5.4.2. Following any Funding Event, any such such invoice from Pfizer to BioNTech shall be payable within [***] from receipt by Pfizer.

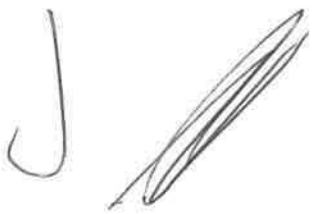
5.4.5. **Capex Costs.** Notwithstanding anything else in this Agreement, each Party shall be solely responsible for its own Capex Costs and any capital expenditures required in connection with this Agreement or the Commercialization Agreement.

5.4.6. **Other Costs.** Except as expressly set forth otherwise in this Agreement), each Party will bear all costs and expenses it incurs in connection with its activities under this Agreement.

5.5. Third Party Funding.

5.5.1. **Third Party Funders.** Pfizer and BioNTech shall, in good faith and acting collaboratively, seek funding from one or more Third Parties for such Third Party to provide financial support to the collaboration between the Parties under this Agreement (each, a "Third Party Funder"). For each potential Third Party Funder, the Parties will agree on (a) the Party to lead the communications and discussions with such Third Party Funder (the "Lead Party") and (b) the activities, costs or expenses for which funding support shall be sought (e.g. funding for Development costs, funding in support of a Party's Capex Costs ("Capex Funding") or both). An initial list of potential Third Party Funders and their allocation as between the Parties is set forth in Schedule 5.5. Notwithstanding the foregoing, Pfizer shall be entitled to secure funding from, and shall be the Lead Party in discussions with, [***], in the event that Pfizer, in its sole discretion, [***], and BioNTech shall be entitled to secure funding from, and shall be the Lead Party in discussions with, [***], in the event that BioNTech, in its sole discretion, chooses to seek funding from [***].

5.5.2. **Discussions with Funders.** The Lead Party will lead any discussions with such Third Parties in any country, provided that the Lead Party will provide regular updates to the JSC and keep the JSC reasonably informed of the status and any developments in such discussions, and shall, at the other Party's reasonable request, update the other Party on any such discussions. The Lead Party shall conduct any such discussions and draft and file any applications for any Third Party Funding in good faith and acting reasonably with respect to its requests for such funding. Where legally possible and unless otherwise agreed between the Parties, each application for any Third Party funding shall be made in both Parties' name unless the Parties have agreed in advance pursuant to Section 5.5.1 that such application shall be in respect of one Party's Capex Funding alone, in which case such application may be made in that Party's own name alone. The Lead Party shall not enter into a written agreement with any Third Party Funder without prior written consent of the other Party (such consent not to be unreasonably withheld, conditioned or delayed) unless the Parties have agreed in advance pursuant to Section 5.5.1 that such agreement shall be in respect of that Lead Party's Capex Funding alone, in which case the Lead Party can conclude such Third Party Funder agreement without consent from the other Party. Notwithstanding the foregoing, (a) Pfizer shall be entitled to seek any funding from [***] without requiring BioNTech's consent; and (b) BioNTech shall be entitled to seek any funding from [***] without requiring Pfizer's consent. Pfizer and BioNTech acknowledge and agree that there is no guaranty that any Lead Party will be successful in securing any funding from any Third Party Funder or that any specific amount of funding will be obtained.



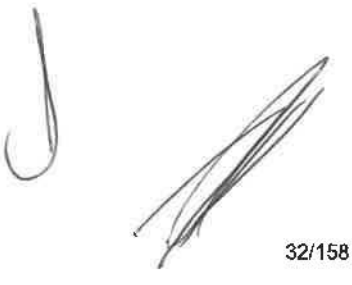
5.5.3. **Allocation of Funds and Balancing Payment.** To the extent possible, any Third Party funding to the extent it relates to activities in relation to which the Parties have agreed to treat the associated Development costs as Shared Development Cost shall be shared equally between the Parties. If such sharing is not possible, a balancing adjustment shall be made in favor of the other Party to the Shared Development Costs to reflect [***] percent of such funding that that Party receives from the Third Party Funder provided that doing so does not breach any applicable Laws or the terms of such funding. Each Party shall promptly report to the other Party in writing if and when it receives any payments from any Third Party Funder funding that relates to activities, costs or expenses that are Shared Development Costs.

5.5.4. **Not Applicable to Loans.** For the avoidance of doubt, this Section 5.5 shall not apply to any traditional loans provided by any Third Party to a Party provided that (a) such loans are repayable by the borrower Party and not, directly or indirectly, by the other Party; (b) this Agreement, the Commercialization Agreement, any other agreement ancillary to this Agreement or the Commercialization Agreement, the BioNTech Technology, Product Technology and Product are not provided as security for, or otherwise encumbered by way of, such loan (excluding, for clarity, any tangible assets). Each Party shall be entitled to seek any such loans from any Third Party without any obligations to the other Party.

5.6. Records and Accounting Principles. Each Party shall keep books and records of any of Shared Development Costs and any Third Party funding in accordance with good industry practice and GAAP or IFRS, as applicable. Each Party shall determine Shared Development Costs using its standard accounting procedures, consistently applied and in accordance with GAAP or IFRS, as applicable (provided that the application of such procedures results, on balance, in outcomes that are fair and equitable to both Parties taking into consideration the interests of both Parties as reflected in this Agreement). All personnel costs of either Party or its Affiliates are excluded from Shared Development Costs.

5.7. Taxes.

5.7.1. **Withholding Taxes.** The Parties agree to use reasonable efforts to cooperate with one another and use commercially reasonable efforts to avoid or reduce, to the extent permitted by applicable Law, tax withholding or similar obligations in respect of royalties, milestone payments, and other payments made by the paying Party to the receiving Party under this Agreement ("Withholding Taxes"). If Withholding Taxes are imposed on any compensation under this Agreement, the liability for such Withholding Taxes shall be the sole responsibility of the receiving Party, and the paying Party shall (a) deduct or withhold such Withholding Taxes from the payment made to the receiving Party, (b) timely pay such Withholding Taxes to the proper taxing authority, and (c) send proof of payment to the receiving Party within [***] following such payment. Each Party shall comply with (or provide the other Party with) any certification, identification or other reporting requirements that may be reasonably necessary in order for the paying Party to not withhold Withholding Taxes or to withhold Withholding Taxes at a reduced rate under an applicable bilateral income tax treaty. Each Party shall provide the other with commercially reasonable assistance to enable the recovery, as permitted by applicable Law, of Withholding Taxes or similar obligations resulting from payments made under this Agreement, such recovery to be for the benefit of the Party bearing the cost of such Withholding Taxes under this Section 5.6 (Taxes and Withholding). Notwithstanding the foregoing, if as a result of any assignment or sublicense by the paying Party, any change in the paying Party's tax residency, any change in the entity that originates the payment, or any failure on the part of the paying Party to comply with applicable



Law with respect to Withholding Taxes (including filing or record retention requirements), Withholding Taxes are imposed that would not otherwise have been imposed ("Incremental Withholding Taxes"), then the paying Party shall be solely responsible for the amount of such Incremental Withholding Taxes and shall increase the amounts payable to the receiving Party so that the receiving Party receives a sum equal to the sum which it would have received had there been no such imposition of Incremental Withholding Taxes.

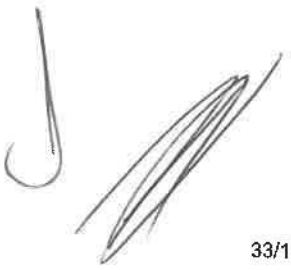
5.7.2. **Value Added Tax.** All payments between the Parties under this Agreement are exclusive of applicable statutory value added tax or similar taxes ("VAT"), if any, which shall be listed separately on each invoice. If and to the extent any VAT will become payable due to any supplies or services rendered under this Agreement and if and to the extent such VAT is to be paid by the Party providing the supply or service to the competent tax authorities, the receiving Party shall pay an amount equal to such VAT to the providing Party upon receipt of a valid invoice allowing for the recovery of such VAT.

5.7.3. **Other.** Except as otherwise set forth in this Section 5.7, each Party shall be solely responsible for the payment of all Taxes imposed on such Party's income arising directly or indirectly from the activities of the Parties under this Agreement.

5.8. Currency, Source of Payments. All amounts payable and calculations under this Agreement will be in United States dollars, [***]. As applicable, all costs and expenses will be translated into United States dollars at the exchange rate used by the relevant Party for public financial accounting purposes. If, due to restrictions or prohibitions imposed by national or international authority, a given payment cannot be made as provided under this Section 5.8, the Parties will consult with a view to finding a prompt and acceptable solution. If the Parties are unable to identify a mutually acceptable solution regarding such payment, then the Party owing the relevant payment may elect, in its sole discretion, to deliver such payment in the relevant jurisdiction and in the local currency of the relevant jurisdiction.

5.9. Method of Payment. Except as permitted pursuant to Section 5.8, each payment hereunder will be made by electronic transfer in immediately available funds via either a bank wire transfer, an ACH (automated clearing house) mechanism, or any other means of electronic funds transfer, at the paying Party's election, to such bank account as the receiving Party will designate in writing to the other Party within [***] of the Signing Date, and thereafter at least [***] before the payment is due. All invoice or billing related questions in relation to Pfizer should be referred to Pfizer's Accounting Department at 800.601.1357 or go to the Accounts Payable Invoice Portal at ap.pfizer.com. Unless otherwise specified herein, each invoice is payable within [***] of receipt of the relevant invoice.

5.10. Audits. Upon [***] prior notice from a Party (the "Auditing Party"), the other Party (the "Audited Party") will permit an independent certified public accounting firm of nationally recognized standing selected by the Auditing Party and reasonably acceptable to the Audited Party, to examine, [***], the relevant books and records of the Audited Party and its Affiliates (and where possible, its subcontractors) as may be reasonably necessary to verify the amounts reported by the Audited Party in accordance with Sections 5.4 and 5.5. An examination by the Auditing Party under this Section 5.10 will occur not more than [***] and will be limited to the pertinent books and records for any Calendar Year ending not more than [***] before the date of the request. The accounting firm will be provided access to such books and records at the Audited Party's or its Affiliates' facility(ies) where such books and records are normally kept and such examination will be conducted during the Audited Party's or its Affiliates' normal business hours. The Audited Party may require the accounting firm to sign a reasonably acceptable non-disclosure agreement before providing the accounting firm with access to the Audited Party's or its Affiliates' facilities or records. Upon completion of the audit, the accounting firm will provide both Pfizer and BioNTech the same written report disclosing any discrepancies in the reports submitted by the Audited Party, and, in each case, the specific details concerning any discrepancies. No other information will be provided to the Auditing Party.



5.10.1. **Underpayments/Overpayments**. If such accounting firm concludes that there are errors in how Shared Development Costs have been charged, allocated or reclaimed, or Third Party funding has not been allocated in accordance with this Agreement by the Audited Party, then adjustments shall be made in accordance with the accounting firm's recommendations in a reconciliation of Shared Development Costs and any overpayment or underpayment by the Audited Party shall be rectified either by a refund to, or payment by, the Audited Party from or to the Auditing Party within [***] of the date the Audited Party receives such accountant's written report. Further, if the amount of any overpayment or overallocation to the Audited Party exceeds more than [***] of the amount that was properly payable due or allocated to the Audited Party, then the Audited Party will reimburse the Auditing Party for the Auditing Party's out-of-pocket costs in connection with the audit.

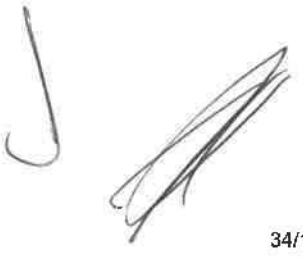
5.10.2. **Confidentiality**. Notwithstanding any provision of this Agreement to the contrary, all reports and financial information of the Audited Party or its Affiliates which are provided to or subject to review by the Auditing Party will be deemed to be Confidential Information of the Audited Party and subject to the provisions of Section 11.1.

5.11. No Guaranty of Success.

5.11.1. Pfizer and BioNTech acknowledge and agree that any milestone payments pursuant to BioNTech hereunder or under the Commercialization Terms: (a) have been included in this Agreement on the basis that they are only payable or otherwise relevant if a certain Product is successfully Developed or Commercialized in accordance with the applicable milestone or event, as applicable; (b) are solely intended to allocate amounts that may be achieved upon successful Development or Commercialization of such Product as applicable, between Pfizer and BioNTech; (c) are not intended to be used as a measure of damages if this Agreement is terminated for any reason; and (d) will only be triggered, and will only be relevant as provided, in accordance with the terms and conditions of such provisions.

5.11.2. Pfizer and BioNTech further acknowledge and agree that nothing in this Agreement, or in any document or presentation provided by Pfizer to BioNTech prior to the Effective Date will be construed as representing any estimate or projection of (a) the successful Development or Commercialization of any Product under this Agreement, (b) the number of Products that will or may be successfully Developed or Commercialized under this Agreement, (c) anticipated sales or the actual value of any Products that may be successfully Developed or Commercialized under this Agreement or (d) the damages, if any, that may be payable if this Agreement is terminated for any reason.

5.11.3. Neither Party makes any representation, warranty or covenant, either express or implied, to the other Party that (a) it will successfully Develop, Manufacture, Commercialize or continue to Develop, Manufacture or Commercialize any Product in any country, (b) if Commercialized, that any Product will achieve any particular sales level, whether in any individual country or cumulatively throughout the Territory or (c) it will devote, or cause to be devoted, any level of diligence or resources to Developing, Manufacturing or Commercializing any Product in any country, or in the Territory.



6. RESEARCH AND DEVELOPMENT PLAN

6.1. Scope of Development and Updating of Plans. Pfizer and BioNTech will collaborate during the Term to conduct research to identify, Develop and evaluate Candidates and Products within the Field in accordance with the binding parts of the Research and Development Plan, the Development Budget, the Manufacturing Plan, and the terms and conditions set forth in this Section 6. The Research and Development Plan may be modified by agreement and approval of the JSC pursuant to Section 7, provided that the JSC shall have no right or authority to (a) modify the Research and Development Plan in a way not permitted under Section 7.3; or (b) modify the Research and Development Plan so as to amend the contractual provisions of this Agreement. The initial [***] of each of the Research and Development Plan, the Manufacturing Plan and the Development Budget shall be agreed between the Parties by [***], the first [***] of each are binding upon the Parties and the second [***] are indicative but non-binding. At least [***] prior to the expiration of such initial [***] binding period, the JSC shall decide and mutually agree on the following [***] period of each of the Research and Development Plan, the Manufacturing Plan and the Development Budget which period, upon agreement, shall be binding upon the Parties subject to Section 7.3.4. At least [***] days prior to the expiration of the initial [***] period following the Effective Date, the JSC shall establish a rolling [***] process to decide on and update each of the Research and Development Plan, the Development Budget and the Manufacturing Plan for subsequent [***] periods, each of which shall be updated by the JSC no later than [***] prior to the expiration of the then binding [***] period.

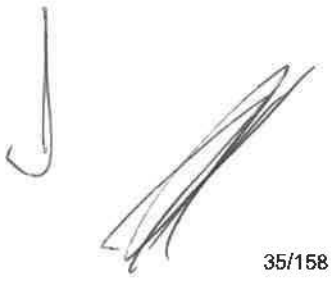
6.2. Research and Development Plan. The Research and Development Plan shall (a) include a broad non-binding overview of the first [***] of the planned Development program (specifying in reasonable detail all material Development activities) to generate the preclinical, clinical, CMC, regulatory and other information required for submitting a marketing authorization application for Regulatory Approval for the Candidate or Product and to achieve such Regulatory Approval for the Candidate or Product in one or more selected country(ies) of the Territory; (b) include a more detailed and binding part of the plan for the initial binding period described in Section 6.1, which will be updated in accordance with Section 6.1; and (c) set forth those obligations assigned to each Party with respect to the performance of the Development activities contemplated by such Research and Development Plan.

6.3. Allocation of Responsibilities.

6.3.1. **General**. Each Party will use Commercially Reasonable Efforts to perform its obligations and activities identified under the binding parts of the Research and Development Plan or as allocated to it by the JSC in a professional manner in accordance with any target dates set forth in Research and Development Plan. Further, each Party will perform its obligations under the binding parts of the Research and Development Plan or as allocated to it by the JSC in compliance with all Laws applicable to its activities under the Research and Development Plan.

6.3.2. **Mutations.** If and to the extent Mutations of the SARS-CoV-2 virus arise [***]

6.3.3. **Label Extensions**. If a Party wishes to extend the label or approved indication of any Product Developed hereunder to other indications (including any outside of the Field), it may so notify the JSC. In such event, the JSC shall discuss such label extension in good faith. If the JSC agrees by unanimous consent that Development should be undertaken to support the label extension, the Parties shall include the Development activities required to be undertaken to support



such label extension in the Research and Development Plan and, if appropriate, amend the Field accordingly to cover such extension. Any external cost or expense (other than Capex Cost) incurred by either Party (or its Affiliates) solely and specifically in connection with such Development activities [***].

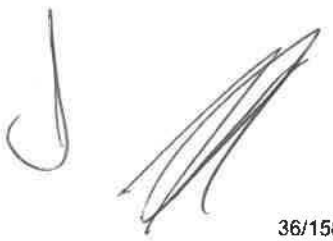
6.3.4. **Subcontractors**. Either Party may subcontract its responsibilities under the binding parts of the Research and Development Plan or those allocated to it by the JSC without the other Party's prior written consent; *provided* that such Party shall be responsible for the management of all permitted subcontractors (which will include any Affiliate of a Party). The engagement of any Third Party subcontractor by a Party shall be in writing. The engagement of any subcontractor (whether Affiliate or Third Party) shall not relieve such Party of its obligations under this Agreement or the binding parts of the Research and Development Plan. Any agreement between the Party or its Affiliate and a subcontractor pertaining to the Research and Development Plan activities shall be consistent with the provisions of this Agreement including (a) an obligation to assign all Intellectual Property Rights generated during its performance of such Research and Development Plan to the Party free of any encumbrance such that the Party may fulfil its obligations hereunder and (b) terms and conditions under which such Third Party is obligated to preserve the confidentiality of the Research and Development Program, Research and Development Program Technology and any Confidential Information are at least as restrictive as those described in Section 11.2.1.

6.3.5. **Flexibility of Resources**. Due to practical consequences arising from the outbreak of the virus that is the subject of the Field, it may become difficult or temporarily impossible (including as classified as a force majeure event) for a Party to fulfil all of its responsibilities under the Research and Development Plan or as allocated to it by the JSC. Accordingly, a Party, in its effort to collaborate, may therefore agree to swap, substitute or perform any of the other Party's responsibilities that were allocated to it in the Research and Development Plan or by the JSC. The JSC shall be responsible for coordinating any such changes, which must be finally approved in writing by the Parties where the change results in a Party taking on additional financial cost and responsibility.

6.3.6. **Personnel Matters**. Each Party acknowledges and agrees that it is solely responsible for the compensation of its personnel assigned to the Research and Development Plan, and shall be responsible for withholding all national, state, local or other applicable taxes and similar items for such personnel. Each Party also shall be responsible for all other of its employer related obligations, including providing appropriate insurance coverage and employee benefits, and making all other deductions required by law affecting the gross wages of each of its employees. BioNTech personnel assigned to the Research and Development Plan activities are not nor shall they be deemed to be employees of Pfizer, and Pfizer personnel assigned to the Research and Development Plan activities are not nor shall they be deemed to be employees of BioNTech.

7. CONTRACT GOVERNANCE.

7.1. Alliance Managers. Each Party will appoint a single individual to act as the primary point of contact between the Parties to support the activities under the Research and Development Plan and the Manufacturing Plan (the "Alliance Managers"). Each Party may change its designated Alliance Manager at any time upon written notice to the other Party. As of the Effective Date, the Alliance Manager for Pfizer will be [***] and the Alliance Manager for BioNTech will be [***]. The Alliance Managers will:



7.1.1. use good faith efforts to attend (either in person or by telecommunications) all meetings of the JSC, but will be non-voting members at such meetings; and

7.1.2. be the first point of referral for all matters of conflict resolution and bring disputes to the attention of the JSC in a timely manner.

7.2. Program Directors. Each Party will appoint a program director to oversee all activities conducted under the Research and Development Plan (each, a "Program Director"). Each Party may change its designated Program Director at any time upon written notice to the other Party. The Program Directors will coordinate the efforts of their respective Party in conducting activities under the Research and Development Plan. As of the Effective Date, the Program Directors for Pfizer and BioNTech are [***], respectively.

7.3. Joint Steering Committee.

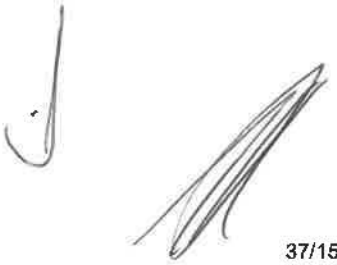
7.3.1. **Composition**. As of the Effective Date, the Parties will establish a Joint Steering Committee, comprised of at least [***] representatives of BioNTech (including the Alliance Manager for BioNTech) and at least [***] representatives of Pfizer (including the Alliance Manager for Pfizer). The JSC representatives for each of Pfizer and BioNTech will be referred to herein as the "Pfizer JSC Members" and the "BioNTech JSC Members" respectively. As of the Effective Date, the Pfizer JSC Members shall be [***] and the BioNTech JSC Members shall [***].

Each Party may replace its representatives to the JSC at any time upon notice to the other Party, *provided that* at all times an equal number of representatives from each Party are appointed to the JSC and each Party shall be responsible for ensuring any replaced representative is fully briefed and apprised of the Research and Development Program. Each Party shall procure that its JSC representatives shall make themselves available to attend JSC meetings upon reasonable notice and in accordance with this Agreement. Each Party may invite non-voting employees and consultants to attend meetings of the JSC. All members of the JSC and any invitees of either Party described above will agree in writing to be bound to obligations of confidentiality and assignment of Intellectual Property Rights no less restrictive than those that bind the Parties under this Agreement.

7.3.2. **Committee Chair**. The JSC will be chaired by a BioNTech JSC Member (the "JSC Chair"). BioNTech may replace the JSC Chair at any time upon notice to Pfizer. The responsibilities of the JSC Chair will be:

7.3.2.1. to notify each Party at least [***] Business Days in advance of each JSC meeting;

7.3.2.2. to collect and organize agenda items for each JSC meeting; and



7.3.2.3. to prepare the written minutes of each JSC meeting and circulate such minutes for review and approval by the Parties and identify action items to be carried out by the Parties.

7.3.3. **Meetings.** Until the initiation of a Phase I Clinical Trial or Expedited Trial Pathway, the JSC shall meet at least weekly, unless otherwise unanimously agreed. Thereafter, the JSC will meet on at least bi-weekly basis (or less or more frequently as the JSC so determines), either in-person or by audio or video teleconference. Meetings of the JSC will occur at such times and places as mutually agreed by the Parties. Any sub-committees or working groups established in accordance with Section 7.3.4 may meet via audio or video teleconference on a regular basis and in-person at such times and places as the Parties may agree. Meetings of the JSC will only occur if at least two representatives of each Party are present at the meeting or participating by teleconference or videoconference. Each Party will be responsible for, and will not be entitled to any reimbursement from the other Party with respect to, any and all personnel costs or expenses (including travel expenses) which are incurred by or on behalf of its personnel in connection with participation in any JSC meetings or sub-committee or working group meetings, or any other travel required to be undertaken by either Party's personnel in connection with the performance of the Agreement. The JSC Chair will use good faith efforts to (a) prepare and circulate to BioNTech and Pfizer each JSC meeting agenda on or before the day prior to the scheduled date for each JSC meeting and (b) circulate for review and approval by BioNTech and Pfizer written minutes of each JSC meeting within [***] Business Days after such meeting. The Parties will agree on the minutes of each meeting promptly, but in no event later than the day before the next meeting of the JSC.

7.3.4. **Responsibilities**. The JSC will coordinate and provide operational and strategic oversight of the Development and Manufacturing activities to be performed under the Research and Development Plan and the Manufacturing Plan by each Party and, within such scope will:

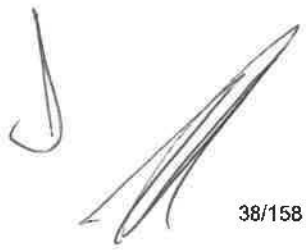
7.3.4.1. review and approve all proposals of whether to seek funding from a Third Party Funder, and the terms of any proposed agreement with a Third Party Funder, which (with the exceptions specified in Section 5.5.2 for [***] and [***]) will require unanimous consent of the JSC;

7.3.4.2. monitor and assess the progress of activities under the Research and Development Plan and the Manufacturing Plan;

7.3.4.3. decide on the Candidates or Products that will be studied in the Clinical Trials;

7.3.4.4. decide on the design of the Clinical Trials, including the protocol governing the Clinical Trials;

7.3.4.5. decide on and revise and approve any revisions of the Research and Development Plan, the Development Budget and the Manufacturing Plan (including in accordance with the mechanism described in Section 6.1 and any adjustments pursuant to Section 6.3.3 and 6.3.5), each of which shall require unanimous consent of the JSC except as expressly set forth in Section 7.3.5;



7.3.4.6. discuss any Intellectual Property Rights of a Third Party which may be relevant to Candidates and Products;

7.3.4.7. oversee the Development of Manufacturing processes relating to the Candidates or Products, establishment of Manufacturing capacity, and endorse a strategy for Manufacturing Candidates and Product for both the Clinical Trials and planned Commercialization;

7.3.4.8. review and discuss all preclinical data and data arising from Clinical Trials investigating the Candidate or Product in the Territory, including adverse events;

7.3.4.9. review and discuss all preclinical data and data arising from Clinical Trials under the Fosun Agreement, including adverse events;

7.3.4.10. form such other committees and sub-committees as the JSC may deem appropriate, such as a Joint Development Committee, a Joint Manufacturing Committee and the like, *provided that* the JSC may, with unanimous consent, delegate decision-making authority (that is within the JSC's own authority) relevant to such committee's and sub-committee's area of expertise only (and the Parties agree that they will form Joint Manufacturing Committee within [***] days of the Effective Date);

7.3.4.11. address such other matters relating to the activities of the Parties under the Research and Development Plan or the Manufacturing Plan as either Party may bring before the JSC, including any matters that are expressly for the JSC to decide as provided in this Agreement;

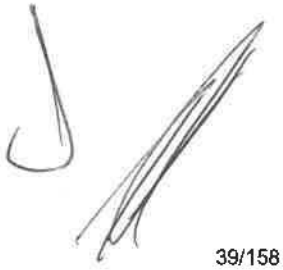
7.3.4.12. agree on a Development Budget, as well as any amendments to such budgets, provided that the Development Budget and any amendments to it shall require unanimous consent of the JSC;

7.3.4.13. discuss, collaborate on and oversee any applications for Regulatory Approvals in respect of the Candidates and Products, both within and outside the Territory;

7.3.4.14. discuss, collaborate on and agree on mutations pursuant to Section 6.3.2 or any label extension pursuant to Section 6.3.3, each of which must be agreed by unanimous consent of the JSC; and

7.3.4.15. attempt to resolve any disputes between the Parties with respect to (a) the performance of activities under the Research and Development Plan or the Manufacturing Plan on an informal basis or (b) matters before the Patent Committee, in each case subject to Section 7.3.5.

7.3.5. **Decision-making.** Notwithstanding the number of Pfizer JSC Members or BioNTech JSC Members, each Party will have one (1) vote, and the JSC will make decisions on a unanimous basis. The JSC will use good faith efforts to reach agreement on any and all matters properly brought before it. If, despite such good faith efforts, the JSC is unable to reach unanimous



agreement on a particular matter, within [***] days after the JSC first meets to consider such matter, or such later date as may be mutually acceptable to the Parties (each such matter, a "Disputed Matter"), then:

7.3.5.1. Pfizer will have final decision making authority in relation to all decisions applicable to the Execution Task where the Decision Making Right is allocated to Pfizer as set out in Schedule 7.3.5; and

7.3.5.2. BioNTech will have final decision-making authority in relation to all decisions applicable to the Execution Task where the Decision Making Right is allocated to BioNTech as set out in Schedule 7.3.5; and

7.3.5.3. all other Disputed Matters (including those for which the Decision Making Right is identified as Mutual) shall be subject to the Parties reaching unanimous or mutual consent (including in respect of the Development Budget).

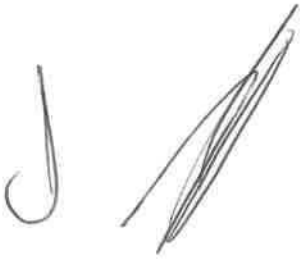
The Parties agree that the JSC will further refine the details of the decision-making rights and processes in accordance with Schedule 7.3.5 and the terms of this Agreement.

7.3.6. **Limits on JSC Authority**. Notwithstanding any provision of this Section 7 to the contrary, (a) each Party will retain the rights, powers and discretion granted to it under this Agreement and no such rights, powers, or discretion will be delegated to or vested in the JSC unless such delegation or vesting of rights is expressly provided for in this Agreement or the Parties expressly so agree in writing, (b) except with respect to modifications to the Research and Development Plan or Manufacturing Plan permitted as set forth in Section 7.3.4.5, the JSC will not have the power to amend this Agreement or otherwise modify or waive compliance with this Agreement in any manner and (c) neither Party will require the other Party to (i) breach any obligation or agreement that such other Party may have with or to a Third Party to the extent such obligation or agreement existed prior to the Effective Date or (ii) perform any activities that are materially different or greater in scope or more costly than those provided for in the Research and Development Plan then in effect. For avoidance of doubt, a joint committee will be formed under the Commercialization Agreement to provide operational and strategic oversight of the Commercialization.

7.3.7. **JSC Term**. The JSC will be dissolved upon expiration of the Term.

7.4. Materials and Permitted Activities.

7.4.1. **Transfer**. From time to time during the Term, Pfizer shall provide BioNTech with tangible chemical or biological materials (the "Pfizer Materials") and BioNTech may provide Pfizer with BioNTech Materials for the other Party's use in accordance with binding parts of the Research and Development Plan. The Party providing its Materials represents and warrants to the other Party that, as of the date of delivery of the Material (a) [***], (b) [***] and (c) [***]. [***].



7.4.2. **Title to Materials.** All right, title and interest in and to the providing Party's Materials (including any modifications or progeny thereof) will remain the sole and exclusive property of such Party notwithstanding the transfer to and use by other Party of the same.

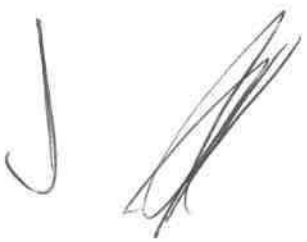
7.4.3. **Permitted Activities.** Notwithstanding anything to the contrary in this Agreement save for each Party's exclusivity obligations and restrictions (including those at Sections 3.1 and 3.10), nothing in this Agreement shall be deemed to prevent or restrict in any way the ability of either Party or its Affiliates to conduct any activities in the Territory, which activities would be allowed under any safe harbor, research exemption, government or executive declaration of urgent public health need, or similar right available in law or equity if conducted by a Third Party.

7.4.4. **Return of Proprietary Materials.** Upon termination or expiration of the Term, each Party receiving the other Party's Materials hereunder shall, either destroy or return all unused Materials to the providing Party.

8. MANUFACTURING

8.1. Development of Manufacture Process. BioNTech and Pfizer shall jointly Develop a scalable process for Manufacture of Candidates and Products in the Field in the Territory in accordance with the binding parts of the Research and Development Plan and the Manufacturing Plan.

8.2. Manufacture of Candidates and Products. Each Party will use Commercially Reasonable Efforts to perform its obligations and activities identified under the binding parts of the Manufacturing Plan or as allocated to it by the JSC in a professional manner in accordance with any target dates set forth in the Manufacturing Plan. Further, each Party will perform its obligations under the binding parts of the Manufacturing Plan or as allocated to it by the JSC in compliance with all Laws applicable to its activities under the Manufacturing Plan. Pfizer and BioNTech will collaborate in the build-up of Manufacturing capacity for the Manufacturing of Candidates and Products for clinical and commercial purposes in accordance with the binding parts of the Manufacturing Plan and the terms and conditions set forth in this Section 8. The Manufacturing Plan may be modified by unanimous consent of the JSC pursuant to Section 7. Unless otherwise agreed in the Manufacturing Plan, at a minimum Pfizer will be responsible for the build-up of its Manufacturing site(s) in the USA for quantities of Product to be agreed as part of the Manufacturing Plan and the commercial supply agreement for such site, and at a minimum BioNTech will be responsible for the extension of its Manufacturing sites in Mainz and Idar-Oberstein for quantities of Product to be agreed as part of the Manufacturing Plan and the commercial supply agreement for such sites. [***] The Manufacturing Plan may also consider one or both Parties engaging Third Party contract manufacturing organizations as a source of Manufacturing. In addition, promptly after the Effective Date, the Parties will agree on a technology transfer plan and continue to perform the technology transfer that the Parties have already started prior to the Effective Date to enable Manufacturing by Pfizer. For the avoidance of doubt, to the extent the technology transferred under this Agreement is identical to the technology to be transferred pursuant to the Flu Collaboration License, the Parties shall cooperate to minimize any duplication of technology transfer efforts under the Flu Collaboration License that unreasonably would be duplicative, wasteful or unnecessary.



8.3. Quality Requirements. Each Party that undertakes or subcontracts any Manufacturing activities in respect of the Candidates or Products, whether for the purposes of this Agreement, the Clinical Trials or pursuant to the commercial supply agreements shall ensure that all Manufacturing activities are undertaken in accordance with (a) applicable GxP standards, applicable Laws, and other regulatory and manufacturing good practice (including record and sample keeping, deviation reporting, testing and quality requirements); and (b) the requirements of the applicable Quality Agreement.

8.4. Manufacturing Agreements.

8.4.1. **Clinical Supply**. Within [***] following the Effective Date, the Parties shall enter into an agreement for clinical supply, as required to ensure the Clinical Trials planned can proceed on the timelines set forth in the binding parts of the Research and Development Plan. All clinical supply of Candidates and Products shall be charged at the Manufacturing Costs. In addition, the Parties will negotiate in good faith and mutually agree on a Quality Agreement with respect to such clinical supply agreement.

8.4.2. **Commercial Supply**. Furthermore, the Parties will negotiate in good faith and mutually agree on one or more commercial supply agreement(s) and Quality Agreement(s) simultaneously with the negotiation of the Commercialization Terms. The commercial supply agreement(s) shall be in accordance with the following commercial terms:

8.4.2.1. The Manufacturing Party shall be entitled to charge the Transfer Price for each batch of Product delivered in accordance with the relevant commercial supply agreement. Such Transfer Price shall be invoiced by the Manufacturing Party upon delivery of the Products and shall be payable by the other Party within [***] from receipt of such invoice.

8.4.2.2. The Transfer Price shall be adjusted on a yearly basis for all commercial supply agreements in accordance with relevant cost developments.

8.4.2.3. The Parties will work together, subject to and observing applicable Laws, and agree the volumes of Product Materials to be purchased from Third Party suppliers for the purposes of this Agreement and to [***] of either Party to source the other Party's requirements for such Product Materials for its Manufacturing activities pursuant to this Agreement and the Commercialization Agreement, which sourced Product Materials shall then be sold, at cost, to that other Party [***].

8.4.2.4. [***]

8.4.3. The supply agreements to be entered into between the Parties pursuant to Sections 8.4.1 and 8.4.2, or the Commercialization Agreements if more appropriate, shall include appropriate accounting mechanisms to allow for true-up payments in respect of (i) Manufacturing Costs, including to account for any mark up on the Manufacturing Costs of Product Materials where permitted in the definition of Manufacturing Costs, and (ii) Manufacturing Variances.

8.5. Allocation of Responsibilities. Section 6.3.1 and Sections 6.3.4 to 6.3.6 shall apply *mutatis mutandis* in respect of each Party's responsibilities under the Manufacturing Plan.

9. DEVELOPMENT, REGULATORY AND PHARMACOVIGILANCE.

9.1. Development Matters.

9.1.1. **Allocation of Development and Regulatory Responsibility.** The Development of Candidates and Products shall be conducted by the Parties, under the direction and oversight of the JSC (and, as applicable, the Joint Development Committee), in accordance with the applicable Research and Development Plan and Development Budget. Pursuant to the initial Research and Development Plan, the Parties shall identify a strategy for Development of the Candidates and Products in the Territory that identifies the Party that is leading the clinical Development of the Candidates or Products in a country in the Territory (the "Lead Development Party"). Notwithstanding the foregoing, the Parties have agreed that (a) Pfizer shall lead the clinical aspects of Development of Candidates and Products in the USA, and (b) BioNTech shall lead the clinical aspects of Development of Candidates and Products in the EU. BioNTech shall be the sponsor and IND/CTA holder for all Clinical Trials in the Territory, in each case, subject to a mutually agreeable strategy with respect to the Development of Candidates and Products. For any Clinical Trial for which Pfizer is the Lead Development Party (but is not the sponsor of such Clinical Trials), BioNTech shall have delegated to Pfizer operational and day-to-day Development activities, decision-making authority and responsibility for such Clinical Trial, including those activities described in Schedule 9.1.1, subject to a protocol approved by unanimous consent by the JSC. For avoidance of doubt, the Lead Development Party shall conduct its Development activities in collaboration with and with active review of the other Party.

9.1.2. **Appointment of Lead Development Party for Future Clinical Trials.** At any time during the term of this Agreement, the JSC may determine by mutual consent that additional clinical Development of the Candidate and Product are warranted and, in such event, unless otherwise agreed by the JSC, (a) Pfizer shall be the Lead Development Party for each additional Clinical Trial in the USA, (b) BioNTech shall be the Lead Development Party for each additional Clinical Trial in the EU and (c) the JSC shall mutually agree on the appointment of one of the Parties to be the Lead Development Party for each additional Clinical Trial on a Clinical Trial-by-Clinical Trial basis in a country or region in the Territory other than the USA and EU ("ROW"), and subject to the mutually agreed upon strategy.

9.1.3. **Clinical Trials.** In respect of Clinical Trials for the Candidates or Products pursuant to this Agreement, the following shall apply:

9.1.3.1. *GxP Standards*. Subject to Section 9.1.3.7, BioNTech as the sponsor for any Clinical Trial in respect of any Candidate or Product pursuant to this Agreement shall ensure the Clinical Trial is conducted in accordance with GxP and all applicable Laws, and will provide to the other Party any significant GxP or non-compliance issues relating to the protocol for such Clinical Trial, which arise or may be identified through monitoring,

9.1.3.2. *Monitoring Plans*. A high-level strategy for monitoring Clinical Trials in respect of any Candidate or Product pursuant to this Agreement will be agreed by the JSC within [***] following the Effective Date. The Lead Development Party of the Clinical Trial will notify the other Party if there are any amendments required to such monitoring plan, and provide such other Party with an opportunity to review and comment on any such amendments, and any amendments shall only be made following approval by the JSC.

9.1.3.3. *IRB/IEC Approval*. BioNTech as the sponsor and Regulatory Approval holder of the Clinical Trials shall ensure that the Clinical Trial is approved by and subject to continuing oversight by an appropriate Institutional Review Board (IRB) or Independent Ethics Committee (IEC), except that BioNTech shall delegate this responsibility to Pfizer for any Clinical Trial for which Pfizer is the Lead Development Party. The Lead Development Party shall provide documentation of both the initial IRB/IEC approval of the final protocol to the other Party and annual renewals of that approval if such renewals are required. To the extent a Party receives notice of any withdrawal or suspension of IRB/IEC approval during the term of this Agreement, it will promptly inform the other Party

9.1.3.4. *Informed Consent*. BioNTech as the sponsor and Regulatory Approval holder for each applicable Clinical Trial will obtain informed consent for each Clinical Trial subject in accordance with the applicable informed consent document and applicable Law and will inform and obtain express consent from each Clinical Trial subject that the data arising from such Clinical Trial may be used in accordance with the terms of this Agreement (including its export from the European Union and its processing by Pfizer or other Third Parties in accordance with the terms of this Agreement and Law), provided however, that BioNTech shall delegate this responsibility to Pfizer for those Clinical Trials for which Pfizer is the Lead Development Party. Notwithstanding the foregoing, the Lead Development Party will share the informed consent document with the other Party for such other Party's review and comment prior to its use in a Clinical Trial in a country in the Territory.

9.1.3.5. *Sponsorship*. Where the Lead Development Party (or its Affiliate or designee) is not the sponsor of a Clinical Trial or Regulatory Approval holder, such Lead Development Party shall not represent to any Third Party, including any Clinical Trial subjects, that the Lead Development Party or its Affiliates are a sponsor.

9.1.3.6. *Reporting*. BioNTech is solely responsible for any and all safety reporting and regulatory obligations associated with the conduct of the Clinical Trial for which it is the sponsor, including, but not limited to, obtaining and maintaining Regulatory Approvals for the conduct of the Clinical Trials, provided, however, that BioNTech shall delegate the safety reporting and regulatory obligations associated with the conduct of each Clinical Trial in the Territory to Pfizer subject to Section 9.3.

9.1.3.7. *Delegation*. Notwithstanding the responsibilities of BioNTech as IND/CTA holder or sponsor of Clinical Trials, where Pfizer is the Lead Development Party for a Clinical Trial Pfizer shall conduct its activities in compliance with GxP and applicable Law with respect to each of the activities which have been delegated to Pfizer pursuant to Schedule 9.1.1.

9.2. Regulatory Matters.

9.2.1. **Lead Development Party.** The JSC shall agree on a strategy to allocate operational responsibility for regulatory activities relating to each Candidate or Product to a Lead Development Party by reference to the country or region within the Territory for which that Party is to act as the Lead Development Party in respect of a Clinical Trial for one or more Candidates or Products. The JSC's initial allocation shall be that Lead Development Party for regulatory activities relating to each Candidate or Product in the EU shall be BioNTech, and the Lead Development Party for regulatory activities relating to each Candidate or Product in the USAshall be Pfizer. Subject to the JSC's mutual consent to seek Regulatory Approval in one or more countries or regions in the ROW, Pfizer shall be the Lead Development Party for regulatory activities relating to each Candidate or Product in such country or region in the ROW. If the JSC cannot agree on whether Regulatory Approval shall be sought for any country or region in the ROW, the Party that wishes to seek Regulatory Approval in such country or region shall be entitled to be the Lead Development Party for regulatory activities relating to each Candidate or Product in such country or region and seek such Regulatory Approval at its own cost. The JSC may vary from the foregoing allocations by mutual consent. The other Party shall cooperate with the Lead Development Party, at its reasonable request, with respect to any regulatory matters for which the Regulatory Approval holder is responsible or to whom regulatory matters have been delegated.

9.2.2. **Regulatory Communications and Filings.** Pfizer shall prepare, file in BioNTech's name, diligently prosecute to grant, and maintain all applications for Regulatory Approvals ("Marketing Authorization Applications") and all Regulatory Approvals obtained therefrom in respect of any Candidates or Products in USA and, subject to Section 9.2.1, the ROW. BionTech shall prepare, file in BioNTech's name, diligently prosecute to grant, and maintain all applications for Marketing Authorization Applications and all Regulatory Approvals obtained therefrom in respect of any Candidates or Products in EU. The JSC may vary from the foregoing allocations by mutual consent. In accordance with Section 9.2.1, each Party shall cooperate with the other Party with respect to any and all regulatory matters for which the other Party is responsible pursuant to this Agreement or the Research and Development Plan. Unless exigent action is required with respect to a given filing before a Regulatory Authority concerning a Candidate or Product, or a material communication with a Regulatory Authority concerning the same, the Party submitting such Marketing Authorization Application shall provide the other Party with copies of all filings relating to such Marketing Authorization Application prior to submission within a reasonable amount of time (but not less than [***] Business Days) to allow such Party to review and comment on such filings, and the Party submitting such Marketing Authorization Application shall consider all comments and proposed revisions from the other Party in good faith prior to submission. The Party responsible for filing such Regulatory Approvals shall consult with the other Party regarding, and keep the other Party informed of, the status of the preparation of all Marketing Authorization Applications and the prosecution thereof, including any material communications

that it receives with respect to the same. Upon request of the other Party, the Lead Development Party responsible for filing applications for such Regulatory Approvals shall provide to the other Party copies of all final Marketing Authorization Applications and filings relating thereto that it submits. The foregoing provisions of this Section 9.2.2 shall also apply to material and substantive communications with Regulatory Authorities.

9.2.3. **Regulatory Meetings.** The Lead Development Party shall consult with the other Party reasonably in advance of the date of any anticipated meeting with a Regulatory Authority relating to any Marketing Authorization Applications or Regulatory Approvals in respect of any Candidate or Product and shall consider any timely and reasonable recommendations made by the other Party in preparation for such meeting. The Parties agree that Pfizer, as the Lead Development Party for the regulatory activities in the USA and ROW shall lead interactions with the Regulatory Authority in the USA and ROW, while BioNTech as the Lead Development Party for the EU, shall lead interactions with the Regulatory Authority in Germany and the EU. The Parties agree that the Party who has been appointed by the JSC as the Lead Development Party shall lead interactions with respect to countries or regions in the Territory. Upon the request of the other Party, and to the extent legally permissible and not opposed by the relevant Regulatory Authority, the Lead Development Party shall permit the other Party to attend any and all meetings with the applicable Regulatory Authority concerning the Candidate or Product. [***]

9.2.4. **Manufacturing Matters.** Where Pfizer is the Lead Development Party and responsible for preparing the filings for Regulatory Approval, BioNTech shall provide all reasonable assistance to Pfizer in such filings, including preparation of the CMC portions of the Common Technical Document in English and supporting ancillary cGMP documents and analytical data as required to meet specific regulatory filing and approval requirements. Each Party shall promptly provide the other with copies of material written correspondence as reasonably necessary to permit each Party to comply with its relevant regulatory obligations described in the Agreement or as otherwise reasonably requested.

9.2.5. **Ownership of Regulatory Filings, Market Authorization Approvals and Pricing and Reimbursement Approvals.** Unless otherwise required under applicable Law or determined by unanimous consent of the JSC (or the JCC with respect to Commercialization Agreement, as applicable), all Regulatory Approvals directed to a Candidate or Product in a country in the Territory and all applications therefor shall be made or held in the name of and owned by BioNTech. Notwithstanding the foregoing BioNTech may, upon giving reasonable notice to Pfizer, elect to transfer to Pfizer or any of its Affiliates one or more Regulatory Approvals in the Territory directed to a Candidate or Product and Pfizer will not withhold its agreement to such transfer if Pfizer or any of its Affiliates is already Commercializing a Pfizer vaccine product in such country and is permitted to hold Regulatory Approvals in such country. Recognizing that the transfer of the foregoing responsibilities or the responsibilities described in 9.2.1 and 9.2.2 and Regulatory Approvals as the case may be requires time, coordination and effort, the Parties will agree a reasonable transition plan for each such transfer and during the transfer period BioNTech shall continue to perform its obligations as Lead Development Party or owner of the Regulatory Approval.

9.2.6. **Notice of Regulatory Investigation or Inquiry.** If any Regulatory Authority (i) contacts a Party with respect to the alleged improper Development, Manufacture, or Commercialization of a Candidate or Product in the Territory, (ii) conducts, or gives notice of its intent to conduct, an inspection at a Party's facilities used in the Development or Manufacturing of a Candidate or Product, or (iii) takes, or gives notice of its intent to take, any other regulatory action with respect to any activity of a Party that could reasonably be expected to adversely affect any Development, Manufacture or Commercialization activities with respect to a Candidate or Product in the Territory, then such Party shall promptly notify the other Party of such contact, inspection or notice. The inspected Party shall provide such other Party with copies of all pertinent information and documentation issued by any such Regulatory Authority within [***] Business Days of receipt, and, to the extent practicable, the JSC or appropriate subcommittee. Such other Party shall have the right to (a) be present at any such inspection, and (b) review and comment upon in advance any responses of the inspected Party that pertain to a Candidate or Product or a Party's activities hereunder.

9.2.7. **Pharmacovigilance and Pharmacovigilance Agreement.**

9.2.7.1. As soon as practicably possible following the Signing Date the Parties shall form a Joint Safety Committee to (a) review and approve each investigator's brochure for the clinical Development of Candidates and Products, (b) review and approve all aggregated data Drug Safety Update Reports, annual IND reports, and other period reports to Governmental Authorities information regarding patient safety (including adverse drug) experiences that are or may be associated with Candidates or Products, (c) review, discuss and agree the outputs of each Party's periodic Candidate and Product related benefit/risk analysis, and (d) such other patient safety-related activities as the Parties may delegate to it from time to time.

9.2.7.2. So long as BioNTech holds the necessary INDs/CTAs/Regulatory Approvals and is acting as sponsor in a country or region in the Territory, BioNTech may initiate clinical Development of the Candidates and Products in the EU prior to the Parties entering into a pharmacovigilance agreement. In such circumstances BioNTech shall be responsible for collecting, monitoring, evaluating, sharing and reporting to applicable Governmental Authorities in the EU information regarding patient safety (including adverse drug) experiences that are or may be associated with Candidates or Products. BioNTech shall be responsible for maintaining a suitable safety database.

9.2.7.3. By no later than the approval of the Investigational New Drug (IND) for Candidate(s) with FDA, the Parties shall have entered into a pharmacovigilance agreement ("Pharmacovigilance Agreement") reflecting the terms set forth in Section 9.3 and Schedule 9.2.7.

9.2.7.4. Following the filing of the IND for Candidate(s) with FDA:

(a) should BioNTech require Pfizer to take over certain activities in relation to collecting, monitoring, evaluating, sharing and reporting to applicable Governmental Authorities, but excluding Ethics Committees, information regarding patient safety (including adverse drug) experiences that are or may be associated with Candidates or Products in the EU, the Parties shall agree and execute an amendment to the Pharmacovigilance Agreement to (i) reflect the additional activities and responsibilities the Parties have agreed Pfizer will perform in the EU, and (ii) set out the procedures the Parties have agreed upon to allow for the reconciliation of BioNTech's safety database with Pfizer's safety database. The effectiveness of the amendment shall be conditional upon BioNTech delivering to Pfizer (x) confirmation from the relevant Governmental Authorities in the EU that they have accepted an amendment to the clinical trial protocol for any on-going clinical trial of Candidates or Product in the EU to reflect the necessary changes (as agreed with Pfizer) in responsibilities and contact information for collecting, monitoring, evaluating, sharing and reporting of information regarding patient safety (including adverse drug) experiences, and (y) written confirmation from BioNTech that it has amended the relevant clinical trial agreements to reflect the change in pharmacovigilance provider and trained the investigators on the new reporting procedures; and,

(b) BioNTech through their Agreement with Fosun shall ensure that Fosun, via BioNTech, deliver to Pfizer (x) a copy of a due diligence report on Fosun's safety data reporting system reasonably acceptable to Pfizer in terms of findings made, (y) a copy of the pharmacovigilance agreement between BioNTech and Fosun which, inter alia, provides for delivery to Pfizer of fully assessed, translated (into English) CIOMS forms for all SAEs: Death / life threatening SUSARs – 5 Business Days from Day 0 (Day 0 being receipt by Fosun from the clinical investigator), or 10 days for all other SAEs, [***] and (z) details of the quality management system used with Fosun to ensure that if late inbound reports are received BioNTech can request root cause analysis and implementation of corrective and preventive actions by Fosun. The Parties agree that prior to Fosun's commencement of clinical activities by Fosun, BioNTech shall have entered into a written agreement with Fosun, reflecting the foregoing.

9.2.7.5. The Pharmacovigilance Agreement and each amendment to it from time to time shall set forth the responsibilities and procedures for (i) collecting, monitoring, evaluating, sharing and reporting to applicable Governmental Authorities information regarding patient safety (including adverse drug) experiences that are or may be associated with Candidates or Products in the countries covered by that agreement and (ii) providing regulatory information to and support of the other Party

with regard to regulatory obligations, provided, that, each such agreement shall include the following guiding principles: acting as BioNTech's delegate for regulatory interactions, Pfizer shall primarily control the regulatory process and regulatory interactions in the countries covered by that agreement, provided, however that the Parties shall work together collaboratively to further the purposes of the collaboration and the activities described in this Agreement. Subject to the proviso in the foregoing sentence, to the extent there is any conflict between the terms and conditions of the Pharmacovigilance Agreement (as amended from time to time) and this Agreement with respect to safety or regulatory matters, the Pharmacovigilance Agreement shall control.

9.2.8. **Audits.** Each Party shall have the right, at its sole cost and expense, to perform audits of the other Party's pharmacovigilance, regulatory, and environmental, health and safety activities concerning any Candidates or Products under this Agreement, including each Party's oversight of any Third Party contracted to perform pharmacovigilance, regulatory or environmental health and safety activities as outlined in this Agreement and in compliance with applicable Laws, which audit right is exercisable at any time during the Term. Upon request, BioNTech shall provide Pfizer with a copy if its latest audit report on Fosun's pharmacovigilance activities.

9.3. Global Safety Database and Safety Reporting. Subject to Section 9.2.7, Pfizer shall maintain the global safety database for the Candidates and Products pursuant to this Agreement and the Commercialization Agreement. Provided that (a) BioNTech (subject to Section 9.1) will be the Lead Development Party with respect to Clinical Trials conducted in the EU, (b) BioNTech will hold a safety database to meet its sponsor responsibilities and regulatory responsibilities in the EU and to hold safety data reports received from China; (c) information shall be exchanged between Pfizer and BioNTech as described in the Pharmacovigilance Agreement to ensure alignment of information between the databases and (d) BioNTech will delegate its responsibilities for the collection, processing, assessment and safety reporting to Regulatory Authorities for all Clinical Trial(s) conducted pursuant to the Research and Development Plan in the Territory upon the approval of the IND for Candidate(s) with FDA. Notwithstanding the foregoing, such responsibility can only be delegated to and Pfizer can only accept this responsibility if the Clinical Trial sites for the Candidates and Products are reporting the safety data, including all individual Serious Adverse Events, translated into English, to Pfizer and for so long as Pfizer has access to all safety data, including all individual Serious Adverse Events, translated into English for any and all active Clinical Trials for the Candidates and Products, including products identical to Candidates or Products conducted under the terms and conditions of the Fosun Agreement (or subsequent agreements with other development partners) to allow Pfizer to meet its regulatory obligations as Lead Development Party in the Territory.

9.4. Product Complaints and Returns. The Parties' rights and obligations with respect to non-conformance and returns of Products shall be governed by, as and to the extent applicable, the applicable supply agreement, the global Quality Agreement, or the Pharmacovigilance Agreement.

9.5. Clinical Trial Register. BioNTech shall, in accordance with Law and its internal policies, register, and publish the summaries and results of, Clinical Trials relating to the Candidate or Product on a clinical trial register maintained by it (or an equivalent register), or as otherwise required by Law. If Pfizer is the Lead Development Party for a Clinical Trial, Pfizer shall prepare such summaries and results in accordance with its internal policies and in a timely manner so as to allow the summaries and results to be published within the mandatory time period, and provide such summaries and results to BioNTech for review and comment. Pfizer will give reasonable consideration to any such comments. BioNTech shall publish such summaries and results on a clinical trial register maintained by it (or an equivalent register), within the mandatory time period.

9.6. Regulatory Exclusivity. The JSC shall oversee the process of applying for and securing exclusivity rights that may be available under the Law of countries in the Territory, including any data or market exclusivity periods such as those periods listed in the FDA's Orange Book or Purple Book (as applicable) or periods under national implementations of Article 10.1(a)(iii) of Directive 2001/EC/83 (including any pediatric exclusivity extensions or other forms of regulatory exclusivity that may be available), and all international equivalents.

9.7. Liability. Subject to Pfizer and its Affiliates compliance with the obligations set forth in Section 9.1.3.7 above, Pfizer and its Affiliates, employees, agents or representatives will not be liable to BioNTech or its Affiliates in respect of any act, omission, default or neglect on the part of Pfizer, its Affiliates, or their respective employees, agents or representatives in connection with the activities undertaken as a Lead Development Party where such activities are undertaken in good faith, unless liability arises from Pfizer's or its Affiliates, employees, agents or representatives gross negligence or willful misconduct.

9.8. Objection Right. Notwithstanding any other provision of this Section 9, as Regulatory Approval holder, BioNTech shall have the right to object to and oppose any intended action of Pfizer as Lead Development Party if BioNTech reasonably believes Pfizer's intended action to be contrary to applicable Law.

9.9. Personal Data. To the extent the Parties shall be required to share Personal Data in connection with this Agreement or the Commercialization Agreement, the Parties shall enter into a legally binding written agreement governing the Parties relationship and their processing activities as required by Applicable Data Protection Law.

10. INTELLECTUAL PROPERTY

10.1. Patent Committee. Within the first [***] following the Effective Date, or as otherwise agreed by the Parties, the Parties will establish a patent committee (the "Patent Committee"), comprised of at least one (1) representative of BioNTech and at least one (1) representative of Pfizer (which representative may be replaced by either Party at any time through written notice to the other Party). The Patent Committee shall coordinate all activities in relation to Patent Rights applicable to the terms of this Agreement. In particular, the Patent Committee shall:

10.1.1. coordinate all activities in relation to the filing and prosecution of Patent Rights relating to this Agreement pursuant to Sections 10.2.1 and 10.3.1 of this Agreement,

10.1.2. discuss any actual, potential or suspected infringement of such Patent Rights pursuant to Section 10.4.1, and

10.1.3. regularly review which BioNTech Patent Rights may be relevant to Candidates and Products.

10.1.4. The Patent Committee shall meet (either in-person or by audio or video conference) as often as determined by the Patent Committee as well as upon the reasonable request of either Party. It is acknowledged that particularly in the case of any Enforcement Action the Patent Committee may need to meet at very short notice and be required to expedite and make decisions very quickly and the Parties shall procure that the Patent Committee shall meet urgently

as quickly as reasonably required in connection with any Enforcement Action. The Patent Committee will be chaired by a Patent Committee member chosen by mutual agreement. The Patent Committee shall operate in good faith and acting reasonably. Sections 7.3.2 and 7.3.3, unless otherwise mutually agreed between the Parties, shall apply *mutatis mutandis*. The Patent Committee will use good faith efforts to reach agreement on all matters properly brought before it. If, despite such good faith efforts, the Patent Committee is unable to reach unanimous agreement on a particular matter, such matter shall be escalated to the JSC for final resolution and decisions of the JSC in this regard must be made by unanimous consent.

10.2. Ownership of Intellectual Property.

10.2.1. **Ownership of Product Technology**. [***]

10.2.2. **Ownership of BioNTech Improvements and Pfizer Improvements**. As between the Parties, (a) BioNTech will own all BioNTech Improvements and (b) Pfizer will own all Pfizer Improvements.

10.2.3. **Ownership of other Research and Development Program Technology**. Except for BioNTech Improvements, Pfizer Improvements and [***] the ownership of other Research and Development Program Technology, will be allocated based on inventorship as defined under the Laws of the United States. Notwithstanding the foregoing, during the Term, and without prejudice to Section 10.3 the Parties (through the Patent Committee) shall cooperate and discuss in good faith with respect to the timing, scope and filing of any Patent Rights claiming or disclosing any Research and Development Program Technology.

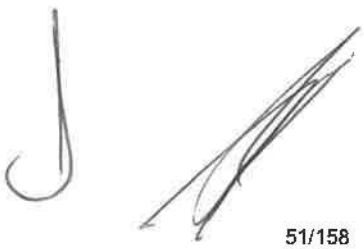
10.2.4. **Ownership of Joint Technology**. Subject to Section 10.2.1, 10.2.2 and 10.2.3, the Parties will jointly own any Joint Technology. Subject to (a) the grant of licenses or sublicenses under Section 3, (b) BioNTech's representations, warranties and covenants under Section 12 and (c) the Parties' other rights and obligations under this Agreement (including Section 3.10), each Party will be free to exploit, either itself or through the grant of licenses to Third Parties (which Third Party licenses may be further sublicensed), Joint Technology throughout the world without restriction, without the need to obtain further consent from or provide notice to the other Party, and without any duty to account or otherwise make any payment of any compensation to the other Party.

10.2.5. **Ownership of Other Intellectual Property**. Except as set forth in Sections 10.2.1, 10.2.4, 10.2.2 and 10.2.1, each Party will own all right, title and interest in and to any and all Know-How, Patent Rights or other Intellectual Property Rights that such Party owns as of the Effective Date or otherwise acquires during the Term. For the purposes of determining ownership under this Agreement, as applicable, inventorship will be determined in accordance with United States patent laws.

10.3. Patent Rights.

10.3.1. **Filing, Prosecution and Maintenance of Patent Rights.**

10.3.1.1. *Prosecution by BioNTech*. BioNTech will have the first right, and a Commercially Reasonable Efforts obligation, to file, prosecute and maintain the BioNTech Patent Rights owned by BioNTech or its Affiliates [***] and Patent Rights claiming BioNTech Improvements (together the "BioNTech Prosecution Patent

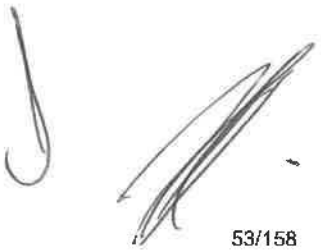


Rights") at BioNTech's sole expense using counsel of its own choice reasonably acceptable to Pfizer in Australia, Canada, the member states of the European Patent Convention including the Major EU Market Countries, Japan, the United States, Brazil, Russia, India, Mexico and South Korea ("Key Patent Jurisdictions"). Upon request of Pfizer, BioNTech shall file one or more BioNTech Prosecution Patent Rights in one or more jurisdictions other than the Key Patent Jurisdictions ("Additional Patent Jurisdictions"), and BioNTech will have the first right, and a Commercially Reasonable Efforts obligation, to file, prosecute and maintain such BioNTech Prosecution Patent Rights in such Additional Patent Jurisdictions at Pfizer's sole expense (until such time as Pfizer elects not to maintain such Patent Rights in such Additional Patent Jurisdictions whereupon BioNTech can elect to abandon or surrender the same or to continue the prosecution and maintenance of such Patent Rights at its own expense) using counsel of its own choice reasonably acceptable to Pfizer. BioNTech will keep Pfizer advised on the status of the preparation, filing, prosecution, and maintenance of the Patent Rights included within BioNTech Prosecution Patent Rights in all the jurisdictions where filed. Further, in respect of any jurisdiction, BioNTech will (a) allow Pfizer a reasonable opportunity and reasonable time to review and provide comments to BioNTech's patent counsel regarding relevant substantive communications to BioNTech and drafts of any responses or other proposed substantive filings by BioNTech before any applicable filings are submitted to any relevant patent office (or Governmental Authority) with respect to any BioNTech Prosecution Patent Rights and (b) reflect any reasonable and timely comments offered by Pfizer in any final filings submitted by BioNTech to any relevant patent office (or Governmental Authority) with respect to any BioNTech Prosecution Patent Rights. If BioNTech elects not to file a Patent Right included in the BioNTech Prosecution Patent Rights in any Key Patent Jurisdiction or Additional Patent Jurisdiction or elects to cease the prosecution or maintenance of one or more Patent Rights included in the BioNTech Prosecution Patent Rights in any Key Patent Jurisdiction or Additional Patent Jurisdiction and, as relevant, no Third Party has agreed to continue the prosecution or maintenance of such Patent Rights under agreements concluded before the Effective Date, BioNTech will provide Pfizer with written notice of its decision not to file, prosecute or maintain not less than [***] before any action is required to avoid abandonment or lapse. In the event of any such notice, if Pfizer elects to file or continue such prosecution or maintenance in the name of BioNTech at Pfizer's sole expense, (x) Pfizer shall be entitled to do so and take all steps in such prosecution and maintenance at its sole discretion; (y) BioNTech will reasonably cooperate to promptly transfer the necessary files and execute the necessary forms regarding such transfer and (z) Pfizer will keep BioNTech advised on the status of such filing, prosecution and maintenance and will reasonably consider any comments made by BioNTech in connection therewith. If Pfizer elects not to file or continue such prosecution or maintenance, then BioNTech may immediately abandon, allow to lapse, or omit to prosecute such Patent Right, as the case may be. BioNTech will promptly, and no later than [***] after written request by Pfizer, by written notice to Pfizer update Schedule 12.3.4 to identify all BioNTech Patent Rights to be added thereto.

10.3.1.2. *Other Patent Rights*. Except as provided in Section 10.3.1.1, each Party will have the sole right, but not the obligation, to file, prosecute and maintain the Research and Development Program Patent Rights or other Patent Rights that it solely owns under this Agreement or to which it otherwise has control of prosecution rights in its sole discretion, provided that at a Party's reasonable request, the other Party will provide status or other requested information for any Research and Development Program Patent Right and will consider in good faith any recommendations made by such Party in regard to the filing, prosecution or maintenance of any such Patent Right.

10.3.1.3. *Reference of Research and Development Program Know-How*. If a Party chooses to file, and thereafter prosecute and maintain, Patent Rights after the expiration of the Term, including any extension to the Term, that Party may use or incorporate Research and Development Program Know-How in the filing or prosecution of such Patent Rights filed after the Term, if it determines in its sole discretion that it is necessary or useful to use or incorporate such Research and Development Program Know-How.

10.3.2. **Joint Patent Rights**. In the event the Parties make any Joint Know-How, the Parties will promptly meet to discuss and determine, based on mutual consent, whether to seek patent protection thereon. Neither Party will file any Joint Patent Right without mutual consent. Unless otherwise agreed between the Parties, if the Parties decide to seek patent protection for any Joint Know-How: (a) BioNTech will have the first right, but not the obligation, to prepare, file, prosecute and maintain any Joint Patent Right predominantly relating to the RNA Technology or RNA Process Technology throughout the world, and (b) Pfizer will have the first right, but not the obligation, to prepare, file, prosecute and maintain any other Joint Patent Right throughout the world, in each case of (a) and (b) with the respective provisions of Section 10.3.1.1 to apply *mutatis mutandis* except as provided in this Section 10.3.2. The non-filing Party will reimburse the filing Party for 50% of the costs reasonably incurred by the filing Party in preparing, filing, prosecuting and maintaining such Joint Patent Rights, which reimbursement will be made pursuant to, and within 75 days of, invoices (including supporting documentation) submitted by the filing Party to the non-filing Party no more often than once per Pfizer Quarter. The non-prosecuting Party will cooperate with the prosecuting Party in taking reasonable measures to control costs and non-prosecuting Party shall be responsible for 100% of (x) any fees or costs related to any correspondence of outside counsel with or instructions to outside counsel by such Party (or any of such Party's Representatives) which is independent of joint prosecution efforts, or (y) any patent office fees, and associated counsel/agent fees and costs, for extensions which are not incurred at the request of, and not due to the actions of, the prosecuting Party. If, once the Parties have agreed to prepare and file an application of Joint Patent Rights, either Party (the "Declining Party") at any time thereafter declines to participate in the preparation, filing, prosecution or maintenance of any Joint Patent Right or share in the costs of filing, prosecuting and maintaining any Joint Patent Right, on a country-by-country basis, the Declining Party will provide the other Party (the "Continuing Party") with 30 days prior written notice to such effect, in which event, the Declining Party will (A) have no responsibility with respect to the filing, prosecution or maintenance of the applicable Joint Patent Right after the end of such 30 day period, (B) have no responsibility for any expenses incurred in connection with such Joint Patent Right after the end of such 30 day period and (C) if



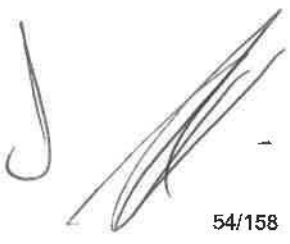
the Continuing Party elects to continue filing, prosecution or maintenance, the Declining Party, upon the Continuing Party's request, will execute such documents and perform such acts, at the Continuing Party's expense, as may be reasonably necessary (1) to assign to the Continuing Party all of the Declining Party's right, title and interest in and to such Joint Patent Right and (2) to permit the Continuing Party to file, prosecute and maintain such Joint Patent Right at its sole expense. Where such Joint Patent Right is assigned to Pfizer as the Continuing Party, BioNTech will retain a non-exclusive, sublicensable, perpetual, irrevocable, royalty-free, fully paid-up worldwide right and license to practice and exploit such Patent Right for any and all purposes excluding, during the Term, in the Field; and where such Joint Patent Right is assigned to BioNTech as the Continuing Party, it will be excluded from the definition of BioNTech Patent Rights, and Pfizer will retain a non-exclusive, sublicensable, perpetual, irrevocable, royalty-free, fully paid-up worldwide right and license to practice and exploit such Joint Patent Right for any and all purposes.

10.3.3. **Prosecution by Third Party Licensors**. Except in the ordinary course of filing continuation applications, BioNTech shall not decline to pay for or participate in the filing, prosecution or maintenance of any Patent Right under any BioNTech Third Party Agreement in any Key Patent Jurisdiction (or other country to the extent doing so may result in BioNTech's loss of license to such Patent Right in such country), to the extent BioNTech is obligated to pay for, or has the right to participate in, such filing, prosecution or maintenance, that is included in the BioNTech Patent Rights and that, in Pfizer's reasonable opinion, covers any Candidate, Product or [***] in the Field in the Territory, and the loss of which would result in loss of right to or would materially diminish the overall protection of such Candidate or Product, without Pfizer's prior written consent, not to be unreasonably withheld or delayed.

10.3.4. **Patent Term Restoration and Extension**. Upon the request of either Party, the Parties will (through the Patent Committee) reasonably discuss patent term extension and supplemental protection certificate strategies in relation to Patent Rights Covering Candidates or Products at any time. Notwithstanding the above, within the time period specified by applicable Law upon receiving Regulatory Approval for a Product in any country in the Territory, [***]. [***]

10.3.5. **Clarifications**. For clarity, prosecution under this Section 10.3 includes opposition, revocation and post-grant review proceedings before the granting patent office or other patent office proceedings ("Prosecution Proceeding"). If such Prosecution Proceedings are concurrent with Third Party litigation under Section 10.4 and are applicable to or part of a coordinated enforcement of such rights, the prosecuting Party and the enforcing Party shall work together and closely align their prosecution and enforcement strategy in accordance with Section 10.5 (including the right for one Party to have final control as stipulated in Section 10.5).

10.3.6. **Liability**. To the extent that a Party is obtaining, prosecuting or maintaining a Patent Right or otherwise exercising its rights under this Section 10.3, such Party, and its Affiliates, employees, agents or representatives, will not be liable to the other Party in respect of any act, omission, default or neglect on the part of any such Party, or its Affiliates, employees, agents or representatives, in connection with such activities undertaken in good faith.



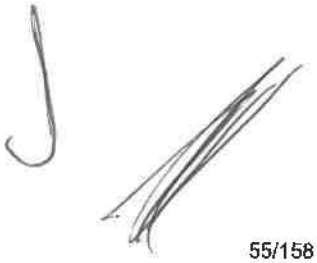
10.3.7. **Recording**. If either Party deems it necessary or useful to register or record this Agreement or evidence of this Agreement with any patent office or other appropriate Governmental Authority(ies) in one or more jurisdictions, the other Party will reasonably cooperate to execute and deliver to such Party any documents accurately reflecting or evidencing this Agreement that are necessary or useful, in such Party's reasonable judgment, to complete such registration or recordation.

10.3.8. **Joint Research Agreement**. This Agreement shall be understood to be a joint research agreement under 35 U.S.C. § 103(c)(3) for pre-AIA Patent Rights and 35 U.S.C. § 100(h) for post-AIA Patent Rights entered into for the purpose of researching, identifying and Developing Candidates and Products.

10.4. Enforcement of Patent Rights.

10.4.1. **Notification of Infringement and Decision about Enforcement Actions**. Each Party will promptly notify the other (through the Patent Committee) in the event of any actual, potential or suspected infringement of a patent under the BioNTech Patent Rights or Research and Development Program Patent Rights by any Third Party. In the event of any such notification, the Parties will (through the Patent Committee) discuss in good faith the relevant actual, potential and suspected infringement and the risks and chances of success as well as chances of settlement connected with the institution of any litigation or other step to remedy infringement (any such steps, or threat of or assertion or enforcement of a Patent Right being an "Enforcement Action") taking into account the possible uses of the relevant Patent Rights by each Party, its respective Affiliates or its or their licensees and the revenues relating to or impacted by such Patent Rights, with the goal to agree on whether or not any Enforcement Action should be taken and, if yes, to closely coordinate so far as reasonably possible their respective efforts and strategies. The Parties acknowledge that time shall be of the essence in connection with any Enforcement Action and each shall move urgently and expeditiously to discuss and seek agreement on any actual or proposed Enforcement Action.

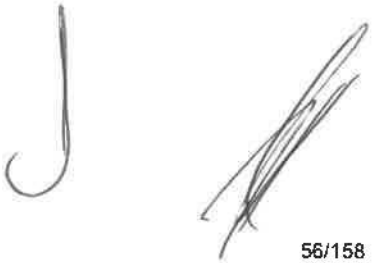
10.4.2. **Enforcement of BioNTech Patent Rights and Product Patent Rights**. Subject to Section 10.4.1, and unless otherwise agreed between the Parties on a case-by-case basis, as between Pfizer and BioNTech, BioNTech shall have the first right, but not the obligation, to institute any Enforcement Action in connection with the BioNTech Patent Rights [***] in the Field in the Territory (the "BioNTech Enforcement Patent Rights"), and any such Enforcement Action will be at BioNTech's expense including BioNTech indemnifying and holding harmless Pfizer and its Affiliates from and against any adverse cost award, where Pfizer or its Affiliates consent to join any such Enforcement Action upon BioNTech's request, or where required by Law or where Pfizer or its Affiliates are enjoined by the counterparty. BioNTech shall not name as a party Pfizer or its Affiliates in any Enforcement Action without Pfizer's prior written consent. In any event, BioNTech will not, without the prior written consent of Pfizer, enter into any compromise or settlement relating to such litigation that (a) admits the invalidity or unenforceability of any BioNTech Enforcement Patent Right or (b) requires BioNTech to abandon any BioNTech Enforcement Patent Right. Upon the request of BioNTech, Pfizer shall have the sole discretion to decide whether or not to join as a party in any such Enforcement Action, and where it elects to do so it shall, at BioNTech's expense, join and cooperate with BioNTech in such Enforcement Action. Pfizer will have the right to consult with, and provide comments to, BioNTech about such Enforcement Action (irrespective of Pfizer or its Affiliate being a party to such Enforcement



Action), and to participate in and be represented by independent counsel in such Enforcement Action at Pfizer's own expense, and BioNTech shall take into account any reasonable comments provided by Pfizer in such Enforcement Action. Neither Party will incur any liability to the other Party (other than that related to a Party's indemnification obligation pursuant to Section 15) as a consequence of any Enforcement Action initiated or pursued pursuant to this Section 10.4 or any unfavorable decision resulting therefrom, including any decision holding any BioNTech Enforcement Patent Rights invalid or unenforceable. Any infringement recoveries resulting from such litigation or steps relating to a claim of Third Party infringement, after deducting BioNTech's out of pocket expenses (including counsel fees and expenses including any adverse cost award) in pursuing such claim, will be treated as Gross Profits for the purposes of the Commercialization Agreement.

10.4.3. **Pfizer's Enforcement Rights**. In respect of an infringement of any BioNTech Enforcement Patent Right in the Field in the Territory in connection with a Competitive Product ("Competitive Product Infringement"), if, following (a) discussion of any potential Enforcement Action pursuant to Section 10.4.1 and (b) a subsequent written request by Pfizer to initiate any Enforcement Action in connection with such Competitive Product Infringement, BioNTech does not initiate any Enforcement Action in connection with such Competitive Product Infringement within thirty (30) days following receipt of such notices, or as soon as possible and in any event no later than ten (10) Business Days if preliminary injunction proceedings are a potential or likely recourse to remedy the infringement), or ten (10) days before the time limit, if any, set forth in the applicable Laws for the filing of such actions, Pfizer shall have the right, but not the obligation, in place of BioNTech to institute any Enforcement Action in connection with such Competitive Product Infringement and any such Enforcement Action will be at Pfizer's expense and the provisions set forth in the first paragraph of this Section 10.4.2 shall apply *mutatis mutandis*. Pfizer's rights with respect to an Enforcement Action for BioNTech Enforcement Patent Rights other than Product Patent Rights shall be limited to (i) Major Market Countries; (ii) Enforcement Actions in countries in which a Competitive Product (or part thereof) reasonably believed to be designated for any Major Market Country is Manufactured; and (iii) Enforcement Actions in Belgium, Ireland or the Netherlands that are in parallel with Enforcement Actions in any of the Major EU Market Countries. [***]

10.4.4. **BioNTech Enforcement outside the Field and/or outside the Territory**. Subject to Section 10.4.1 and unless otherwise agreed between the Parties on a case-by-case basis, as between Pfizer and BioNTech, BioNTech shall have the sole right, but not the obligation, to institute any Enforcement Action outside the Field and/or outside the Territory in connection with any BioNTech Enforcement Patent Rights), and any such Enforcement Action will be at BioNTech's expense including BioNTech indemnifying and holding harmless Pfizer and its Affiliates from and against any adverse cost award, where Pfizer or its Affiliates consent to join any such Enforcement Action upon BioNTech's request, where required by Law or where Pfizer or its Affiliates are enjoined by the counterparty. BioNTech shall not name as a party Pfizer or its Affiliates in any Enforcement Action without Pfizer's prior written consent. In any event, BioNTech will not, without the prior written consent of Pfizer, enter into any compromise or settlement relating to such Enforcement Action that (i) admits the invalidity or unenforceability of any BioNTech Enforcement Patent Rights or (ii) requires BioNTech to abandon any BioNTech Enforcement Patent Rights. Upon the request of BioNTech, Pfizer shall have the sole discretion to decide whether or not to join as a party in any such Enforcement Action, and where it elects to do so it shall, at BioNTech's expense, join and cooperate with BioNTech in such Enforcement Action.



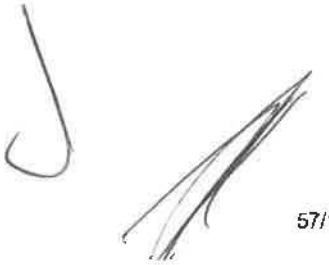
Pfizer will have the right to consult with, and provide comments to, BioNTech about such Enforcement Action (irrespective of Pfizer or its Affiliate being a party to such Enforcement Action), and to participate in and be represented by independent counsel in such Enforcement Action at Pfizer's own expense, and BioNTech shall take into account any reasonable comments provided by Pfizer in such Enforcement Action. Neither Party will incur any liability to the other Party (other than that related to a Party's indemnification obligation pursuant to Section 15 or otherwise in this sub-section) as a consequence of any Enforcement Action initiated or pursued pursuant to this Section 10.4.3 or any unfavorable decision resulting therefrom, including any decision holding any BioNTech Enforcement Patent Rights invalid or unenforceable.

10.4.5. **Pfizer Patent Rights.** Pfizer shall have the sole right, but not the obligation, to institute litigation or take other steps to remedy infringement in connection with any field in respect of any Patent Rights that it solely owns including any Pfizer Patent Right. In the event that any such Patent Rights are based on inventions made or created solely or jointly by BioNTech, its Affiliates or its Representatives acting on BioNTech's behalf, BioNTech shall provide reasonable assistance to Pfizer at Pfizer's expense in connection with such litigation.

10.4.6. **Biosimilar Notices.**

10.4.6.1. *BioNTech Cooperation*. Upon Pfizer's request, BioNTech and Pfizer will use Commercially Reasonable Efforts to assist and cooperate with each other in (A) establishing a strategy for responding to requests for information from Regulatory Authorities and Third Party requestors and (B) preparing submissions responsive to any Biosimilar Notices received by Pfizer or BioNTech; *provided* that BioNTech will make the final decisions with respect to such strategy and any such responses.

10.4.6.2. *Compliance with Biosimilar Notices*. The MA Holder will have the sole right in its discretion to comply with the applicable provisions of 42 U.S.C. § 262(l) (or any amendment or successor statute thereto), any similar statutory or regulatory requirement enacted in the future regarding biologic products in the United States, or any similar statutory or regulatory requirement in any non-U.S. country or other regulatory jurisdiction, in each case, with respect to any Biosimilar Notice received from any Third Party regarding any Product that is being Commercialized in the Field in the Territory in the applicable jurisdiction, and the exchange of information between any Third Party and such MA Holder pursuant to such requirements; *provided that*, prior to any submission of information by MA Holder to a Third Party, the other Party will have the right to review the patent information included in such proposed submission, and to make suggestions as to any changes to such patent information that Pfizer reasonably believes to be necessary; *provided further* that MA Holder will determine the final content of any such submission. In the case of a Product approved in the United States under the PHS Act (or, in the case of a country in the Territory other than the United States, any similar Law), to the extent permitted by applicable Law, the MA Holder, as the sponsor of the application for the Product, will be the "reference product sponsor" under the PHS Act. The MA Holder will give written notice to the other Party of receipt of a Biosimilar Notice received by MA Holder with respect to a Product, and MA Holder will consult with the other Party

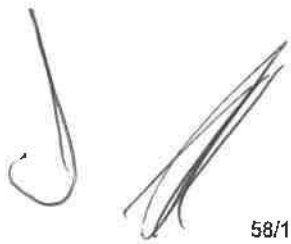


with respect to the selection of any Patent Rights to be submitted pursuant to 42 U.S.C. § 262(l) (or any similar law in any country of the Territory outside the United States); *provided* that the MA Holder will have final say on such selection of Patent Rights. Such other Party agrees to be bound and will cause its Affiliates and use Commercially Reasonable Efforts to cause all Third Party Licensors to be bound by the confidentiality provisions of 42 U.S.C. § 262(l)(1)(B)(iii). In connection with any action brought by such other Party under this Section 10.4.6, such other Party, upon the MA Holder's request, will reasonably cooperate and will cause its Affiliates and use Commercially Reasonable Efforts to cause all Third Party Licensors to reasonably cooperate with MA Holder in any such action, including timely commencing or joining in any action brought by MA Holder under this Section 10.4.6.

10.4.7. **Unified Patent Court.** In respect of BioNTech Enforcement Patent Rights, for each and every such Patent Right having effect anywhere within any member state that was or is, from time to time, a signatory to the UPC Agreement, BioNTech shall have the sole discretion to decide whether to (a) opt in or opt out (and to opt in again), pursuant to Article 83 of the UPC Agreement, of the Unified Patent Court system; and (b) elect if such Patent Rights should, during their prosecution, be designated as a Unitary Patent or a European Patent. The other Party shall promptly do all things necessary and execute all documents and make all necessary elections required to give effect to such decision(s) or election(s).

10.4.8. **Settlement Cross-Licensing**. If pursuant to a bona fide settlement of any Enforcement Action or Infringement Claim controlled by Pfizer, Pfizer, with BioNTech's prior written consent, which shall not be unreasonably withheld, conditioned or delayed, grants to a Third Party (that was a party to the Enforcement Action or Infringement Claim) any sublicense to any of the Patent Rights licensed to Pfizer under this Agreement in respect of that Third Party's Competitive Product, then Pfizer shall pay to BioNTech (a) at a minimum, if such sublicense includes any of the rights granted to Pfizer under a Current License or future BioNTech Third Party Agreement (subject to Sections 3), all royalties due by BioNTech to the relevant Third Party for such sublicense under any Current License and Future BioNTech Third Party Agreement in respect of licensed sales of such Third Party Competitive Product and (b) all other royalties received by Pfizer shall be deemed Gross Profits. For the avoidance of doubt, should the Third Party as part of the same agreement grant any cross-license to Pfizer (sublicensable to BioNTech for the purposes of this Agreement) for any Candidates or Products, such cross-license shall not be deemed "non-cash" consideration for the purpose of the Net Sales definition.

10.5. Other Actions by Third Parties. Separate from Prosecution Proceedings, each Party will promptly notify the other Party in the event of any legal action by any Third Party involving any BioNTech Enforcement Patent Rights of which it becomes aware, including any nullity, revocation, declaratory judgment, interference, *inter partes* reexamination, reexamination or compulsory license proceeding. The right to defend against any such action shall be with the Party controlling the filing, prosecution and maintenance of the affected Patent Right (as determined in accordance with Section 10.3.1), and the provisions of Section 10.3.1 shall apply *mutatis mutandis* in respect of such defense. If any such action has been instituted by any Third Party in response to, or in connection with, any Enforcement Action pursuant to Section 10.4, or any Enforcement Action is to be pursued as a consequence of such action being instituted by any Third Party, the Party controlling the Enforcement Action and the Party controlling the defense shall work together and closely align their enforcement and defense strategy, which may include the (joint) appointment of the same patent counsel for all concurrent Third Party litigation and patent office proceedings taking into account the impact on enforcement and potential for revenues relating to such



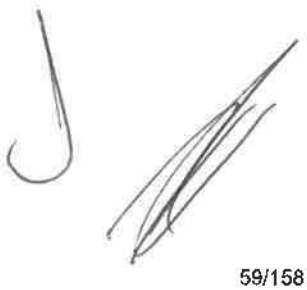
Patent Rights, and in the absence of agreement, the enforcing Party shall have the final say over the Prosecution Proceedings in so far as the Prosecution Proceeding will adversely impact the ongoing enforcement of such right, subject to having given good faith consideration to the comments and suggestions of the prosecuting Party. Further details of such joint proceeding may be agreed between the Parties from time to time.

10.6. Purple Book Listings. To the extent of any BioNTech Enforcement Patent Rights, the Parties shall cooperate with each other to enable BioNTech to make filings with Regulatory Authorities, as required or allowed in connection with (a) in the United States, the FDA's Purple Book and the Biologics Price Competition and Innovation Act and (b) outside the United States, under the national implementations of Article 10.1(a)(iii) of Directive 2001/EC/83 or other international equivalents thereof within the Territory. Pfizer shall consider BioNTech's reasonable requests in connection therewith, including meeting any submission deadlines, in each case, to the extent required or permitted by applicable Law.

10.7. Allegations of Infringement and Right to Seek Third Party Licenses.

10.7.1. **Notice.** If either Party becomes aware that the Development, Manufacture, Commercialization or use of any Candidate or Product, the practice of any BioNTech Technology or Research and Development Program Technology in the Field, or the exercise of any other right granted by BioNTech to Pfizer or any of its Affiliates or Sublicensees hereunder (collectively, the "Licensed Activities") is alleged by a Third Party to infringe, misappropriate or otherwise violate such Third Party's Patent Rights or other Intellectual Property Rights or either Party otherwise identifies any Third Party Patent Rights or other Intellectual Property Rights that may be relevant to such Licensed Activities (collectively, an "FTO Action"), such Party will, as soon as reasonably practicable, notify the other Party in writing and the Parties will discuss the FTO Action in good faith to determine and agree upon a resolution of the same.

10.7.2. **Option to Negotiate.** If the Parties determine that to resolve the FTO Action it is necessary or useful to obtain a license under one or more Patent Rights or other Intellectual Property Rights Controlled by a Third Party, then [***]; will negotiate and enter into a license or other agreement with such Third Party in close coordination with the other Party. If the Parties do not agree that a license from a Third Party is necessary or useful to resolve the FTO Action, the Party who considers a license is necessary or useful to resolve the FTO Action shall be entitled to negotiate and enter into a license or other agreement with such Third Party, but shall do so keeping the other Party reasonably informed. [***] [***].



10.8. Third Party Infringement Suits. Each of the Parties will promptly notify the other in the event that any Third Party files any suit or brings any other action alleging patent infringement by Pfizer or BioNTech or any of their respective Affiliates or Sublicensees with respect to the Development, Manufacture, Commercialization or use of any Candidate or Product or the practice of any BioNTech Technology or Research and Development Program Technology (any such suit or other action referred to herein as an "Infringement Claim"). In the case of any Infringement Claim against Pfizer (including its Affiliates or Sublicensees) alone, or against both Pfizer and BioNTech (including their respective Affiliates), Pfizer will have the right, but not the obligation, to control the defense of such Infringement Claim, including control over any related litigation, settlement, appeal or other disposition arising in connection therewith. BioNTech, upon request of Pfizer, agrees to cooperate with Pfizer at Pfizer's expense. BioNTech will have the right to consult with Pfizer concerning any Infringement Claim and to participate in and be represented by independent counsel in any associated litigation in which BioNTech is a party at BioNTech's own expense. If Pfizer elects to control the defense of any Infringement Claim and BioNTech is obligated under Section 15.3 to indemnify Pfizer (including any Pfizer Indemnified Party) with respect to such Infringement Claim, then (a) Pfizer will bear 100% of its own attorneys' fees incurred in investigating, preparing or defending such Infringement Claim notwithstanding the provisions of Section 15.3 and (b) BioNTech will otherwise indemnify Pfizer and any applicable Pfizer Indemnified Parties to the full extent provided for under Section 15.3, provided that Pfizer shall not enter into any compromise or settlement with the Third Party in respect of such Infringement Claim without BioNTech's prior written consent (such consent not to be unreasonably withheld, conditioned or delayed) where such compromise or settlement requires the payment of monetary penalty or damages that are indemnified by BioNTech under this Agreement. In the case of any Infringement Claim against BioNTech alone, Pfizer will have the right to consult with BioNTech concerning such Infringement Claim and Pfizer, upon request of BioNTech, will reasonably cooperate with BioNTech at BioNTech's expense. Neither Party will enter into any compromise or settlement in respect of an Infringement Claim admitting or implying that the Development, Manufacture, Commercialization or use of any Candidate or Product or the practice of any BioNTech Technology or Research and Development Program Technology infringes Third Party patents without the other Party's written consent.

11. CONFIDENTIALITY

11.1. Confidentiality. Except to the extent expressly authorized by this Agreement, the Parties agree that, during the Term and for [***] years thereafter (except to the extent a longer period is required by a Current License applicable for such Confidential Information disclosed pursuant to that Current License), each Party (the "Receiving Party") receiving any Confidential Information of the other Party (the "Disclosing Party") hereunder will: (a) keep the Disclosing Party's Confidential Information confidential; (b) not disclose, or permit the disclosure of, the Disclosing Party's Confidential Information; and (c) not use, or permit to be used, the Disclosing Party's Confidential Information for any purpose other than as expressly permitted under the terms of this Agreement (including under any license or right of use granted hereunder).

11.2. Authorized Disclosure.

11.2.1. **Disclosure to Party Representatives**. Notwithstanding the foregoing provisions of Section 11.1, the Receiving Party may disclose Confidential Information belonging to the Disclosing Party to the Receiving Party's Representatives who (a) have a need to know such Confidential Information in connection with the performance of the Receiving Party's obligations or the exercise of the Receiving Party's rights under this Agreement and (b) have agreed in writing to non-disclosure and non-use provisions with respect to such Confidential Information that are at least as restrictive as those set forth in this Section 10.1.

11.2.2. **Disclosure to Third Parties.** Notwithstanding the foregoing provisions of Section 11.1, each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary:

11.2.2.1. to Governmental Authorities to the extent useful, to (a) obtain or maintain Regulatory Approvals for any Candidate or Product within the Territory; or (b) obtain or maintain Regulatory Approvals for a product comprising a Candidate in the Field outside of the Territory; and (c) in order to respond to inquiries, requests or investigations (i) relating to Candidates or Products or this Agreement within the Territory; or (ii) relating to any product comprising a Candidate in the Field outside of the Territory; *provided, however*, that BioNTech may not disclose any Pfizer Confidential Information to Fosun or its Affiliates without the prior written consent of Pfizer, other than to the extent necessary for Fosun or its Affiliates (or , such other collaboration partner in or for China) to undertake fill/finish of a product identical to any Product in China or to comply with information requirements of the China National Medical Products Administration relating to such product required under applicable Law, in each case so far as such use is licensed under Sections 3.4.2(b) or 3.4.4(b);

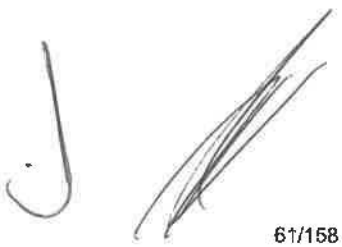
11.2.2.2. to outside consultants (including any professional advisor), potential acquisition partners (including any potential successors in interest), private investors or financing sources, contractors, advisory boards, managed care organizations, and non-clinical and clinical investigators, in each case to the extent useful to develop, register or market any Candidate or Product within the Territory; *provided* that the Receiving Party will obtain the same confidentiality obligations from such Third Parties as it obtains with respect to its own similar types of confidential information;

11.2.2.3. in connection with filing or prosecuting Research and Development Program Patent Rights, Product Patent Rights or Trademark rights as permitted by this Agreement;

11.2.2.4. in connection with any prosecution or litigation actions or defenses undertaken pursuant to Section 10 or any other litigation directly related to a Candidate or Product in the Field in the Territory;

11.2.2.5. subject to the provisions of Section 11.5.2, in connection with or included in scientific presentations and publications relating to Candidates or Products, including abstracts, posters, journal articles and the like, and posting results of and other information about clinical trials to clinicaltrials.gov or PhRMA websites;

11.2.2.6. by either Party in respect of Confidential Information belonging to the other Party (including the terms of the Agreement) to any bona fide or potential subcontractor under this Agreement in connection with the Development of the Candidate or Product in the Territory, in each case who has agreed in writing to non-disclosure and non-use provisions with respect to such Confidential Information that are at least as restrictive as those set forth in this Section 10.1; and



11.2.2.7. to the extent necessary or useful in order to enforce its rights under this Agreement.

Notwithstanding anything herein to the contrary, each Party acknowledges and agrees that the use by a Party of the other Party's Confidential Information disclosed under the Flu Collaboration License in the performance of this Agreement is not a breach of the confidentiality obligations under this Agreement or the Flu Collaboration License, and vice versa. If a Party deems it reasonably necessary to disclose Confidential Information belonging to the other Party pursuant to clause (a) or any of clauses (c) through (e) of this Section 11.2.2, then the Disclosing Party will to the extent possible give reasonable advance written notice of such disclosure to the other Party and take such measures to ensure confidential treatment of such information as is reasonably required by the other Party, at the other Party's expense.

11.3. SEC Filings and Other Disclosures. Either Party may disclose the terms of this Agreement and make any other public written disclosure regarding the existence of, or performance under, this Agreement, to the extent required, in the reasonable opinion of such Party's legal counsel, to comply with (a) applicable Law, including the rules and regulations promulgated by the United States Securities and Exchange Commission or (b) any equivalent Governmental Authority, securities exchange or securities regulator in any country. Before disclosing this Agreement or any of the terms hereof pursuant to this Section 11.3, the Parties will consult with one another on the terms of this Agreement to be redacted in making any such disclosure, with the Party disclosing pursuant to this Section 11.3 providing as much advance notice as is feasible under the circumstances, and giving consideration to the comments of the other Party. Further, if a Party discloses this Agreement or any of the terms hereof in accordance with this Section 11.3, such Party will, at its own expense, seek such confidential treatment of confidential portions of this Agreement and such other terms, as may be reasonably requested by the other Party and limit its disclosure of such Confidential Information to only that required to comply with applicable Law.

11.4. Residual Knowledge Exception. Notwithstanding any provision of this Agreement to the contrary, Residual Knowledge will not be considered Confidential Information for purposes of this Section 10.1; provided that, for clarity, a Party's rights to Residual Knowledge hereunder shall not include the right to practice any Patent Right owned or Controlled by the other Party that claims such Residual Knowledge unless otherwise expressly granted in another provision of this Agreement or in another agreement between the Parties.

11.5. Public Announcements; Publications.

11.5.1. **Announcements**. Except as may be expressly permitted under Section 11.3, neither Party will make any public announcement regarding this Agreement without the prior written approval of the other Party. The Parties agree that the Parties will issue a mutually agreed upon joint press release regarding the signing of this Agreement following the Signing Date.

11.5.2. **Publications**. During the Term, each Party will submit to the other Party for review and approval (such approval not to be unreasonably withheld, delayed or conditioned) any proposed publication or public presentation proposed by a Party or its Affiliates or any of their respective Representatives that relates to the activities conducted under this Agreement, including the Research and Development Plan ; *provided* that notwithstanding the requirement for approval (a) neither Party shall be prevented from submitting any publication or making a presentation in respect of a Clinical Trial for which the Party is either the IND holder or the Lead Development Party to

the extent such publication or presentation is required under applicable Law or such Party's internal publication policies, but such publishing Party shall not disclose the other Party's confidential information in respect of its technology and Intellectual Property Rights, and shall take on board and reasonably consider any reasonable requests of the other Party with respect to such proposed publication or presentation; (b) the Party whose approval is sought shall not unreasonably withhold or condition such approval; and (c) nothing shall prohibit a Party from making any press release or statement where required pursuant to applicable Law or stock exchange rule, subject to such publishing Party shall take on board and reasonably consider any reasonable requests of the other Party with respect to such proposed publication or presentation. Each Party's review and approval will be conducted only for the purposes of identifying if confidential information should be modified or deleted so as to preserve the value of the technology owned by such Party or its Affiliates and the rights granted to each Party hereunder. Written copies of such proposed publication or presentation required to be submitted hereunder will be submitted as soon as practically possible before submission for publication or presentation (the "Review Period"). The reviewing Party will provide its comments with respect to such publications and presentations within 7 Business Days of its receipt of such written copy. The Review Period may be extended for an additional 10 Business Days in the event a Party can, within 7 Business Days of receipt of the written copy, demonstrate reasonable need for such extension including for the preparation and filing of patent applications. Each Party will comply with standard academic practice regarding authorship of scientific publications and recognition of contribution of other parties in any publication governed by this Section 11.5.2, including International Committee of Medical Journal Editors standards regarding authorship and contributions.

11.6. Non-Disclosure in China. For the avoidance of doubt, nothing in this Agreement authorizes or permits BioNTech to disclose to Fosun, its Affiliates or any other collaboration partner in or for China any Pfizer Confidential Information without the prior written consent of Pfizer other than to the extent necessary for Fosun or its Affiliates (or such other collaboration partner in or for China) to undertake fill/finish of a product identical to any Product in China or to comply with information obligations required by the China National Medical Products Administration relating to such product in accordance with applicable Law, in each case so far as such use is licensed under Sections 3.4.2(b) or 3.4.4(b).

11.7. Obligations in Connection with Change of Control. If a Party is subject to a Change of Control or if a Party or any of its Affiliates acquires or merges with a Third Party during the Term ("Change of Control Party"), such Change of Control Party will, and it will cause its Representatives to, ensure that no Confidential Information of the other Party is released to (a) any Affiliate of the Change of Control Party that becomes an Affiliate of the Change of Control Party as a result of the Change of Control or (b) any other Representatives of the Change of Control Party (or of the relevant surviving entity of such Change of Control) who become Representatives of the Change of Control Party as a result of the Change of Control, unless such Affiliate or other Representatives, as applicable, have signed individual confidentiality agreements which include equivalent obligations to those set out in this Section 11. Upon occurrence of a Change of Control, the Change of Control Party will promptly notify the other Party, share with the other Party the policies, procedures and technical and organizational measures it plans to implement in order to protect the confidentiality of the other Party's Confidential Information prior to such implementation and make any adjustments to such policies and procedures that are reasonably requested by the other Party.

12. REPRESENTATIONS AND WARRANTIES

12.1. Mutual Representations and Warranties. Each of BioNTech and Pfizer hereby represents and warrants to the other Party that:

12.1.1. it is duly organized, validly existing and in good standing under the laws of the jurisdiction of its organization;

12.1.2. the execution, delivery and performance of this Agreement by such Party has been duly authorized by all requisite action under the provisions of its charter, bylaws and other organizational documents, and does not require any action or approval by any of its shareholders or other holders of its voting securities or voting interests;

12.1.3. it has the power and authority to execute and deliver this Agreement and to perform its obligations hereunder;

12.1.4. this Agreement has been duly executed and is a legal, valid and binding obligation on each Party, enforceable against such Party in accordance with its terms; and

12.1.5. the execution, delivery and performance by such Party of this Agreement and its compliance with the terms and provisions hereof does not and will not conflict with or result in a breach of or default under any Binding Obligation existing as of the Effective Date.

12.2. Mutual Covenants. In addition to the covenants made by the Parties elsewhere in this Agreement, each of BioNTech and Pfizer hereby covenants to the other Party that, from the Effective Date until expiration or termination of this Agreement it will perform its obligations under this Agreement in compliance with applicable Laws.

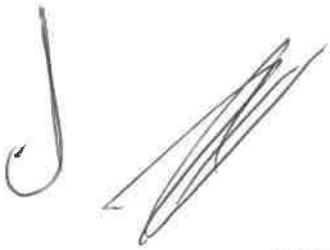
12.3. Representations and Warranties of BioNTech. BioNTech hereby represents and warrants to Pfizer that, unless otherwise disclosed in Schedule 12.3 (or otherwise as accepted to have been disclosed between BioNTech's external counsel and Pfizer's external counsel other than in writing), and provided that those provisions of the Current Licenses set forth in Schedule 1.36 shall be deemed disclosed against the representations and warranties given by BioNTech at sections 12.3.1, 12.3.2, 12.3.4, 12.3.10 and 12.3.11 of this Agreement and provided further that all disclosures made under the Flu Collaboration License shall be deemed disclosed also under this Agreement:

12.3.1. as of the Signing Date, except with respect to BioNTech Technology Controlled by BioNTech pursuant to a Current License, BioNTech or its Affiliates are the sole and exclusive owner of the BioNTech Technology, and all BioNTech Technology is free and clear of any claims, liens, charges or encumbrances;

12.3.2. as of the Signing Date, BioNTech has, and to its knowledge will have, the full right, power and authority to (a) grant all of the right, title and interest in the licenses and other rights granted or to be granted to Pfizer, Pfizer's Affiliates or Pfizer's Sublicensees under this Agreement and (b) perform its obligations under this Agreement;

12.3.3. Schedule 1.17 sets forth a true and complete list of all Candidates relevant to the Field discovered, developed or Controlled by BioNTech or its Affiliates on or prior to the Signing Date;

12.3.4. as of the Signing Date, (a) Schedule 12.3.4 sets forth a true and complete list of all Patent Rights (i) owned or otherwise Controlled by BioNTech or its Affiliates or (ii) to which BioNTech or its Affiliates have been granted or otherwise transferred any right to practice under, in each case of (i) and (ii), that relate to the Candidates, the Products, the BioNTech Technology, or the Parties' activities in the Research and Development Program, (b) each such Patent Right is in full force and effect and, so far as BioNTech is aware, valid and enforceable, (c) BioNTech or



its Affiliates have timely paid, or caused the appropriate Third Parties to pay, all filing and renewal fees payable with respect to such Patent Rights; (d) BioNTech Controls all Patent Rights listed in Schedule 12.3.4; and (e) other than those licensed hereunder, there are no other Patent Rights owned or Controlled by BioNTech that Candidates or Products would infringe;

12.3.5. as of the Signing Date, BioNTech is not aware of any material adverse event, or medical or scientific concern or doubt regarding the safety, contraindications or effectiveness of the use of the BioNTech Technology or the Candidates that have not previously been disclosed in writing to Pfizer;

12.3.6. to BioNTech's knowledge as of the Signing Date, (a) no Third Party (i) is infringing any BioNTech Patent Right or (ii) has challenged or threatened in writing to challenge the ownership, scope, validity or enforceability of, or BioNTech's or any Current Licensor's rights in or to, any BioNTech Patent Right (including, by way of example, through the institution or written threat of institution of interference, nullity or similar invalidity proceedings before the United States Patent and Trademark Office or any analogous foreign Governmental Authority);

12.3.7. as of the Signing Date, BioNTech has independently developed all BioNTech Know-How and BioNTech Materials or otherwise has a valid right to use, and to permit Pfizer, Pfizer's Affiliates and Pfizer's Sublicensees to use, the BioNTech Know-How and BioNTech Materials for all permitted purposes under this Agreement;

12.3.8. except with respect to BioNTech Technology Controlled by BioNTech pursuant to a Current License, BioNTech or its Affiliates have obtained from all inventors of BioNTech Technology existing as of the Signing Date, valid and enforceable agreements assigning to BioNTech or its Affiliates each such inventor's entire right, title and interest in and to all such BioNTech Technology (except to the extent applicable Law provides that all right, title and interest in and to such BioNTech Technology automatically vests in BioNTech or its Affiliates by operation of law);

12.3.9. in respect of BioNTech Technology solely or jointly owned by BioNTech existing as of the Signing Date, neither BioNTech nor its Affiliates are subject to any funding agreement with any government or Governmental Authority;

12.3.10. as of the Effective Date (a) there are no BioNTech Third Party Agreements other than the Current Licenses set forth in Schedule 1.36, (b) true and complete copies of each Current License (other than the Fosun Agreement) have been provided to Pfizer, (c) except as provided in the Current Licenses, no Third Party has any right, title or interest in or to, or any license under, any BioNTech Technology in the Field, (d) no rights granted by or to BioNTech or its Affiliates under any Current License conflict with any right or license granted to Pfizer or its Affiliates hereunder and (e) BioNTech and its Affiliates are in compliance in all material respects with all Current Licenses;

12.3.11. as of the Signing Date, to BioNTech's knowledge, the use by BioNTech or Pfizer (or their respective Affiliates or Sublicensees) of the BioNTech Technology in accordance with this Agreement, and the Development, Manufacture or Commercialization of those Candidates listed in Schedule 1.17 or Products incorporating such Candidates in accordance with this Agreement (a) does not and will not infringe any Patent Right of any Third Party or (b) will not infringe the claims of any published Third Party pending Patent Right when and if such claims issue;

12.3.12. as of the Effective Date, there is no (a) written claim, demand, suit, proceeding, arbitration, inquiry, investigation or other legal action of any nature, civil, criminal, regulatory or otherwise, pending or, to BioNTech's knowledge, made or threatened (irrespective of whether or not in writing) against BioNTech or any of its Affiliates or (b) judgment or settlement against or owed by BioNTech or any of its Affiliates, in each case in connection with the BioNTech Technology, the Current Licenses, any Candidate or Product or relating to the transactions contemplated by this Agreement;

12.3.13. as of the Signing Date, BioNTech and its Affiliates (a) have claimed and remunerated all employee inventions of their respective employees comprised within the GEIA Technology in accordance with the provisions of the GEIA; and (b) are entitled to unrestrictedly claim all rights to employee inventions of their employees comprised within the GEIA Technology;

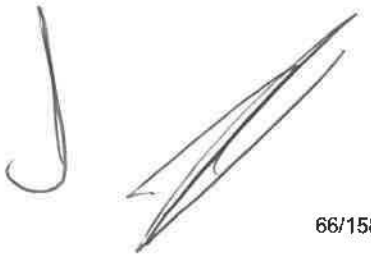
12.3.14. as of the Signing Date, BioNTech has obtained all necessary assignment documents for the BioNTech Technology inventions in its files and maintains written track records of the proper claiming of any inventions made by employees of BioNTech, its Affiliates or Third Parties included in BioNTech Technology or Research and Development Program Technology by the employer and/or the proper assignment of the inventors of their rights in the invention, including the right to claim priority to said invention, to the employer;

12.3.15. as of the Signing Date, BioNTech has no knowledge of (a) any inequitable conduct or fraud on any patent office with respect to any of the BioNTech Patent Rights or (b) any Person (other than Persons identified in the applicable patent applications or patents, as inventors of inventions disclosed in the BioNTech Patent Rights) who claims to be an inventor of an invention disclosed in the BioNTech Patent Rights;

12.3.16. as of the Signing Date, BioNTech and its Affiliates are not, and to BioNTech's knowledge, no Current Licensor or Representative of BioNTech (in each case, as applicable) is, debarred by any Regulatory Authority or the subject of debarment proceedings by any Regulatory Authority and, in the course of the discovery or pre-clinical development of any Candidate or Product, BioNTech and its Affiliates have not and, to the knowledge of BioNTech, no Current Licensor or Representative of BioNTech (in each case, as applicable) have used any employee or consultant that is debarred by any Regulatory Authority or, to the knowledge of BioNTech, is the subject of debarment proceedings by any Regulatory Authority;

12.3.17. BioNTech, its Affiliates, and to BioNTech's knowledge, all third parties and Representatives acting on BioNTech's behalf, have and will comply in all material respects with all applicable Law and accepted pharmaceutical industry business practices in connection with this Agreement, including, to the extent applicable, the FD&C Act (21 U.S.C. § 301, et seq.), the Anti-Kickback Statute (42 U.S.C. § 1320a-7b), Civil Monetary Penalty Statute (42 U.S.C. § 1320a-7a), the False Claims Act (31 U.S.C. § 3729 et seq.), comparable state statutes, the regulations promulgated under all such statutes, and the regulations issued by the FDA, consistent with the 'Compliance Program Guidance for Pharmaceutical Manufacturers' published by the Office of Inspector General, U.S. Department of Health and Human Services;

12.3.18. with respect to any Candidates, Products, or payments or services provided under this Agreement, BioNTech, its Affiliates, and to its knowledge all third parties and Representatives acting on BioNTech's behalf, have not taken and will not during the Term take any action directly or indirectly to offer, promise or pay, or authorize the offer or payment of, any money or anything of value in order to improperly or corruptly seek to influence any Government Official or any other person in order to gain an improper advantage, and has not accepted, and will not accept in the future such payment;



12.3.19. BioNTech, its Affiliates, and to its knowledge all third parties and Representatives acting on BioNTech's behalf, have and will continue to comply with the laws and regulations of the countries where it operates, including Anti-Corruption Laws, accounting and record keeping laws, and laws relating to interactions with HCPs, Governments and Government Officials;

12.3.20. BioNTech has implemented policies and procedures, including but not limited to anti-corruption policies and procedures, commensurate with its current risk profile, and shall review said policies from time to time setting out rules governing interactions with HCPs and Government Officials, engagement of Third Parties, including, where appropriate, due diligence ("Policies"), and its Policies will mandate a robust set of internal controls, including accounting controls, designed to ensure the making and keeping of fair and accurate books, records and accounts, on its operations around the world and apply worldwide to all its employees, subsidiaries, and Third Parties acting on its behalf to provide reasonable assurance that BioNTech, its subsidiaries and such Third Parties will comply with Laws, including but not limited to Anti-Corruption Laws to the extent required by such Laws. BioNTech will reasonably monitor its operations and the operations of its Affiliates with the purpose of ensuring its Policies are effective at the reasonable assurance level and make necessary changes from time to time, in particular as its business activities expand;

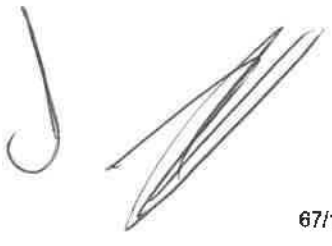
12.3.21. the Impf Group does not own or Control any Intellectual Property Rights used by BioNTech or that BioNTech may reasonably require or be useful to exploitation of any of the RNA Technology.

12.4. Accuracy of Representations and Warranties.

12.4.1. BioNTech will take no action which would render any representation or warranty made by BioNTech and contained in Section 12.1 or Section 12.2 inaccurate or untrue; provided that such covenant shall not apply to representations and warranties expressly given as of the Effective Date;

12.4.2. BioNTech will promptly notify Pfizer of any lawsuits, claims, administrative actions, regulatory inquiries or investigations, or other proceedings asserted or commenced against BioNTech or its Representatives involving in any material way the ability of BioNTech to deliver the rights, licenses and sublicenses granted herein; and

12.4.3. BioNTech will promptly notify Pfizer in writing of any facts or circumstances which come to its attention and which cause, or through the passage of time may cause, any of the representations and warranties contained in Section 12.1, Section 12.2, Section 16.10 or otherwise in this Agreement to be untrue or misleading in any material respect at any time during the Term; and in addition to the foregoing, with regard to any of the representations under Section 16.10, BioNTech will suspend all affected activities (including making any related payments) under this Agreement, unless and until Pfizer determines that such activities may be resumed; provided that such covenant shall not apply to representations and warranties expressly given as of the Effective Date.



12.5. BioNTech Covenants. In addition to the covenants made by BioNTech elsewhere in this Agreement, BioNTech hereby covenants to Pfizer that, from the Effective Date until expiration or termination of this Agreement:

12.5.1. BioNTech will not, and will cause its Affiliates not to (a) license, sell or assign (other than in a connection with a permitted assignment of this Agreement by BioNTech pursuant to Section 16.1) or otherwise transfer to any Person (other than Pfizer or its Affiliates or Sublicensees pursuant to the terms of this Agreement) any BioNTech Technology or Research and Development Program Technology (or agree to do any of the foregoing) or (b) incur or permit to exist, with respect to any BioNTech Technology or Research and Development Program Technology, any lien, encumbrance, charge, security interest, mortgage, liability, assignment, grant of license or other Binding Obligation, in each case of (a) and (b) that is inconsistent with the licenses and other rights granted (or that may be granted) to Pfizer or its Affiliates under this Agreement;

12.5.2. Except as explicitly permitted under this Agreement, BioNTech will not (a) take, or omit to take, any action that diminishes the rights under the BioNTech Technology or Research and Development Program Technology granted (or that may be granted) to Pfizer or Pfizer's Affiliates under this Agreement or (b) take, or omit to take, any action that is reasonably necessary to avoid diminishing the rights under the BioNTech Technology or Research and Development Program Technology granted (or that may be granted) to Pfizer or Pfizer's Affiliates under this Agreement (for the avoidance of doubt, BioNTech shall not be in breach of the covenants set forth in this Section 12.5.2 due to any reasonable act or position taken in connection with the filing, prosecution, maintenance, defense or enforcement of BioNTech Technology or Research and Development Program Technology as permitted in Section 10);

12.5.3. BioNTech will (a) not enter into any BioNTech Third Party Agreement that adversely affects (i) the rights granted (or that may be granted) to Pfizer, Pfizer's Affiliates or Sublicensees hereunder or (ii) BioNTech's ability to fully perform its obligations hereunder; (b) not amend or otherwise modify any BioNTech Third Party Agreement (including any Current License) or consent or waive rights with respect thereto in any manner that (A) adversely affects the rights granted (or that may be granted) to Pfizer or Pfizer's Affiliates or Sublicensees hereunder or (B) BioNTech's ability to fully perform its obligations hereunder; (c) promptly furnish Pfizer with true and complete copies of all (1) amendments to the Current Licenses and (2) BioNTech Third Party Agreements and related amendments executed following the Effective Date (in each case with redactions only in respect of sensitive information which is not relevant for the purposes of this Agreement); (d) remain, and cause its Affiliates to remain, in compliance in all material respects with all BioNTech Third Party Agreements; and (e) furnish Pfizer with copies of all notices received by BioNTech or its Representatives relating to any alleged breach or default by BioNTech or its Representatives under any BioNTech Third Party Agreement within ten (10) Business Days after receipt thereof (in each case with redactions only in respect of sensitive information which is not relevant for the purposes of this Agreement); and

12.5.4. BioNTech will not enter into or otherwise allow itself or its Representatives to be subject to any agreement or arrangement, other than the Current Licenses, which limits the ownership or licensed rights of Pfizer or its Affiliates with respect to, or limits the ability of Pfizer or its Affiliates to grant a license, sublicense or access, or provide or provide access or other rights in, to or under, any Intellectual Property Right or material (including any Patent Right, Know-How or other data or information), in each case, that would, but for such agreement or arrangement, be included in the rights licensed or assigned (or that may be licensed or assigned) to Pfizer or its Affiliates pursuant to this Agreement

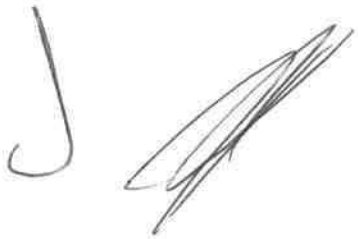
12.5.5. BioNTech and its Affiliates will maintain or obtain valid and enforceable agreements with or from all inventors of BioNTech Technology or Research and Development Program Technology who are employed by or otherwise acting on behalf of BioNTech or its Affiliates assigning to BioNTech or its Affiliates each such inventor's entire right, title and interest in and to all such BioNTech Technology or Research and Development Program Technology (except to the extent applicable Law provides that all right, title and interest in and to such BioNTech Technology or Research and Development Program Technology automatically vests in BioNTech or its Affiliates by operation of law).

12.5.6. BioNTech will unrestrictedly claim and remunerate (and procure that its Affiliates will unrestrictedly claim and remunerate) all employee inventions of their respective employees comprised within the GEIA Technology in accordance with the provisions of the GEIA.

12.5.7. In respect of GEIA Technology created after the Effective Date to which Pfizer shall obtain a license hereunder, BioNTech will use Commercially Reasonable Efforts (and will procure that its Affiliates use Commercially Reasonable Efforts) to conclude agreements with BioNTech employee inventors regarding the respective inventions by which the respective inventors: (a) waive the employer's obligation to release the employee invention and to enable the employee inventor upon request to apply for foreign Intellectual Property Rights for such foreign countries in which it does not intend to apply for Intellectual Property Rights (Sec. 14 GEIA); and (b) waive the employer's obligation to notify the employee inventor and to transfer the right in the invention to the employee inventor at the latter's request and expense, if it does not intend to pursue the application for the grant on an Intellectual Property Right for the invention any further or if it does not want to maintain the Intellectual Property Right granted for the job-related invention (Sec. 16 GEIA); and (c) waive the employer's obligation to acknowledge protectability of the invention in case the employer decides not to file a registration, but to keep the invention secret (Sec. 17 GEIA);

12.5.8. To the extent BioNTech Technology or Research and Development Program Technology is created after the Effective Date by inventors employed by or acting on behalf of BioNTech's or its Affiliates' Third Party subcontractors, BioNTech will (a) use Commercially Reasonable Efforts (and will procure that its Affiliates use Commercially Reasonable Efforts) to obtain valid and enforceable agreements with their respective Third Party subcontractors imposing on their Third Party subcontractors the obligation to claim the rights in the invention in accordance with applicable Law and to conclude agreements with its employee inventors assigning to the respective Third Party subcontractor each such inventor's entire right, title and interest in and to all such BioNTech Technology or Research and Development Program Technology (except to the extent applicable Law provides that all right, title and interest in and to such BioNTech Technology or Research and Development Program Technology automatically vests in the Third Party subcontractor by operation of law) and, (b) to the extent GEIA applies to such BioNTech Technology or Research and Development Program Technology, use Commercially Reasonable Efforts to obtain a waiver of inventor in his rights in Sec. 14, 16 and 17 GEIA;

12.5.9. with respect to any BioNTech Technology or Research and Development Program Technology to which Pfizer shall obtain a license hereunder that is made after the Effective Date in the jurisdiction of the GEIA by an inventor on behalf of BioNTech or its Affiliates who is employed by a university pursuant to Sec. 42 GEIA (e.g. university professors, research assistants), BioNTech will use Commercially Reasonable Efforts (and will procure that its Affiliates use Commercially Reasonable Efforts) to obtain valid and enforceable trifold agreements with such inventor and the respective university by which the university (a) waives its entire right, title and interest in and to that BioNTech Technology or Research and Development Program Technology made by the



inventor, (b) the inventor assigns its rights, title and interest in and to that BioNTech Technology or Research and Development Program Technology to BioNTech or its Affiliates, (c) the inventor waives its rights pursuant to Sec. 14, 16 and 17 GEIA as well as (d) waives its negative publication right (Sec. 42 Nr. 2 GEIA) vis-a-vis BioNTech or its Affiliates;

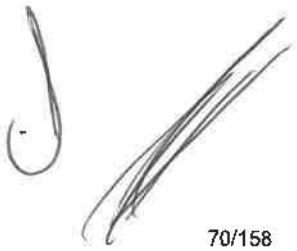
12.5.10. with respect to animals used in conducting activities under this Agreement, BioNTech will, and will cause its Affiliates and permitted subcontractors to, comply with its policies on animal care and use which shall be no less strict than Pfizer's Corporate Policy regarding Animal Care and Use, attached hereto as Exhibit C (except where in conflict with applicable Law);

12.5.11. with respect to Human Material used, including collection or transfer, by BioNTech, its Affiliates or permitted subcontractors in conducting activities under this Agreement, (a) such use shall be in accordance with the binding part of the Research and Development Plan and shall be within the scope of and consistent with its ethical approval policies, (b) BioNTech will, and will cause its Affiliates or permitted subcontractors to, handle and use the Human Material in accordance with all applicable Laws and the ICF, which shall permit Pfizer to use the Human Material for the research purposes contemplated by this Agreement, (c) BioNTech will provide the ICF to Pfizer upon request by Pfizer, (d) the Human Material will be used for research purposes only and not be used for treatment of or administration to humans and (e) if BioNTech procures any Human Material from a Third Party such as a sample bank, it will ensure that the collection and transfer of the Human Material and the use of the Human Material for purposes of the Research and Development Plan is in accordance with all applicable Laws and recognized international standards for the protection of human research subjects;

12.5.12. BioNTech shall, at all times, maintain and enforce a compliance and ethics program containing adequate systems, policies and procedures for the detection, investigation, documentation, and remediation of any allegations, reports or findings related to a potential violation of applicable Law, including Anti-Corruption Laws, with respect to the Candidates, Products, payments and services under this Agreement, which policies shall be not less strict than Pfizer's Anti-Bribery and Anti-Corruption Principles attached hereto as Exhibit B. Such policies and procedures should set out rules governing interactions with HCPs, Government Officials, the engagement of Third Parties, and where appropriate, conducting due diligence, and the investigation, documentation and remediation of any allegations, reports or findings related to a potential violation of applicable Laws, and BioNTech shall, upon Pfizer's request, require any persons acting on behalf of BioNTech in connection with this Agreement to complete anti-corruption compliance training provided by Pfizer, and will notify Pfizer of any persons that require or may require such training during the Term of this Agreement;

12.5.13. if BioNTech finds, following an investigation, credible evidence of a violation of any applicable policies and procedures that are designed to ensure compliance with any applicable Laws, including any criminal, civil or administrative laws or regulations, or violations of policies or procedures related to scientific misconduct or data integrity, BioNTech shall promptly inform Pfizer of the occurrence and the steps taken by BioNTech to remediate the occurrence; and

12.5.14. in it undertaking, sponsoring, or having regulatory oversight over any Clinical Trials, BioNTech shall ensure and procure that all documentation for such Clinical Trials shall comply with, and take advantage of, any applicable Laws that serve to limit product liability claims and losses having regard to the pandemic status of COVID-19, including any requirements under any declarations pursuant to the Public Readiness and Emergency Preparedness (PREP) Act in the USA or any equivalent, similar or comparable legislation in the Territory.



12.6. Pfizer Covenants. In addition to the covenants made by Pfizer elsewhere in this Agreement, Pfizer hereby covenants to BioNTech that, from the Effective Date until expiration or termination of this Agreement,

12.6.1. Pfizer and its Affiliates maintain or will obtain valid and enforceable agreements with or from all inventors of Pfizer Improvements or Research and Development Program Technology who are employed by or otherwise acting on behalf of Pfizer or its Affiliates valid and enforceable agreements assigning to Pfizer or its Affiliates each such inventor's entire right, title and interest in and to all such Pfizer Improvements or Research and Development Program Technology (except to the extent applicable Law provides that all right, title and interest in and to such Pfizer Improvements or Research and Development Program Technology automatically vests in Pfizer or its Affiliates by operation of law), and Pfizer and its Affiliates have made or will make any payments owing to any such inventors in respect of any Pfizer Improvements or Research and Development Program Technology or any other Person that is required in connection with the creation or exploitation of or transfer of rights to such Pfizer Improvements or Research and Development Program Technology;

12.6.2. with respect to Human Material used, including collection or transfer, by Pfizer, its Affiliates or permitted subcontractors in conducting activities under this Agreement, (a) such use shall be within the scope of and consistent with its ethical approval policies, (b) Pfizer will, and will cause its Affiliates or permitted subcontractors to, handle and use the Human Material in accordance with all applicable Laws and the ICF, (c) Pfizer will provide the ICF to BioNTech upon request by BioNTech, (d) the Human Material will be used for research purposes only and not be used for treatment of or administration to humans and (e) if Pfizer procures any Human Material from a Third Party such as a sample bank, it will ensure that the collection and transfer of the Human Material and the use of the Human Material for purposes of the Research and Development Plan is in accordance with all applicable Laws and recognized international standards for the protection of human research subjects; and

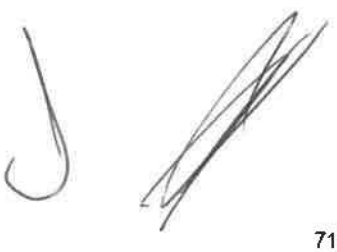
12.6.3. Pfizer will comply with the provisions of the Current Licenses set forth in Schedule 1.36 in respect of BioNTech Technology sublicensed to Pfizer under the respective Current Licenses insofar as Pfizer is using such BioNTech Technology;

12.6.4. Pfizer shall comply with its Anti-Bribery and Anti-Corruption Principles attached hereto as Exhibit B and its Corporate Policy regarding Animal Care and Use, attached hereto as Exhibit C; and

12.6.5. in it undertaking, sponsoring, or having regulatory oversight over any Clinical Trials, Pfizer shall ensure and procure that all documentation for such Clinical Trials shall comply with, and take advantage of, any applicable Laws that serve to limit product liability claims and losses having regard to the pandemic status of COVID-19, including any requirements under any declarations pursuant to the Public Readiness and Emergency Preparedness (PREP) Act in the USA or any equivalent, similar or comparable legislation in the Territory.

12.7. Notifications. During the Term. BioNTech will promptly notify Pfizer in writing or orally in the event that it learns of:

12.7.1. any prior art or other facts that BioNTech believes would result in the invalidity or unenforceability of any of the claims included in any of the BioNTech Patent Rights or Research and Development Program Patent Rights; or



12.7.2. any inequitable conduct or fraud on the patent office with respect to any of the BioNTech Patent Rights or Research and Development Program Patent Rights; or

12.7.3. any Person (other than Persons identified as inventors of inventions disclosed in the BioNTech Patent Rights or Research and Development Program Patent Rights) who claims to be an inventor of an invention disclosed in the BioNTech Patent Rights or Research and Development Program Patent Rights; and

12.7.4. any lawsuits, claims, administrative actions, government inquiries or investigations, or other proceedings related to the activities contemplated under this Agreement.

12.8. Representation by Legal Counsel. Each Party hereto represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption will exist or be implied against the Party which drafted such terms and provisions.

12.9. BioNTech's knowledge. All references in this Section 12 to BioNTech's knowledge (or equivalent) shall refer to the actual knowledge after reasonable internal inquiry of BioNTech's management comprising those individuals set forth in Schedule 12.9.

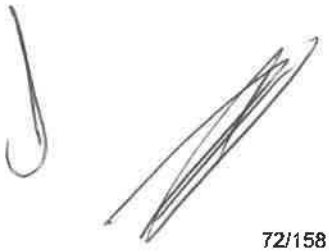
12.10. Disclaimer. THE FOREGOING REPRESENTATIONS AND WARRANTIES OF EACH PARTY ARE IN LIEU OF ANY OTHER REPRESENTATIONS AND WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR ANY IMPLIED WARRANTIES OF FITNESS FOR A PARTICULAR PURPOSE, ALL OF WHICH ARE HEREBY SPECIFICALLY EXCLUDED AND DISCLAIMED.

13. GOVERNMENT APPROVALS; TERM AND TERMINATION

13.1. Government Approvals. Each of BioNTech and Pfizer will cooperate with the other Party and to make all registrations, filings and applications, to give all notices and to obtain as soon as practicable all governmental or other consents, transfers, approvals, orders, qualifications authorizations, permits and waivers, if any, and to do all other things necessary or useful for the consummation of the transactions as contemplated hereby including the collection of Human Material.

13.2. Term. The term of this Agreement (the "Term") will commence on the Effective Date and shall continue, unless terminated earlier in accordance with this Section 13, until the later of (a) completion of all Development and Manufacturing obligations of each Party set out herein; and (b) the termination or expiry of the Commercialization Agreement or, in the absence of a Commercialization Agreement, Pfizer ceasing to pursue Commercialization activities pursuant to the Commercialization Terms.

13.3. Termination for Cause by a Party. Either Party may terminate this Agreement for cause, at any time during the Term, by giving written notice to the other Party in the event that such other Party commits a material breach of its obligations under this Agreement and such material breach remains uncured for at least 90 days, in each case measured from the date written notice of such material breach is given to Pfizer; *provided, however*, that if any breach is not reasonably curable within [***] and if the Party accused of breach is making a bona fide effort/using Commercially Reasonable Efforts to cure such breach, such termination will be delayed for a time period to be agreed by both Parties in order to permit the Party accused of a breach a reasonable period of time to cure such breach. If the alleged material breach relates to non-payment of any amount due under this Agreement, the cure period will be tolled pending resolution of any bona fide dispute between the Parties as to whether such payment is due.



13.4. Termination by Pfizer Convenience. [***], Pfizer may terminate this Agreement for convenience upon [***] prior written notice (which notice period may be shortened by BioNTech in BioNTech's sole discretion through written notice to Pfizer at any time after BioNTech's receipt of such termination notice) without any liability to BioNTech.

13.5. Termination by Pfizer for [***]

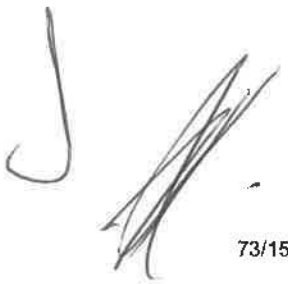
13.6. Effects of Termination.

13.6.1. **Termination for Cause by a Party.** In the event that a Party terminates this Agreement for cause pursuant to Section 13.3, all rights and obligations of each Party hereunder will cease (including all rights and licenses and sublicenses granted by either Party to the other Party hereunder, and all sublicenses granted to Affiliates or Third Parties under the rights granted hereunder), except as otherwise expressly provided herein.

13.6.2. **Termination for Pfizer's Convenience.** Upon Pfizer's termination pursuant to Section 13.4 (a) [***]; and (b) [***].

13.6.3. **No Effect on Related Agreements.** Unless explicitly agreed otherwise, termination or expiration of this Agreement shall not affect any other agreements concluded hereunder, including the Commercialization Agreement or any Manufacturing agreements pursuant to Article 8.

13.6.4. **Continuation of Pfizer Licenses.** Except in the event of Pfizer's termination pursuant to Section 13.3 or 13.7.1, (a) [***], (b) [***], (c) [***], and (d) [***].



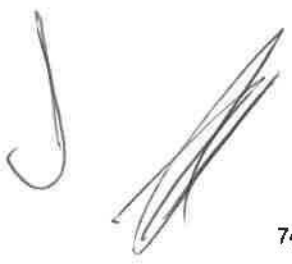
13.6.5. **Exclusivity.** In the event of Pfizer's termination pursuant to Section 13.3 or 13.7, the Parties' obligations pursuant to Section 3.10.3 shall survive the termination or expiration of this Agreement for a period of [***] years provided that BioNTech shall not be prevented from using the Product within the Field. In the event of Pfizer's termination pursuant to Section 13.4 or 13.5, Pfizer shall not be entitled to enter into any collaboration or license agreement with any Third Party to Develop or Commercialize in the Territory an immunogenic composition comprising mRNA in the Field for a period of [***] months commencing on the date of the termination notice served by Pfizer, provided that such obligation shall not (i) restrict Pfizer's or its Affiliates' right to work as contract manufacturer for a Third Party, (ii) prohibit Pfizer or its Affiliate from acquiring any Third Party, or being acquired by any Third Party, that at the time of acquisition is active in the Development or Commercialization of an immunogenic composition comprising mRNA in the Field, or (iii) prohibit Pfizer or its Affiliate from undertaking non-clinical research work.

13.6.6. **Accrued Rights.** Expiration or termination of this Agreement for any reason will be without prejudice to any right which will have accrued to the benefit of either Party prior to such termination, including damages arising from any breach under this Agreement. Expiration or termination of this Agreement will not relieve either Party from any obligation which is expressly indicated to survive such expiration or termination.

13.6.7. **Survival Period.** The following sections, together with any sections that expressly survive, will survive expiration or termination of this Agreement for any reason: Sections 1 (Definitions), 3.5 (additional licenses), 5.4.2(a) through (d) only (Repayment of BioNTech Deferred Development Costs) (except in the event of a termination by Pfizer pursuant to Section 13.4), 5.6 (Records and Accounting Principles), 5.7.1 (Withholding Taxes), 5.10 (Audits), 5.10.1 (Underpayments/Overpayments), 5.10.2 (Confidentiality), 7.4.2 (Title to Pfizer Materials and BioNTech Materials), 7.4.4 (Return of Proprietary Materials), 9.2.5, first sentence only (Ownership of Regulatory Filings), 9.7 (Liability), 10.2 (Ownership of Intellectual Property), 10.3.1.2, 10.3.1.3 and 10.3.2 (Filing, Prosecution and Maintenance of Patent Rights), 11 (Confidentiality), 13.6 (Effects of Termination), 13.7 (Provision for Insolvency), 15.1 (No Consequential Damages), 15.2 (Indemnification by Pfizer), 15.3 (Indemnification by BioNTech), 15.4 (Procedure), 16 (Miscellaneous) and, to the extent an Enforcement Action or Infringement Claim is active, live or pending at the time of expiry or termination, Sections 10.4 or 10.8, as applicable.

13.7. Provision for Insolvency.

13.7.1. **Termination Right.** BioNTech will be deemed a "Debtor" under this Agreement if, at any time during the Term (a) a case is commenced by or against BioNTech under the Bankruptcy Code, (b) BioNTech files for or is subject to the institution of bankruptcy, reorganization, liquidation or receivership proceedings (other than a case under the Bankruptcy Code), (c) BioNTech assigns all or a substantial portion of its assets for the benefit of creditors, (d) a receiver or custodian is appointed for BioNTech's business or (e) a substantial portion of BioNTech's business is subject to attachment or similar process; *provided, however*, that in the case of any involuntary case under the Bankruptcy Code, BioNTech will not be deemed a Debtor if the



case is dismissed within 60 days after the commencement thereof. If BioNTech is deemed a Debtor, then Pfizer may terminate this Agreement by providing written notice to BioNTech. If Pfizer terminates this Agreement pursuant this Section 13.7.1, then: (i) all licenses granted to Pfizer under this Agreement will become irrevocable and perpetual, and Pfizer will have no further obligations to BioNTech under this Agreement other than (A) those obligations that expressly survive termination in accordance with Section 13.6.7 and (B) an obligation to pay royalties with respect to Net Sales of Products in an amount equal to 100% of the amount that would otherwise have been payable under this Agreement, such amount to be paid in accordance with and subject to the other terms of this Agreement governing the payment of royalties; (ii) such termination will not be construed to limit BioNTech's right to receive payments that accrued before the effective date of such termination; (iii) Pfizer will have the right to offset, against any payment owing to BioNTech as provided for under clause (i), above, any damages found or agreed by the Parties to be owed by BioNTech to Pfizer; and (iv) nothing in this Section 13.7.1 will limit any other remedy Pfizer may have for any breach by BioNTech of this Agreement.

13.7.2. **Rights to Intellectual Property.** All rights and licenses now or hereafter granted by BioNTech to Pfizer under or pursuant to any Section of this Agreement, including Sections3.1.1, 3.2.1, 3.3, 3.4.1 and 3.5.1 and Section 10 hereof, are rights to "intellectual property" (as defined in the Bankruptcy Code). The Parties hereto acknowledge and agree that the payments provided for under Sections 5 and all other payments by Pfizer to BioNTech hereunder or under the Commercialization Agreement do not constitute royalties within the meaning of Section 365(n) of the Bankruptcy Code or relate to licenses of intellectual property hereunder. If (a) a case under the Bankruptcy Code is commenced by or against BioNTech, (b) this Agreement is rejected as provided in the Bankruptcy Code and (c) Pfizer elects to retain its rights hereunder as provided in Section 365(n) of the Bankruptcy Code, then BioNTech (in any capacity, including debtor-in-possession) and its successors and assigns (including any trustee) will provide to Pfizer all Intellectual Property Rights licensed hereunder, and agrees to grant and hereby grants to Pfizer and its Affiliates a right to access and to obtain possession of and to benefit from and, in the case of any chemical or biological material or other tangible item of which there is a fixed or limited quantity, to obtain a pro rata portion of, each of the following to the extent related to any Candidate or Product, or otherwise related to any right or license granted under or pursuant to this Agreement: (i) copies of pre-clinical and clinical research data and results; (ii) all of the following (to the extent that any of the following are so related): BioNTech Materials, cell lines, antibodies, assays, reagents and other biological materials; (iii) samples or Candidates and Products; (iv) BioNTech Technology, Product Technology, and RNA Technology, (v) laboratory notes and notebooks; (vi) Candidate and Product data or filings, and (vii) rights of reference in respect of filings for and Regulatory Approvals, all of which constitute "embodiments" of intellectual property pursuant to Section 365(n) of the Bankruptcy Code, and (viii) all other embodiments of such intellectual property, whether any of the foregoing are in BioNTech's possession or control or in the possession and control of any Third Party but which BioNTech has the right to access or benefit from and to make available to Pfizer. BioNTech will not interfere with the exercise by Pfizer or its Affiliates of rights and licenses to Intellectual Property Rights licensed hereunder and embodiments thereof in accordance with this Agreement and agrees to use Commercially Reasonable Efforts to assist Pfizer and its Affiliates to obtain such Intellectual Property Rights and embodiments thereof in the possession or control of Third Parties as reasonably necessary or useful for Pfizer or its Affiliates or Sublicensees to exercise such rights and licenses in accordance with this Agreement.

13.7.3. **No Limitation of Rights.** All rights, powers and remedies of Pfizer provided in this Section 13.7 are in addition to and not in substitution for any and all other rights, powers and remedies now or hereafter existing at Law or in equity (including the Bankruptcy Code) in the event of the commencement of a case under the Bankruptcy Code involving BioNTech. To the extent

equivalent rights exist under the Bankruptcy Code existing from time to time in the jurisdiction where BioNTech is established the foregoing provisions shall be interpreted in accordance with such equivalent rights, and where such equivalent rights to not exist Pfizer shall be entitled to avail of itself all remedies and rights available to it as a creditor and licensee of Intellectual Property Rights under such local Bankruptcy Code.

14. CHANGE OF CONTROL

14.1. Change of Control. If a Change of Control occurs with respect to a Party and a Third Party during the Term, or if a Party or any of its Affiliates acquires or merges with a Third Party during the Term, (in either case such Party being the "Affected Party"):

14.1.1. if such Third Party is, at the time of such Change of Control or acquisition or merger, conducting activities that would cause the Affected Party or one of its Affiliates to violate Section 3.10.1 (such activities, a "Acquisition Program"), then such Affected Party or such Third Party shall be permitted to continue such Acquisition Program and such continuation will not constitute a violation of Section 3.10.1;

14.1.2. the provisions of Section 11.7 shall apply and no Confidential Information of the other Party or its Affiliates may be disclosed to the Third Party and shall not be used in any Acquisition Program (if any) and the Affected Party shall implement and maintain, in accordance with such Affected Party's internal commercially reasonable practices, an information and personnel barrier between the working teams involved in the day to day conduct of such Affected Party's internal program of Development and Manufacture of Candidates and Products under this Agreement, and any activities of the Third Party, including under any Acquisition Program; and

14.1.3. if BioNTech is the Affected Party then:

14.1.3.1.[***];

14.1.3.2.[***];

14.1.3.3.[***];

14.1.3.4.[***]; and

14.1.3.5.[***].

14.2. Effects of Change of Control. In the event of a Change of Control of BioNTech by during the Term, the following provisions of this Section 14 shall also apply:

14.2.1. **BioNTech Intellectual Property.** All BioNTech Technology and Research and Development Program Technology, Controlled by BioNTech immediately prior to such BioNTech Change of Control shall continue to be BioNTech Technology and Research and Development Program Technology licensed to Pfizer for purposes of this Agreement.

14.2.2. **Existing Acquirer Intellectual Property**. Patent Rights and Know-How that were Controlled by the entity acquiring BioNTech or such entity's Affiliates that were not Affiliates of BioNTech prior to such BioNTech Change of Control (collectively, the "Acquirer") shall not be included within the licenses granted to Pfizer hereunder.

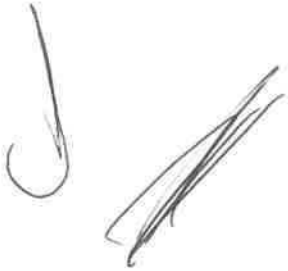
14.2.3. **Independent Intellectual Property**. Patent Rights and Know-How that, following such BioNTech Change of Control, are developed, made or otherwise acquired or Controlled by the Acquirer outside of the Research and Development Plan or the Manufacturing Plan and without use of Pfizer's Technology, Pfizer's Confidential Information, Research and Development Program Technology, BioNTech Improvements or BioNTech Technology shall not be included within the Research and Development Program Technology or BioNTech Technology or BioNTech Third Party Agreements (it being understood, however, for the avoidance of doubt, that all BioNTech Technology, Research and Development Program Technology, and Intellectual Property Rights developed by BioNTech or the Acquirer in the course of, or used by BioNTech or the Acquirer under the Research and Development Plan or used in the Manufacture of the Candidates or Products by BioNTech shall be licensed to Pfizer pursuant to the licenses set forth in this Agreement).

14.2.4. **Research and Development Program Technology.** No Research and Development Program Technology Controlled by Pfizer including Pfizer Improvements shall be licensed or sub-licensable to the Acquirer, and no Confidential Information of Pfizer or its Representatives shall be disclosed to the Acquirer, in each case without the prior written consent of Pfizer.

14.2.5. **Effect on Certain Agreement Provisions.** From and after the effective date of a BioNTech Change of Control by a Specified Person, the Acquirer shall not be considered an "Affiliate" for the purposes of this Agreement, provided that the Acquirer does not engage in any activities otherwise restricted under Section 3.10 using any Research and Development Program Technology, Pfizer Technology, Pfizer Improvements or Confidential Information of Pfizer.

15. LIMITATION ON LIABILITY, INDEMNIFICATION AND INSURANCE

15.1. No Consequential Damages. Except with respect to liability arising from a breach of Sections 10 or 10.1, from any willful misconduct or intentionally wrongful act, or to the extent such Party may be required to indemnify the other Party under this Section 15, in no event will either Party or its Representatives be liable under this Agreement for any special (only as related to indirect, incidental or



consequential damages), indirect, incidental, consequential or punitive damages, whether in contract, warranty, tort, negligence, strict liability or otherwise, including loss of indirect profits or revenue suffered by the other Party or any of its Representatives. Without limiting the generality of the foregoing, "consequential damages" will be deemed to include, and neither Party will be liable to the other Party or any of such other Party's Representatives or stockholders for any damages based on or measured by loss of projected or speculative future sales of the Products, any development, regulatory, launch or sales threshold milestone payments due or any other unearned, speculative or otherwise contingent payments provided for in this Agreement.

15.2. Indemnification by Pfizer. Pfizer will indemnify, defend and hold harmless BioNTech, each of its Affiliates, and each of its and its Affiliates' employees, officers, directors and agents (each, a "BioNTech Indemnified Party") from and against any and all claims, causes, or allegations (whether threatened or pending), judgments, expenses, damages, liabilities, obligations, fees (including the reasonable fees of attorneys and other consulting or testifying professionals), costs and losses (collectively, "Liabilities") that the BioNTech Indemnified Party may be required to pay to one or more Third Parties resulting from or arising out of (a) use of the Pfizer Technology, Pfizer Materials, and/or Pfizer Know-How disclosed by or on behalf of Pfizer in accordance with the rights licensed under this Agreement, (b) use of the Pfizer name or logo in accordance with the rights licensed under this Agreement or (c) the material breach by Pfizer of any of its representations, warranties or covenants set forth in Section 7.4.1, Section 12.1 or Section 12.2 or Section 12.6; except, in each case, to the extent caused by the negligence, recklessness or intentional acts of BioNTech or any BioNTech Indemnified Party.

15.3. Indemnification by BioNTech. BioNTech will indemnify, defend and hold harmless Pfizer, its Affiliates, Sublicensees, contractors, distributors and each of its and their respective employees, officers, directors and agents (each, a "Pfizer Indemnified Party") from and against any and all Liabilities that the Pfizer Indemnified Party may be required to pay to one or more Third Parties resulting from or arising out of (a) use of the BioNTech Technology [***], BioNTech Materials, and/or BioNTech Know-How disclosed by or on behalf of BioNTech in accordance with the rights licensed under this Agreement, (b) the Candidates or Products in accordance with the rights licensed under this Agreement, save to the extent the Liabilities are in respect of (i) the exploitation of Pfizer Technology infringing a Third Party Patent Right or (ii) [***]; (c) use of the BioNTech name or logo in accordance with the rights licensed under this Agreement, (d) rights or obligations under the GEIA relating to inventions made by employees of BioNTech or its Affiliates or Third Party Licensors in relation to BioNTech Technology or Research and Development Program Technology used in any Candidate or Product; or (e) the material breach by BioNTech or any of its Representatives of any of its representations, warranties or covenants set forth in Section 9, Section 12.1, Section 12.2, Section 12.3, or Section 12.5 except to the extent caused by the negligence, recklessness or intentional acts of Pfizer or any Pfizer Indemnified Party.

15.4. Procedure.

15.4.1. **Notice**. Each Party will notify the other Party in writing in the event it becomes aware of a claim for which indemnification may be sought hereunder. In the event that any Third Party asserts a claim or other proceeding (including any governmental investigation) with respect to any matter for which a Party (the "Indemnified Party") is entitled to indemnification hereunder (a "Third Party Claim"), then the Indemnified Party will promptly notify the Party obligated to indemnify the Indemnified Party (the "Indemnifying Party") thereof; *provided, however,* that no delay on the part of the Indemnified Party in notifying the Indemnifying Party will relieve the Indemnifying Party from any obligation hereunder unless (and then only to the extent that) the Indemnifying Party is prejudiced thereby.

15.4.2. **Control**. Subject to either Party's right to control any actions described in Section 10 (even where the other Party is the Indemnifying Party), the Indemnifying Party will have the right, exercisable by notice to the Indemnified Party within ten Business Days after receipt of notice from the Indemnified Party of the commencement of or assertion of any Third Party Claim, to assume direction and control of the defense, litigation, settlement, appeal or other disposition of the Third Party Claim (including the right to settle the claim solely for monetary consideration) with counsel selected by the Indemnifying Party and reasonably acceptable to the Indemnified Party; provided that (a) the Indemnifying Party has sufficient financial resources, in the reasonable judgment of the Indemnified Party, to satisfy the amount of any adverse monetary judgment that is sought, (b) the Third Party Claim seeks solely monetary damages and (c) the Indemnifying Party expressly agrees in writing that as between the Indemnifying Party and the Indemnified Party, the Indemnifying Party will be solely obligated to satisfy and discharge the Third Party Claim in full (the conditions set forth in clauses (a), (b) and (c) above are collectively referred to as the "Litigation Conditions"). Within ten Business Days after the Indemnifying Party has given notice to the Indemnified Party of its exercise of its right to defend a Third Party Claim, the Indemnified Party will give notice to the Indemnifying Party of any objection thereto based upon the Litigation Conditions. If the Indemnified Party reasonably so objects, the Indemnified Party will continue to defend the Third Party Claim, at the expense of the Indemnifying Party, until such time as such objection is withdrawn. If no such notice is given, or if any such objection is withdrawn, the Indemnifying Party will be entitled, at its sole cost and expense, to assume direction and control of such defense, with counsel selected by the Indemnifying Party and reasonably acceptable to the Indemnified Party. During such time as the Indemnifying Party is controlling the defense of such Third Party Claim, the Indemnified Party will cooperate, and will cause its Affiliates and agents to cooperate upon request of the Indemnifying Party, in the defense or prosecution of the Third Party Claim, including by furnishing such records, information and testimony and attending such conferences, discovery proceedings, hearings, trials or appeals as may reasonably be requested by the Indemnifying Party. In the event that the Indemnifying Party does not satisfy the Litigation Conditions or does not notify the Indemnified Party of the Indemnifying Party's intent to defend any Third Party Claim within ten Business Days after notice thereof, the Indemnified Party may (without further notice to the Indemnifying Party) undertake the defense thereof with counsel of its choice and at the Indemnifying Party's expense (including reasonable, out-of-pocket attorneys' fees and costs and expenses of enforcement or defense). The Indemnifying Party or the Indemnified Party, as the case may be, will have the right to join in (including the right to conduct discovery, interview and examine witnesses and participate in all settlement conferences), but not control, at its own expense, the defense of any Third Party Claim that the other party is defending as provided in this Agreement.

15.4.3. **Settlement**. The Indemnifying Party will not, without the prior written consent of the Indemnified Party, enter into any compromise or settlement that commits the Indemnified Party to take, or to forbear to take, any action. The Indemnified Party will have the sole and exclusive right to settle any Third Party Claim, on such terms and conditions as it deems reasonably appropriate, to the extent such Third Party Claim involves equitable or other non-monetary relief, but will not have the right to settle such Third Party Claim to the extent such Third Party Claim involves monetary damages without the prior written consent of the Indemnifying Party. Each of the Indemnifying Party and the Indemnified Party will not make any admission of liability in respect of any Third Party Claim without the prior written consent of the other party, and the Indemnified Party will use reasonable efforts to mitigate Liabilities arising from such Third Party Claim.

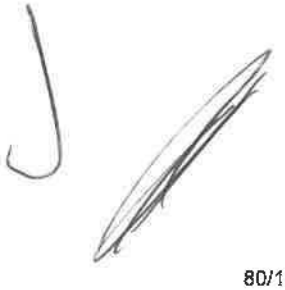
15.5. Insurance. Each Party further agrees to obtain and maintain, during the Term, commercial general liability insurance, including products liability insurance (or clinical trials insurance, if applicable), with minimum "A-" A.M. Best rated insurance carriers to cover its indemnification obligations under Section 15.2 or Section 15.3, as applicable, in each case with limits of not less than $[***] ([***] U.S. Dollars) per occurrence and in the aggregate. All deductibles and retentions will be the responsibility of the named insured. Within [***] days of the Effective Date, BioNTech will amend its existing insurance policies in such a way that (a) Pfizer Inc. and its Affiliates will be indemnified as principal on BioNTech's commercial general liability and products liability policies (or clinical trials insurance, if applicable) and (b) Pfizer Inc. and its Affiliates will be provided a waiver of subrogation on BioNTech's commercial general liability and products liability policies (or clinical trials insurance, if applicable). For U.S. exposures, additional insured status on BioNTech's commercial general liability and products liability policies shall be via form CG20101185 or its equivalent. Products liability coverage shall be maintained for three years following termination of this Agreement. To the extent of its culpability or negligence, all coverages of BioNTech will be primary and non-contributing with any similar insurance, carried by Pfizer. Notwithstanding any provision of this Section 15.5 to the contrary, Pfizer may meet its obligations under this Section 15.5 through self-insurance. Neither Party's insurance will be construed to create a limit of liability with respect to its indemnification obligations under this Section 15.

16. MISCELLANEOUS

16.1. Assignment. Neither this Agreement nor any interest hereunder will be assignable by a Party without the prior written consent of the other Party, except as follows: (a) subject to the provisions of this Agreement in respect of Change of Control, as applicable, a Party may assign its rights and obligations under this Agreement by way of sale of itself or the sale of the portion of its business to which this Agreement relates, through merger, sale of assets and/or sale of stock or ownership interest, *provided that* the assignee will expressly agree to be bound by such Party's obligations under this Agreement and that such sale is not primarily for the benefit of its creditors, (b) such Party may assign its rights and obligations under this Agreement to any of its Affiliates, *provided that* the assignee will expressly agree to be bound by such Party's obligations under this Agreement and that such Party will remain liable for all of its rights and obligations under this Agreement. In addition, Pfizer may assign its rights and obligations under this Agreement to a Third Party where Pfizer or its Affiliate is required, or makes a good faith determination based on advice of counsel, to divest a Product in order to comply with Law or the order of any Governmental Authority as a result of a merger or acquisition, *provided that* the assignee will expressly agree to be bound by Pfizer's obligations under this Agreement. Each Party will promptly notify the other Party of any assignment or transfer under the provisions of this Section 16.1. This Agreement will be binding upon the successors and permitted assigns of the Parties and the name of a Party appearing herein will be deemed to include the names of such Party's successors and permitted assigns to the extent necessary to carry out the intent of this Agreement. Any assignment not in accordance with this Section 16.1 will be void.

16.2. Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments, and to do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of the Agreement.

16.3. Force Majeure. Each Party will be excused from the performance of its obligations under this Agreement to the extent that such performance is prevented by force majeure (defined below) and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse will be continued so long as the condition constituting force majeure continues and the nonperforming Party takes Commercially Reasonable Efforts to remove the condition. For purposes of this Agreement, "force majeure" will include conditions beyond the control of the Parties, including an act of God, voluntary or involuntary compliance with any regulation, Law or order of any government, war, act of terror, civil commotion, labor strike or lock-out, epidemic, failure or default of public utilities or common carriers, destruction of production facilities or materials by fire, earthquake, storm or like catastrophe.



16.4. Interpretation. Except where the context expressly requires otherwise, (a) the use of any gender herein will be deemed to encompass references to either or both genders, and the use of the singular will be deemed to include the plural (and vice versa), (b) the words "include", "includes" and "including" will be deemed to be followed by the phrase "without limitation", (c) the word "will" will be construed to have the same meaning and effect as the word "shall", (d) any definition of or reference to any agreement, instrument or other document herein will be construed as referring to such agreement, instrument or other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein), (e) any reference herein to any Person will be construed to include the Person's successors and assigns, (f) the words "herein", "hereof" and "hereunder", and words of similar import, will be construed to refer to this Agreement in its entirety and not to any particular provision hereof, (g) all references herein to Sections, Exhibits or Schedules will be construed to refer to Sections, Exhibits or Schedules of this Agreement, and references to this Agreement include all Exhibits and Schedules hereto, (h) the word "notice" means notice in writing (whether or not specifically stated) and will include notices, consents, approvals and other written communications contemplated under this Agreement, (i) provisions that require that a Party, the Parties or any committee hereunder "agree," "consent" or "approve" or the like will require that such agreement, consent or approval be specific and in writing, whether by written agreement, letter, approved minutes or otherwise (excluding e-mail or instant messaging, but a signed PDF document being acceptable), (j) references to any specific law, rule or regulation, or article, section or other division thereof, will be deemed to include the then-current amendments thereto or any replacement or successor law, rule or regulation thereof, and (k) the term "or" will be interpreted in the inclusive sense commonly associated with the term "and/or".

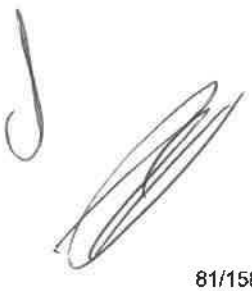
16.5. Notices. Any notice or notification required or permitted to be provided pursuant to the terms and conditions of this Agreement (including any notice of force majeure, breach, termination, change of address, etc.) will be in writing and will be deemed given upon receipt if delivered personally or by facsimile transmission (receipt verified), and upon delivery if mailed by registered or certified mail or courier. Where delivery occurs outside normal working hours, notice will be deemed given at the start of normal working hours on the next Business Day. Notice shall be given to the Parties at the following addresses or facsimile numbers (or at such other address or facsimile number for a Party as will be specified by like notice, *provided, however*, that notices of a change of address will be effective only upon receipt thereof):

All correspondence to Pfizer will be addressed as follows:

Pfizer Inc.
Notices: [***]

with a copy to:

Pfizer Inc.
Notices: Pfizer Legal Division
[***]



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To help expedite Pfizer's awareness and response, copies of notices may be provided to Pfizer by email but must be supplemented by one of the following methods: (a) personal delivery, (b) first class certified mail with return receipt requested, or (c) next-day delivery by major international courier, with confirmation of delivery. Electronic copies may be sent via email to [***].

All correspondence to BioNTech will be addressed as follows:

BioNTech SE
[***]

16.6. Amendment. No amendment, modification or supplement of any provision of this Agreement will be valid or effective unless made in writing and signed by a duly authorized officer of each Party.

16.7. Waiver. No provision of this Agreement will be waived by any act, omission or knowledge of a Party or its agents or employees except by an instrument in writing expressly waiving such provision and signed by a duly authorized officer of the waiving Party. The waiver by either of the Parties of any breach of any provision hereof by the other Party will not be construed to be a waiver of any succeeding breach of such provision or a waiver of the provision itself.

16.8. Severability. If any clause or portion thereof in this Agreement is for any reason held to be invalid, illegal or unenforceable, the same will not affect any other portion of this Agreement, as it is the intent of the Parties that this Agreement will be construed in such fashion as to maintain its existence, validity and enforceability to the greatest extent possible. In any such event, this Agreement will be construed as if such clause of portion thereof had never been contained in this Agreement, and there will be deemed substituted therefor such provision as will most nearly carry out the intent of the Parties as expressed in this Agreement to the fullest extent permitted by applicable Law.

16.9. Descriptive Headings. The descriptive headings of this Agreement are for convenience only and will be of no force or effect in construing or interpreting any of the provisions of this Agreement.

16.10. Global Trade Control Laws. The Parties acknowledge that certain activities covered by or performed under this Agreement may be subject to laws, regulations or orders regarding economic sanctions, import controls or export controls ("Global Trade Control Laws"). Each of the Parties will perform all activities under this Agreement in compliance with all applicable Global Trade Control Laws. Furthermore, with respect to the activities performed under this Agreement, each of the Parties represents, warrants and covenants that:

16.10.1. Each Party will not, for activities under this Agreement, (a) engage in any such activities in a Restricted Market; (b) involve individuals ordinarily resident in a Restricted Market; or (c) include companies, organizations, or Governmental Authorities from or located in a Restricted Market. "Restricted Market" for purposes of this Agreement means the Crimean Peninsula, Cuba, the Donbass Region, Iran, North Korea, Sudan, and Syria, or any other country or region sanctioned by the United States or European Union.

16.10.2. Each Party represents and warrants that it is not a Restricted Party and is not owned or controlled by a Restricted Party. With respect to activities performed under this Agreement, neither Party will engage or delegate to any Restricted Parties for any activities under this Agreement. Each Party will screen all relevant Third Parties involved by such Party in the activities under this Agreement under the relevant Restricted Party Lists. "Restricted Parties" for purposes of this Agreement means any individual or entity on any of the following "Restricted Party Lists": the list of sanctioned entities maintained by the United Nations; the Specially Designated Nationals List and the Sectoral Sanctions Identifications List of the U.S. Treasury Department's Office of Foreign Assets Control; the U.S. Denied Persons List, the U.S. Entity List, and the U.S. Unverified List of the U.S. Department of Commerce; entities subject to restrictive measures and the Consolidated List of Persons, Groups and Entities Subject to E.U. Financial Sanctions, as implemented by the E.U. Common Foreign & Security Policy; the List of Excluded Individuals / Entities published by the U.S. Health and Human Services' Office of Inspector General; any lists of prohibited or debarred parties established under the U.S. Federal Food Drug and Cosmetic Act; the list of parties suspended or debarred from contracting with the U.S. government; and similar lists of restricted parties maintained by the Governmental Authorities of the countries that have jurisdiction over the activities conducted under this Agreement.

16.10.3. Neither Party will knowingly transfer to the other Party any goods, software, technology or services that are (a) controlled under the U.S. International Traffic in Arms Regulations or at a level other than EAR99 under the U.S. Export Administration Regulations; or (b) specifically identified as an E.U. Dual Use Item or on an applicable export control list of another country.

16.11. Dispute Resolution. If any dispute or disagreement arises between Pfizer and BioNTech in respect of this Agreement, they will follow the following procedures in an attempt to resolve the dispute or disagreement:

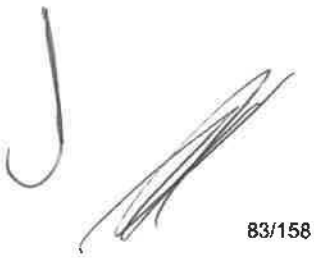
16.11.1. The Party claiming that such a dispute exists will give notice in writing ("Notice of Dispute") to the other Party of the nature of the dispute.

16.11.2. Within 30 days of receipt of a Notice of Dispute and in advance of any meeting pursuant to Section 16.11.3, the receiving Party will provide a written response to the other Party's claims regarding the dispute.

16.11.3. Within 45 days of receipt of a Notice of Dispute, the Chief Scientific Officer, Vaccine Research and Development of Pfizer and the Chief Scientific Officer of BioNTech AG will meet at a mutually agreed-upon time and location for the purpose of resolving such dispute to discuss the dispute or disagreement.

Notwithstanding any provision of this Agreement to the contrary, either Party may immediately initiate litigation in any court of competent jurisdiction seeking any remedy at law or in equity, including the issuance of a preliminary, temporary or permanent injunction, to preserve or enforce its rights under this Agreement. The provisions of this Section 16.11 will survive for five years from the date of termination or expiration of this Agreement.

16.12. Governing Law. This Agreement is governed by, and all disputes arising under or in connection with this Agreement shall be resolved in accordance with, laws of England and Wales, without regard to conflict of law principles thereof.



16.13. Consent to Jurisdiction and Venue. The Parties irrevocably submit to the exclusive jurisdiction of the courts of England and Wales as regards any claim, dispute or matter (whether contractual or non-contractual) arising out of or in connection with this Agreement (including its formation). Notwithstanding the foregoing, this clause shall not prevent either Party from being entitled to seek urgent interim or emergency relief (such as a preliminary injunction) before any other court of competent jurisdiction in respect of any claim, dispute or matter (whether contractual or non-contractual) arising out of or in connection with this Agreement (including its formation).

16.14. Entire Agreement. This Agreement constitutes and contains the complete, final and exclusive understanding and agreement of the Parties and cancels and supersedes any and all prior negotiations, correspondence, understandings and agreements, whether oral or written, between the Parties respecting the subject matter hereof and thereof, including (a) that certain [***] (which is hereby terminated effective as of the Effective Date, *provided that* such Confidential Disclosure Agreement will continue to govern the treatment of Confidential Information disclosed by the Parties prior to the Effective Date in accordance with its terms), (b) that certain [***] (which is hereby terminated effective as of the Effective Date, *provided that* the terms of this Agreement shall also apply to all activities made under the [***] (which is hereby terminated effective as of the Effective Date).

16.15. Flu Collaboration. Except as provided in Section 8.2, nothing in this Agreement varies, amends or otherwise supersedes or replaces the provisions and rights under the Flu Collaboration License, and the Flu Collaboration License and this Agreement shall be treated as separate arm's length transactions.

16.16. Independent Contractors. Both Parties are independent contractors under this Agreement. Nothing herein contained will be deemed to create an employment, agency, joint venture or partnership relationship between the Parties hereto or any of their agents or employees, or any other legal arrangement that would impose liability upon one Party for the act or failure to act of the other Party. Neither Party will have any express or implied power to enter into any contracts or commitments or to incur any liabilities in the name of, or on behalf of, the other Party, or to bind the other Party in any respect whatsoever.

16.17. Counterparts. This Agreement may be executed in two (2) counterparts, each of which will be an original and both of which will constitute together the same document. Counterparts may be signed and delivered by facsimile or digital (e.g., PDF) file, each of which will be binding when received by the applicable Party.

16.18. No Third Party Rights or Obligations. No provision of this Agreement will be deemed or construed in any way to result in the creation of any rights or obligation in any Person not a Party to this Agreement, and this Agreement does not give rise to any rights under the Contracts (Rights of Third Parties) Act 1999 to enforce any term of this Agreement. However, Pfizer may decide, in its sole discretion, to use one or more of its Affiliates to perform its obligations and duties hereunder, *provided that* Pfizer will remain liable hereunder for the performance by any such Affiliates of any such obligations.

(Signature page follows)

IN WITNESS WHEREOF, authorized representatives of the Parties have duly executed this Agreement as of the Effective Date to be effective as of the Effective Date.

PFIZER INC.

By _____

Name:

Title:

BIONTECH SE

By _____

Name:

Title:

By _____

Name:

Title:

[Signature page to Collaboration Agreement]

"HE15"

Restoring the pharmaceutical industry's reputation

Mark Kessel

Big pharma's storehouse of trouble has fostered consumer mistrust and a negative view of the industry. How does the industry go about restoring its flagging reputation?

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It wasn't that long ago that the pharmaceutical industry was considered among the most respected industries and Merck (Whitehouse Station, NJ, USA) the most admired corporation in the United States. This is in sharp contrast to consumer attitudes today, when the industry's reputation is not much better than that of the financial sector or tobacco companies[1]. Why has an industry in the business of developing lifesaving drugs garnered such a negative reputation, and how should it go about fixing it?

AP Photo/Alexander F. Yuan, File

The GlaxoSmithKline office in Beijing, China, was the center of a 2013 scandal in which local managers were accused of paying millions of dollars in bribes to Chinese doctors to prescribe the company's drugs. Numerous other scandals and ethical lapses across the industry have contributed to a decline in reputation.

Deconstructing a reputation

According to Alexander Brigham and Stefan Linssen of the consulting firm Ethisphere Institute[2] (New York), over the past three decades, the percentage of a company's value attributable to tangible assets has dropped from 90% to just 25%. Other estimates[2,3] also suggest that it is the intangible assets of a company (including reputation) that currently represent as much as 40–60% of a corporation's market capitalization. Thus, a company's reputation is among its most valuable assets.

Corporate reputation depends on both the past experience that people have had with a company and the extent or nature of their communication with it through the media and word of mouth. It is thus a mixture of perception by its different stakeholders as well as the reality of its policies, practices, systems and performance. According to public relations consultant Karen Harrison[4], a person's past experience with a company can account for about two-thirds of their view of that company.

For companies in the pharmaceutical sector, how stakeholders view companies is influenced primarily by the lay professional media (through print, TV, radio and online) and the internet (blogs and social media). In addition to companies themselves, key contributors to the conversation include the following: trade bodies, such as the Pharmaceutical Research and Manufacturers of America, the European Federation of Pharmaceutical Industries and Associations and the Biotechnology Industry Organization; regulatory and government agencies, such as the US Food and Drug Administration (FDA) and the US Department of Justice; professional bodies, such as the American Medical Association; patient groups; and lawyers representing patients. Indeed, a key differentiator of the pharmaceutical sector from other industry sectors is that its consumers are also patients.

A recent PatientView survey[5] that asked patient groups (~80% from Europe, with the rest from North America) their opinions on the reputation of the pharmaceutical industry as a whole and of its leading companies found that only 34% believed that multinational drug companies have an excellent or even good reputation (a 19% decline from the prior year).

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e-mail: mark@symphonycapital.com

Box 1 Changing attitudes of stakeholders

The pharmaceutical industry is different from other industries. Its business is focused on improving the lives of patients while at the same time generating profits to satisfy the needs of shareholders and funding further research. George Merck believed these objectives were not inconsistent with each other—if Merck served patients, the profits would naturally follow. Over time, however, there has been a shift in ideology of corporations that the only social responsibility is to increase profits and enhance investor returns, and pharma has followed this mantra. As Jurgen Drews, the former head of Roche research, candidly stated in 2003, in the pharmaceutical business today "the ethics of successful business have replaced those of medicine. The supreme loyalty of today's companies is not primarily directed at patients and their physicians but at shareholders. Consequently, the most influential figures in today's pharmaceutical companies are no longer the heads of R&D but the heads of marketing and finance"[13]. Tellingly, when pharma executives were polled about the reputation of the industry, 85% agreed that patient-centricity is the best route to future profitability[14]. And yet, it is hard to reconcile the views of these executives with their record in balancing patient needs with those of shareholders.

Patients as consumers. The shifting emphasis on shareholder value of pharmaceutical company management must also be considered in the context of shifting attitudes of patients. As the past century has progressed, consumer expectations have shifted. In the early twentieth century, access to drugs was viewed as a luxury available to those who could afford it. Today, in the West, the provision of medicine is viewed as an entitlement and even a human right. This has led to disillusionment with an industry perceived as placing profits above the rights of patients to access medicine. Headlines attacking pharmaceutical pricing practices for putting needed medicines out of reach of patients foster the view that the pharma industry has pivoted away from patients to financial goals. Patients and the public do not relate to the measure of financial success that these corporations trumpet in relation to their performance. In the public eye, pharmaceutical organizations are also perceived differently from companies in other sectors, because in the provision of medicine, traditional market forces do not apply; the market for drugs is not like buying a new garment or an iPhone. Sick patients must have access to a pharmaceutical product if they are sick—the consequence of not having access to a drug is very often a matter of life or death. In this way, the pharmaceutical industry is perceived differently from other industrial sectors like technology or household products, both in terms of economics and in terms of consumer choice.

At the same time, deciding which vacuum cleaner to buy is a very different prospect from the types of complex healthcare decisions that patients face and have traditionally worked through with their personal physicians. And yet in the United States, for example, drugs are now promoted to patients using DTC advertising, along the lines of other consumer products. Industry defends such advertising under the guise of 'informing consumers'. But DTC ads have resulted in the emergence of consumer self-prescription and shifted the balance and trust in the relationships between patients and prescribing physicians.

Physicians as consumers. Physicians have long been targeted by big pharma's marketing activities, which has affected them indirectly and directly. Indirect effects have resulted from DTC "ask your doctor" ads, which have eroded physician relationships with patients; for example, patients may come to the doctor's office demanding a new drug seen on a DTC ad with the implicit threat that they will seek out another doctor who will prescribe them the DTC medication if the physician refuses to prescribe for valid medical reasons. So a physician's role as gatekeeper of information has been eroded through big pharma's consumer marketing campaigns.

Direct effects of big pharma marketing on physicians relate to paid consultancy work and promotional activities, such as cruises, free drugs and other gifts. It also relates to continuing medical education of doctors, which in the United States is driven by key opinion leaders, who are often on the payroll of industry. All of these factors have in their turn had a negative knock-on effect for the reputation of doctors themselves and eroded the doctor-patient relationship.

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Those surveyed pointed to several industry shortcomings: a failure to assist patients in securing medications in a difficult economic environment; offering drugs with only short-term health benefits; not serving the needs of neglected patient groups; inappropriate marketing of drugs; a lack of fair pricing policies; making drugs unaffordable to many patients; a lack of transparency in corporate activities, adverse news about products; not having a patient-centered strategy; and not acting with integrity. This is a fairly strong indictment of an industry that promotes itself as a lifesaver.

The impact of this reputational decline needs to be viewed in the context that approximately two-thirds of people's willingness to say positive things about a company is influenced by their perception of the company and only one-third by what they think of its products. Such results have been shown to be similar across multiple stakeholder groups—policymakers, regulators, media, investors, employees and government bodies[6]. Therefore, the tarnished reputation of the pharmaceutical industry, mainly through self-inflicted wounds, has had a major impact on its business and value in the marketplace.

Root causes of reputational decline

The relationships between the pharmaceutical industry and its various stakeholders have changed over the past few decades (Box 1). These changes have contributed to the loss of reputation, which has been due to numerous factors. Each factor taken in isolation would not have been sufficient to have brought about the decline all in itself; it is the combination of these factors that has brought about the loss of prestige.

Big pharma and big business. To some extent, reputational decline can be attributed simply to the fact that many pharma companies are large multinational corporations that are now facing strategic issues that require an adjustment to the traditional business model. The increasing price and cost pressure, patent expirations on blockbuster drugs leading to aggressive generic competition, public policy and changes in how consumers access medicine are leading to erosion of profit margins. Big pharma, like other industries, is not immune from the pressure of having to meet Wall Street quarterly earnings expectations; indeed, today's companies are measured on how well their stock performs and boards of directors incentivize management accordingly to meet Wall Street's demands. The needs of patients are secondary. This has resulted in a greater emphasis on a return on investment from R&D and reducing the amount of capital it is allocated. In turn, this has increased offshoring, the elimination of in-house teams and the flight of scientific expertise into the biotech/biopharmaceutical sector.

Box 1 Changing attitudes of stakeholders (continued)

Industry has also played a hidden role in biasing the clinical literature that physicians rely on to practice evidence-based medicine. It is increasingly clear that cherry picking of results and selective publishing practices directed by pharmaceutical company marketing teams to highlight favorable trial results and drive product sales have corrupted the literature; in some cases, the obfuscation of damaging side effect risks associated with the use of certain products (e.g., Vioxx in pain and Paxil in adolescents) has misled physicians, encouraging them to prescribe drugs in inappropriate clinical situations. These revelations have driven a wedge between professional physician societies and associations such that industry researchers are often unable to present their work at conferences or contribute reviews to the literature.

An increasingly disenfranchised workforce. After decades of layoffs and offshoring of R&D as well as the scaling down of sales reps, there are now many disgruntled pharmaceutical employees and ex-pharmaceutical company employees around the world. Disenfranchised employees can fuel negative information in the media and on the internet, and are often critical of decision making by pharma management.

Many of these R&D employees question the corporate line that industry remains focused on R&D and true innovation when it seems more effort is placed on share buybacks or extending existing franchises through incremental innovation, with accounts of promising discovery programs shelved, not because of scientific challenges, but rather because of the reassignment of corporate priorities. In addition, some disgruntled sales employees have become whistleblowers, speaking out against questionable practices in the marketing and detailing of pharmaceutical products.

Journalists and the new media. As information travels more quickly around the world, coupled with the 24/7 news cycle and trial by Twitter, industry lapses in business ethics, regulatory violations, manufacturing failures and other wrongdoing have been magnified and propelled around the globe at the speed of the internet. Not only is the web providing a wealth of health information at newsbyte speed, but also that information frequently may be false or of poor quality, gratuitously demonizing the pharmaceutical industry and blaming it for all manner of healthcare ills when culprits may lie elsewhere.

A further issue for an industry involved in the complex process of the creation, development and provision of medicine is the dwindling expertise of journalists with relevant expertise about health and the industry in the mainstream media. This means that media coverage of pharmaceutical industry issues is increasingly less likely to present a balanced discussion or nuanced view, particularly in relation to drug pricing, marketing and conflicts of interest.

The above changes to the media have exacerbated the problems encountered by big pharma corporate communications departments, particularly when dealing with internal wrongdoing. Often, pharmaceutical companies and their public relations teams cannot be assured that they will have the luxury of time to try to mitigate reputational damage in the media. In addition, the legally neutered communications that originate from large companies often come across as corporate, anodyne and dehumanized to members of the general public.

Lawyers and class-action lawsuits. Lawyers who have targeted asbestos and tobacco manufacturers in the past are increasingly turning their attention to drug companies, alleging that they have hidden the harm caused by medicines from consumers. With their ability to advertise, class-action tort lawyers have created a cottage industry over the safety issues that have arisen with respect to drugs. These follow a familiar formula: "Have you or a loved one endured a negative reaction" to a drug? If so, "legal action is an option for you and your family," often with a listing of the millions of dollars won in previous lawsuits. These lawyers are not solo practitioners with limited resources but a well-financed trial bar that can afford to advertise and attract thousands of claimants. Some of the more prominent litigation brought by these firms involved Pfizer's (New York) Rezulin, GSK's Paxil, Wyeth's (now Pfizer) diet drugs Fen-phen, Merck's (Whitehouse Station, NJ, USA) Vioxx and the list goes on. These suits reinforce the view that pharma cares less about their patients than profits.

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At the same time, consolidation in the industry continues unabated with the aim of furthering revenue growth and circumventing corporate taxes. Recently, mega mergers (by means of a so-called inversion into a company located in a jurisdiction with lower taxes than the jurisdiction in which the acquirer is located) overtly take place without reference to benefits to patients; indeed, such deals often emphasize that such mergers are valuable because they reduce US tax burden for a company—all against a background where the public outcry about tax dodges by big business and "the 1%" is becoming ever more strident. Although pharmaceutical executives have trumpeted that these consolidations result in more efficient R&D organizations, the true import has been the further curtailment of R&D spending devoted to high-risk, high-reward R&D—all to the detriment of patients. The fact that such consolidations have been discredited has not tempered the appetite in boardrooms to pursue this growth strategy. None of this goes down well with consumers.

R&D restructuring has had other reputational consequences. These decisions, involving local companies that employ hundreds or even thousands of people, may threaten large swathes of a nation's economy, employment and business (e.g., Pfizer and AstraZeneca's aborted merger in the spring, which prompted a UK parliamentary enquiry). Also several multinational pharmaceutical companies already present in a particular country have reorganized or relocated their R&D centers to other countries on the basis of short-term decisions to meet Wall Street expectations or short-term financial performance, which again can decimate local economies, leading to hardship and disenchantment with large pharmaceutical companies.

In the United States, big business has an increasingly long reach into policymaking in Washington, DC. As large corporations, US drug companies spend more than any other sector on lobbying each year: $234 million in 2012, according to the Center for Responsive Politics (CRP), a nonprofit research group in Washington, DC. Prominent companies have sought to influence the outcome of elections through campaign donations and the activities of elected legislators. It is doubtful that the public perceives this lobbying power as fostering patient interests over industry profits.

Lastly, as companies bridge many different markets in a globally interconnected world, differences between ethical standards in different national jurisdictions can translate into scandals for pharma on an international scale. The Chinese government's recent clampdown on the Shanghai office of GlaxoSmithKline (GSK, London) for its practices in marketing medicines is a case in point. Many of the practices (e.g., paying hospital doctors to prescribe)

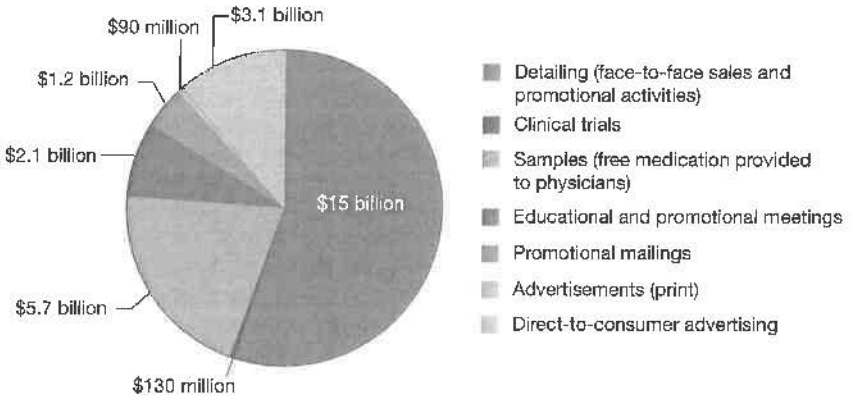

Figure 1 Main areas in which pharmaceutical marketing departments spent funds in 2012. Source: Pewtrusts.org

were detailed by a shocked media and are indeed unacceptable and criminalized in the West; however, Western media coverage often failed to highlight that such practices are not unusual in the Chinese drug marketplace. Even so, the negative publicity in the West has a detrimental effect on the company's (and therefore the industry's) reputation, even though it may have been acting in line with common business practice in China at the time. The question for multinational companies is, which national ethical standards should they follow?

Dubious marketing practices. It needs to be recognized that many of the industry's marketing practices have alienated patients and influenced the medical profession. During 2012, the pharmaceutical industry spent over $27 billion on promoting drugs, of which $24 billion was on marketing to physicians with the balance spent on consumers (**Fig. 1**). The majority or about $15 billion was spent on detailing—face-to-face promotional activities aimed at doctors and pharmacy directors, including wining and dining doctors, and promotional gifts. As of 2012, ~72,000 pharmaceutical sales representatives were employed in the United States alone. The next largest expenditure, $5.7 billion, was in samples—the free medication given to physicians—which has been shown to result in substantial increases in new prescriptions for the promoted drug. Big pharma companies assert that samples are intended to benefit indigent patients. Yet, research has shown that free medications are dispensed mostly to insured patients whose medications are covered[7]. These patients ultimately incur higher prescription costs than those who are not provided with samples because they are then prescribed the sampled drug rather than a less-expensive generic alternative.

The list of activities that are designed to influence physician prescription practices goes on: educational and promotional meetings at restaurants; promotional mailings highlighting a drug's benefits in trials sponsored by the company, which have been shown to be highly biased in favor of the company's drug; journal and web advertisements criticized by the FDA for highlighting a drug's effectiveness without pointing out its risks; and direct-to-consumer (DTC) ads encouraging consumers to ask doctors for the more expensive branded drug. Indirect marketing has also been effective in promoting drug sales. For example, continuing medical education, which used to function as veiled marketing, is now regulated but is still perceived as a marketing initiative; grants to health advocacy organizations intended to galvanize patients around a disease have the effect of promoting the drugs manufactured by the sponsoring company for these diseases.

All such marketing practices have inured to the detriment of patients. The historical focus on blockbuster drugs has been regarded by critics of big pharma as emphasizing sales volume over whether patients receiving a drug actually derive any benefit from it. The ubiquitous DTC ads in the United States not only promote a drug but increasingly reframe and medicalize human traits to create a need for the drug—Paxil (paroxetine) for social anxiety disorder or general anxiety disorder (shyness), Rogaine (minoxidil)/Propecia (finasteride) for baldness (male-pattern), Viagra (sildenafil) for erectile dysfunction (andropause, aging) or recently marketed low testosterone and 'low T' (andropause, aging). Big pharma is no longer just marketing drugs; it now markets diseases to consumers. Again, to many in the public, these DTC ads give the perception that industry's focus is more on peddling elixirs for trivial human conditions rather than focusing on finding drugs that ameliorate or cure debilitating diseases. Also, big pharma's use of 'pay-for-delay' deals and patent evergreening—in which intellectual property is used to enable line extensions of 'me-too' drugs and prevent generic competition—not only does nothing to reburnish its image as an innovative industry searching for cures but also has gotten pharma in the crosshairs of regulators. Last month, in a widely publicized lawsuit, the US Federal Trade Commission (FTC) alleged that the AbbVie (Deerfield, IL, USA) and TEVA Pharmaceuticals (Petach Tikva, Israel) pay-for-delay deal for AndroGel forced consumers to overpay hundreds of millions for that drug. The FTC said that it is hoping to get a billion dollar settlement in this and similar cases.

Big pharma's marketing practices have also alienated the medical profession. Allegations of companies withholding or failing to report negative data about marketed products—even making payments to certain physicians to overstate the benefits of drugs—have dogged the sector. Legislators have moved to pass legislation to counter corruption and conflicts of interest that have been attributed to companies in the pharmaceutical sector. Last month, the Open Payments Program of the Physician Payment Sunshine Act, a part of the 2010 Affordable Care Act came online, creating a database of drug company financial interactions with physicians and hospitals. Counterintuitively, it is possible that more transparency in these interactions will in the short term create more reputational damage for the pharmaceutical industry (and for doctors), particularly if distorted media coverage of the extent of industry-physician collaborations shocks a public who is unaware of the interaction between the two worlds and who wrongly assumes physicians and academics work in isolation from industry.

Finally, the preeminence of the marketing imperative in big pharma has meant industry has played a prominent role in the suppression of negative data in academic publications and in restricting the freedom of academics to disclose such data. These allegations have caused a backlash in several quarters. First, it has damaged the credibility of industry-sponsored publications so that prescribers have become increasingly skeptical about the data presented and increasingly concerned about the data supporting the safety and efficacy of the drugs they are prescribing. Second, it has angered many of the thought leaders and prominent medical journal editors like Catherine DeAngelis (*Journal of the American Medical Association*), who have become outspoken critics of the pharma industry in general. Books written by these leaders (e.g., *The Truth about Drug Companies, Overdosed America* and *Bad Pharma*) are read widely by the public and reviewed and discussed in the popular media.

Critical editorials and articles have been circulating for several decades in the

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scientific literature, but they have been more prominent of late. Journals like the *British Medical Journal* have considered banning all submissions from industry authors; the *Lancet* and the *New England Journal of Medicine* decline to publish any review articles by industry authors; and several clinical conferences no longer allow big pharma speakers to present their results. The fact that infractions by industry are not exceptional is what has prompted these blanket measures to be taken by clinical journals and learned societies.

Pricing and access to drugs. The high price of drugs is a problem increasingly blamed on the pharmaceutical industry (despite the fact that drug prices are not the biggest contributor to healthcare costs as a whole). In the US reimbursement system, the burden of high drug costs falls upon individuals, and state and local governments and insurers, which will need to balance access and affordability to an increasing extent. Such costs are unsustainable for healthcare systems that are facing infinite demand and finite resources, but in particular for the way in which these costs are being passed on to patients, in some cases leading them to bankruptcy.

Although industry cites the high costs of bringing a proprietary drug to market and the relatively short time of market and data exclusivity available to recoup these costs before generic competition, an increasingly strident group of physicians, legislatures and pharmacy benefit managers have weighed in, questioning whether the cost of these drugs are reasonable. For example, Zaltrap (ziv-aflibercept), a newly approved drug marketed by Sanofi at $11,000 per month, garnered national headlines when physicians at Memorial Sloan-Kettering Cancer Center in New York declared they would not include it in the formulary because of its high price in relation to benefit, causing Sanofi to effectively drop its price in half[8]. Interestingly, although big pharma has had its fair share of criticism over the pricing of its products, more often than not the most exorbitant prices are being charged by smaller biotech or biopharma companies (which spend substantial resources on differentiating their image and reputations from big pharma).

One recent case concerns the hepatitis C drug Sovaldi (sofosbuvir) from Gilead Sciences (Foster City, CA, USA), which has been subject to mounting criticism from the World Health Organization (Geneva), healthcare companies and patients over the drug's $1,000-a-day price. The debate has moved the US Senate Finance Committee to request information about the cost, and pharmacy benefit manager CVS Caremark has joined Express Scripts in urging Gilead to price its drug more reasonably. Other stakeholders like the National Coalition on Health Care and America's Health Insurance Plans also have criticized the cost of treatment, which could total $84,000 to $200,000 per patient, depending on the length of treatment. This represents about 10 to 20 times the cost of the current treatment regimen. It should not be lost on industry leaders that this furor has the echoes of past criticism of the pharmaceutical industry when it was accused of putting lifesaving HIV drugs out of reach of poorer populations.

Table 1 Endemic problems of criminal behavior and civil infringements across the sector

Date	Company	Fine ($ millions)	Infringement
February 2014	Endo Health Solutions and its subsidiary Endo Pharmaceuticals (Dublin)	192.7	Criminal and civil liabilities arising from Endo's marketing of the prescription drug Lidoderm (lidocaine). As part of the agreement, Endo admitted that it intended that Lidoderm be used for unapproved indications and that it promoted Lidoderm to healthcare providers this way.
November 2013	Johnson & Johnson	2,200	Criminal and civil allegations relating to illegal promotion of the prescription drugs Risperdal (risperidone), Invega (paliperidone) and Natrecor (Nesiritide) for uses not approved as safe and effective by the FDA, the targeting of elderly dementia patients in nursing homes, and the payout of kickbacks to physicians and to the nation's largest long-term care pharmacy provider, Omnicare.
December 2012	Amgen (Thousand Oaks, CA, USA)	762	Criminal and civil charges that the company illegally introduced and promoted several drugs, including Aranesp (darbepoetin alfa), a drug to treat anemia. Amgen pleaded guilty to illegally selling Aranesp to be used at doses that the FDA had explicitly rejected, and for an off-label treatment that FDA had never approved.
	Sanofi-Aventis (Paris)	109	Allegations that company gave doctors free units of Hyalgan (hyaluronate injection to relieve knee pain) to encourage sales, lowered the effective price by promising doctors free samples, while at the same time obtaining inflated prices for the drug from government programs by submitting false price reports.
October 2012	Boehringer Ingelheim	95	Allegations that company promoted several drugs including Aggrenox (aspirin/dipyridamole), Atrovent (ipratropium), Combivent (Ipratropium/albuterol) and Micardis (telmisartan) for nonmedically accepted uses.
July 2012	GSK	3,000	Civil and criminal liabilities regarding misbranding of Paxil for treating depression in patients under 18, even though the drug had never been approved for that age group as well as failure to disclose safety information about Avandia to the FDA.
May 2012	Abbott	1,500	Illegal promotion of Depakote (divalproex) in indications for which it had never been approved: schizophrenia and control of aggression and agitation in elderly dementia patients.
November 2011	Merck	950	Illegal promotion of Vioxx as a treatment for rheumatoid arthritis before it had been approved for that use and misrepresentation of the drug's heart safety to increase sales.
April 2010	AstraZeneca (London)	520	Allegations of illegal promotion of Seroquel (quetiapine) for a variety of unapproved uses, such as aggression, sleeplessness, anxiety and depression. The company paid the fine but denied the allegations.
September 2009	Pfizer	2,300	Misbranding Bextra with "the intent to defraud or mislead," promoting the drug to treat acute pain at dosages the FDA had previously deemed dangerously high. Bextra was pulled from the market in 2005 due to safety concerns. The government alleged that Pfizer also promoted three other drugs illegally: Geodon (ziprasidone), Zyvox (linezolid) and Lyrica (pregabalin).
January 2009	Eli Lilly	1,420	Off-label promotion of Zyprexa (olanzapine) to elderly populations to treat dementia. The US government also alleged that Lilly targeted primary care physicians to promote Zyprexa for unapproved uses and "trained its sales force to disregard the law."

Source: Department of Justice

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In response to the uproar, Gilead announced in September that it will allow seven Indian generic companies to make and market Sovaldi in >90 countries in the developing world to provide more affordable access. Even so, some organizations still criticized Gilead for excluding from this arrangement other highly burdened countries, such as China and Brazil, that represent potential lucrative markets.

A second issue is the inflexible drug pricing schemes that these companies are bringing to emerging economies, in many cases leading governments to issue compulsory licenses as a last ditch means of bringing affordable drugs to their countries. Given the fact that many large pharmaceutical companies are still highly profitable and frequently engage in share buybacks or dividends for the benefit of shareholders, industry should not be surprised that its lack of impetus to find solutions to providing its products to developing countries has a negative effect on its reputation.

Prominent public censure of industry malpractice. Industry has now been subjected to numerous regulatory and congressional investigations, billion-dollar fines for illegal marketing (gabapentin (Neurontin)), misleading DTC ads, off-label promotion of drugs, enquiries about pricing (Solvadi), lawsuits for the sale of drugs with known safety risks (e.g., Merck's Vioxx (rofecoxib)), and allegations of price fixing and kickbacks (including arrangements to delay access to generics). The list of companies fined in the billions of dollars by the US Department of Justice for violating the False Claims Act and the Federal Food, Drug & Cosmetic Act has not dampened such activities over time (**Table 1**).

Pharmaceutical companies are seemingly oblivious to the consequences of these fines to their reputations, even if they shrug them from their balance sheets as the cost of doing business. These activities, at times in violation of criminal statutes, are publicized in many different media outlets across the world for all to see. This has led consumers to espouse that there is too little regulation of the industry. How can industry continue to engage in these activities and not expect its reputation to be damaged?

Restoring a reputation

Once a company's reputation declines, some sources[3] estimate that it takes about 3.5 years to rebuild it, even in the best of circumstances. Given the many missteps of the pharmaceutical industry over the years, there is no single panacea to fix the current reputation problem. And the process of restoring reputation will be complex, requiring the rebuilding of trust among multiple stakeholders. Therefore, improving the pharmaceutical industry's standing is going to require both industry as a whole (through its trade bodies and other organizations) and individual pharmaceutical companies to come to grips with the factors precipitating reputational decline and seek to address them. The following are some of the steps that can start the industry on the road to recovery.

Refocus on patient's needs. Among the main components that are used in reputational measurement are ethics (the company behaves ethically and is trustworthy) and customer focus (the company cares about and is strongly committed to its customers). As can be gleaned from patient surveys, the pharmaceutical industry has fallen short in these key ingredients in recent years. Therefore, a good place to start rebuilding the reputation of the pharmaceutical industry is to focus on its key stakeholder—its consumers. This is a large task, and it will require establishing a sense of caring about patients on an industry-wide basis.

The public needs to be convinced that pharmaceutical companies are concerned about them and about curing their maladies. Thus, George W. Merck's admonition "We try to remember that medicine is for the patient. We try never to forget that medicine is for the people. It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear. The better we have remembered it, the larger they have been" needs to be inculcated in the center of big pharma's core values and its behavior. This requires programs that reach out and forge bonds with patients and their physicians. A good place to start is to collaborate with patient organizations to understand patient needs and how to fulfill them, by developing creative support programs, providing educational as opposed to marketing materials to patients, and where needed, cost-effective patient access to drugs. For example, lack of adherence to drug regimens is a serious health issue, especially among the elderly. Companies could develop adherence programs for their drugs. Through the use of social media, drug companies can implement this and other programs and engage in an effective dialog with patients. Recently, Pfizer (New York) has taken this tack by launching a social media campaign using the hashtag, #FOGO (fear of getting old), which attempts to stimulate a dialog related to the aging process and its import. This is intended to burnish the Pfizer brand rather than promote particular products.

Cease DTC advertising. The industry needs to take a critical look at DTC advertising and determine whether it strengthens the perception of patients that drugs companies care more about selling more drugs to enhance earnings than they do about patients. These ads are ubiquitous on television, tend to demean the image of the companies, generally talk down to patients and detract from the benefits that the drugs are intended to provide to the appropriate patient population. The ads may also promote inappropriate use of the drugs by patients deriving their information from the advertisement rather than from their personal physicians.

Price for prestige as well as profit. Among the many perceptions that patients have of pharmaceutical companies is that their current focus is on improving their earnings rather than the lives of patients. Clearly, the cost of developing a truly innovative drug is expensive and can exceed $1 billion when failures are factored into the equation. But is the pricing justified?

There is a need to educate stakeholders about the costs associated with drug development and to justify the pricing of a new drug by describing the benefit to affected patients and the cost savings to the healthcare system. Even then a drug company should consider whether its pricing policy should still be tempered to avoid the potential outcry from its stakeholders and the longer term impact on its reputation.

Restore an ethical culture. The ethics of a company are at the top of many reputational measurement systems. Thus, it should not come as a surprise that ethical lapses attributed to pharmaceutical employees garner much of the attention of the pharmaceutical stakeholders, including regulators. A corporation's culture is a system of shared values that guides the behavior of the company's members. To foster an ethical culture, the boards of directors of companies need to question whether the company is run with ethical leadership, which is inculcated throughout the organization. If companies tolerate unethical behavior from senior management and give them a free pass, then it sends a message within the organization that it is fine to weigh ethical conduct on a cost-benefit basis or to seek ways to circumvent potential liability. As pharmaceutical companies conduct operations globally, the industry needs to take steps to instill its ethical framework into diverse cultures where the respect for such conduct is often wanting. Executives should always consider whether they would be comfortable if their company decisions involving ethics were ever made public.

If the fundamental culture of the pharmaceutical industry is principally focused on promoting corporate profit, ethical conduct will suffer. Therefore, boards of directors should

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consider whether the percentage of executive compensation based on equity is fostering the wrong behavior. Twenty years ago, about 20% of an executive's compensation was in the form of stock; today, in large companies, it accounts for about 60% (ref. 9). With such a large amount of value tied to a stock's performance, are boards fostering the wrong behavior in company leadership? Absent the right culture, ethical lapses will just continue to be the cost of doing business. Big pharma needs to take steps, such as Johnson & Johnson (New Brunswick, NJ, USA) management did in the 1980s when it pulled Tylenol capsules from the market nationwide because of tampering in Chicago, or as Merck executives did when they developed a drug for river blindness at a cost of hundreds of million of dollars, and provided it free to victims living in abject poverty.

To be sure, restoring ethical behavior in today's profit-driven environment is not without its challenges. It has been reported that GSK, in an attempt to be the poster child for ethical behavior, has taken steps to reform its marketing practices by altering its pay structure and incentives to drug detailing representatives, severing the connection between sales and their compensation and eliminating compensation to doctors for promoting its products. Some analysts are concerned, however, that these reforms may be responsible for the deteriorating sales of some of GSK's products. It is notable that other big pharma companies have not followed the GSK lead[10].

Stop flaunting regulations and law. From January 2009 through February 2014, 11 pharmaceutical companies (including Merck and Johnson & Johnson) agreed to pay over $13 billion in fines stemming from allegations running the gamut of fraudulent marketing practices to failure to report safety-related data. Despite the adverse media publicity stemming from these billions of dollars in fines, the public does not believe that senior management ever was held accountable. To avert such failings in the future, the industry needs to restore ethical behavior, put in place better controls and punish misconduct of executives responsible for the infractions. Interestingly, there has not been the same clamor for the government to hold pharma's management to account for such wrongdoing as there has been in relation to the financial sector's malfeasance.

Implement data transparency. Drug companies have been accused of a reckless disregard for patient safety. In April of this year, a jury in the United States ordered Takeda (Tokyo) and Eli Lilly (Indianapolis) to pay $9 billion in damages for hiding evidence possibly linking their drug Actos (pioglitazone) to a form of cancer. Although the size of this award is not likely to stand, it reflects the public's disdain for the lack of transparency of drug industry data affecting patients. Allegations also abound that pharmaceutical companies publish successful trial data and withhold from publication negative data, and rig study designs to foster favorable outcomes. Such a controversy surrounds Tamiflu, where Roche (Basel) spent years resisting efforts by the Cochrane Collaboration to obtain missing efficacy data from clinical trials. Although some attempts have been made for greater sharing of data—GSK, Roche and Johnson & Johnson have taken steps to make data available to those who request it—the industry as a whole has not embraced data sharing with open arms. Indeed, in 2013, AbbVie even filed a lawsuit (which has subsequently been dropped) to stop the European Medicines Agency from releasing clinical trial data for its blockbuster drug Humira (adalimumab) to the public. Although industry argues that confidential business information needs to be protected, there is no excuse for withholding safety data that could affect clinical decision making—whether before or after the drug has been approved by the regulators. The continued lack of data transparency further gives credence to industry critics and the public that drug companies have lost their ethical compass.

Change industry messaging. Although it is the actions of big pharma that have really hammered its reputation, industry's messaging has also played a role. The sector has not had an effective program to educate consumers and other stakeholders on how it has improved lives and the difficulty and costs associated with bringing new therapies to patients. In this respect, it should think about two key aspects.

First, industry needs to focus on its messengers. Surveys have shown that more than half of a company's reputation can be attributed to the CEO. In the past, pharmaceutical companies were run by CEOs who had both scientific training and credibility in the marketplace and were perceived as individuals concerned about patient well-being and devoted to their health. In recent times, large drug companies have often been run by lawyers or individuals coming out of sales and marketing, who are not likely to garner the same respect among stakeholders. Thus, companies need to overcome this perception. For example, it would behoove pharmaceutical companies to encourage executives grounded in science to interact more frequently with the relevant stakeholders in connection with the launch of an expensive drug. Such discussion could explain a new drug's benefits and why it is worth the high cost, its development expenses, the company's program to provide it to patients not fully covered by insurance and other relevant information. Having the CEO or CFO crow about a new drug's impact on the bottom line to securities analysts and the financial and trade press is not effective messaging to the greater public and stakeholders.

Second, beyond the usual trite epithets about caring for patients, industry needs to educate the public about what it really does, the value it brings to the discovery of medicines, and the complexity and time involved in bringing a new drug to market. Because the lay media is constantly bombarding readers with reports of breakthroughs in genomics and new technologies that promise to revolutionize drug discovery, the average consumer is unaware that it can take as many as 15 years to bring a drug to patients, or that the odds of a chemical going from discovery to launch are 5,000 to 1, and the cost of developing a new drug is in the hundreds of millions of dollars. For the foreseeable future, drug discovery and development will continue to be a long and costly process. What's more, industry needs to counter the misinformation from certain academics, politicians and pharmascolds who claim that it is academia and the US National Institutes of Health that bring drugs to market, not industry. Therefore, instead of squandering funds on DTC, pharmaceutical companies and the industry's trade associations should consider investing in a communications strategy designed to deliver this information.

Reduce government lobbying. For years, the pharmaceutical industry has been spending well over $200 million per year on lobbying activities in the United States. At the same time, these expenditures have not totally diminished congressional criticism of the industry. The industry has been criticized by both the US Congress and the FDA for several activities, ranging from violations for misleading advertising to targeting children with candy-flavored nicotine replacement products. A Congressional report even concluded that GSK tried to intimidate independent scientists and deliberately misrepresent medical data to rebut safety concerns over its Avandia (rosiglitazone) drug to treat diabetes. And when the US Congress goes after the FDA for its handling of Vioxx or Avandia, it is likely to have a ripple effect on the pharmaceutical industry's relationship with its principal regulator.

This type of conduct makes governmental bodies and regulators look askance at drug companies. Companies thus need to present the facts with complete candor to restore

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confidence in both their testimony and their data.

Do good and do it loudly. History is replete with examples where companies addressed social issues, which at the same time fostered the interest of the company. A recent *New York Times* article[11] entitled "Motivating corporations to do good" points out that corporations in the past not only were motivated by self-interest but also addressed some social and economic issues and listed a few of the more prominent examples: Henry Ford doubling his worker's pay; Eastman Kodak Company providing profit sharing, retirement and sickness benefits; and Coca-Cola pronouncing that corporate executives served workers, customers and the community and not just stockholders.

Today, like other large companies in other sectors, big pharma corporate ethos is to 'make the shareholder king'. Restoring reputation will mean placing more emphasis on patients and convincing shareholders this is worth the effort. For example, there is a dearth of innovation to develop new antibiotics to combat antibiotic-resistant infections. Big pharma has shunned development of these drugs and has proclaimed publicly that there are insufficient economic incentives for development programs to go forward. Shouldn't pharma, with its vast amount of resources—and a track record of producing antibiotic innovations in the past—reenter this area rather than bowing out? If no pharma company is willing to go it alone, perhaps a consortium could take on the development program.

To this end, the pharmaceutical industry needs to effectively communicate how it has reformed unethical practices (tiptoeing around the specter of class-action lawsuits), so that past dubious practices will not be repeated. It can also counter negative publicity by being more vocal about altruistic activities, such as philanthropic drug access programs, or other forms of assistance to community and humanitarian causes, including to the developing world. Pharma can also garner goodwill by embracing environmentally friendly technology and emphasize sustainability and moving toward the use of green chemistry and away from environmentally harmful processes. Finally, it should communicate how it is promoting research through investment, establishing private research institutes and foundations, and providing grants and scholarships to support young scientists.

But perhaps the most fruitful avenue in terms of restoring reputation is for big pharma to be seen as engaged in activities that promote and aid patients and patient groups. As much as possible, the pharmaceutical industry needs to find better routes to reach foundations, which are skeptical of industry's motives, in promoting research, and it should expand its consultations with patients to garner and incorporate their feedback. Ultimately, if the pharmaceutical industry can gain the support of patient groups who communicate with the media and public on its behalf, such communication will have substantially more weight with the public than any communications coming from a pharmaceutical company internal public relations department.

Conclusions

A strong reputation can benefit a pharmaceutical company in manifold ways—increasing sales from its various customer groups; enhancing relationships with collaborating companies; attracting and retaining a strong employee talent pool; improving relationships with regulators and governmental bodies; enhancing loyalty from its various stakeholders in the event of negative publicity or crisis; ensuring an ability to obtain premium prices for its products; and enabling better patient enrollment in its clinical trials. And yet the industry has neglected to address many of the factors that are damaging its name, resulting in a reputation that is worse than at any other time in its recent history.

The public's trust in big pharma is likely to worsen unless both individual companies and the industry sector as a whole make a concerted effort to address the fundamental problems that are eroding reputation. Rebuilding this lost reputation will be difficult and will take years. In addition, as the reputation of a single company is affected by the actions of others in the same industry, rebuilding reputations in an industry that is itself declining will be even more arduous.

To restore its good name, the pharmaceutical industry has to radically alter the way it is perceived by the public. The good news is that as the damage was self-inflicted, it should be possible to address it. However, this will require a change from an industry mindset that has been focused on profits and meeting the goals of securities analysts to a mindset that reemphasizes patients. This can only happen if the industry's corporate leadership and Wall Street believe that profits will naturally follow. Perhaps pharmaceutical executives can take their cue from recently arisen benefit-type corporations that have as their mission social as well as business goals, proving that investors do not view these goals as incompatible[12]. This may mean that rather than denying AIDS drugs to the poor populations of Africa and being vilified for it, drug companies take the high road. Merck did this when freely providing its drug for river blindness, which garnered enormous goodwill.

Brand reputation has come to represent a most valuable asset. Shouldn't the pharmaceutical industry treat its brand reputation with the same care it does its other assets and manage it and invest in it accordingly?

COMPETING FINANCIAL INTERESTS
The author declares no competing financial interests.

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BENZINGA

Pfizer Hits Deadlock With India Over Vaccine Indemnity Issue: Reuters

Vandana Singh

May 21, 2021 · 2 min read

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Pfizer Inc (NYSE: PFE) and the Indian government are at loggerheads over a demand by the company for legal protection from any claims linked to the use of its COVID-19 vaccine, said Reuters citing two sources.

What Happened: India has not given any manufacturer of a COVID-19 vaccine indemnity against the costs of compensation for any severe side effects.

"The whole problem with Pfizer is the indemnity bond. Why should we sign it?" an Indian government source with direct knowledge of the matter told Reuters.

"If something happens, a patient dies, we will not be able to question them (Pfizer). If somebody challenges in a court of law, the central government will be responsible for everything, not the company," the source added.

Pfizer declined to comment, citing ongoing discussions with the government.

The Indian health ministry also did not reply to Reuter's requests for comment.

The second source said Pfizer has been consistent in its position on indemnity and is not planning to change its approach for a deal with India.

Why It Matters: Last month, India pledged to fast-track approvals for overseas vaccine makers, including Pfizer, **Moderna Inc** (NASDAQ: MRNA), and **Johnson and Johnson** (NYSE: JNJ).

However, none have since sought permission from India's drug regulator to sell their vaccine in the country, which has a population of 1.35 billion.

Pfizer withdrew its application for emergency use authorization for the vaccine developed with **BioNTech SE** (NASDAQ: BNTX) in February after India insisted

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Price Action: PFE shares are down 0.15% at $40.06, while BNTX shares are down 1.33% at $201 during the market session on the last check Friday.

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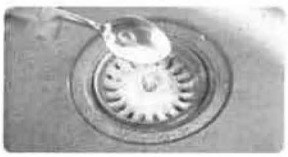

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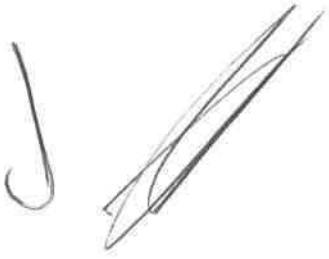

"HE17"

INDIA TOP NEWS FEBRUARY 5, 2021 / 7:30 AM / UPDATED 2 YEARS AGO

Pfizer drops India vaccine application after regulator seeks local trial

By Krishna N. Das 3 MIN READ

NEW DELHI (Reuters) - Pfizer Inc said on Friday it had withdrawn an application for emergency-use authorisation of its COVID-19 vaccine in India, after failing to meet the drug regulator's demand for a local safety and immunogenicity study.

A vial and syringe are seen in front of a displayed Pfizer and Biontech logo in this illustration taken January 11, 2021. REUTERS/Dado Ruvic/Illustration/File Photo

The decision means the vaccine will not be available for sale in the world's two most populous countries, India and China, in the near future. Both countries are running their immunisation campaigns using other products.

Unlike other companies conducting small studies in India for foreign-developed vaccines, Pfizer had sought an exception citing approvals it had received elsewhere based on trials done in countries such as the United States and Germany.

Indian health officials say they generally ask for so-called bridging trials to determine if a vaccine is safe and generates an immune response in its citizens. There are, however, provisions under India's rules to waive such trials in certain conditions.

The U.S. company, which was the first drugmaker to seek emergency approval in India for its vaccine developed with Germany's BioNTech, made the withdrawal decision after a meeting with India's Central Drugs Standard Control Organisation (CDSCO) on Wednesday.

The drug regulator said on its website its experts did not recommend the vaccine because of side effects reported abroad were still being investigated. It also said Pfizer had not proposed any plan to generate safety and immunogenicity data in India.

"Based on the deliberations at the meeting and our understanding of additional information that the regulator may need, the company has decided to withdraw its application at this time," Pfizer said in a statement.

"Pfizer will continue to engage with the authority and re-submit its approval request with additional information as it becomes available in the near future."

Reuters was the first to break the news.

Pfizer had sought authorisation for its vaccine in India late last year, but the government in January approved two much cheaper shots - one from Oxford University/AstraZeneca and another developed in India by Bharat Biotech with the Indian Council of Medical Research.

Both companies had applied for approval of their vaccines after Pfizer, and their trials are ongoing in India. Local company Dr. Reddy's Laboratories Ltd is running trials for Russia's Sputnik V vaccine, which is expected to be approved this month or next.

Reporting by Krishna N. Das; additional reporting by Anuron Kumar Mitra; editing by Raju Gopalakrishnan and Jason Neely

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"AM2"

Curing the pandemic of misinformation on COVID-19 mRNA vaccines through real evidence-based medicine - Part 2

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Background: Authorities and sections of the medical profession have supported unethical, coercive, and misinformed policies such as vaccine mandates and vaccine passports, undermining the principles of ethical evidence-based medical practice and informed consent. These regrettable actions are a symptom of the 'medical information mess': The tip of a mortality iceberg where prescribed medications are estimated to be the third most common cause of death globally after heart disease and cancer.

Aim: To identify the major root causes of these public health failures.

Methods: A narrative review of both current and historical driving factors that underpin the pandemic of medical misinformation.

Results: Underlying causes for this failure include regulatory capture – guardians that are supposed to protect the public are in fact funded by the corporations that stand to gain from the sale of those medications. A failure of public health messaging has also resulted in wanton waste of resources and a missed opportunity to help individuals lead healthier lives with relatively simple – and low cost – lifestyle changes.

Conclusion: There is a strong scientific, ethical and moral case to be made that the current COVID vaccine administration must stop until all the raw data has been subjected to fully independent scrutiny. Looking to the future the medical and public health professions must recognise these failings and eschew the tainted dollar of the medical-industrial complex. It will take a lot of time and effort to rebuild trust in these institutions, but the health – of both humanity and the medical profession – depends on it.

Contribution: This article highlights the importance of addressing metabolic health to reduce chronic disease and that insulin resistance is also a major risk factor for poor outcomes from COVID-19.

Keywords: COVID-19; mRNA vaccine; cardiac arrests; real evidence-based medicine; shared decision making.

A pandemic of misinformation

What has become clear with regard to the coronavirus disease 2019 (COVID-19) vaccines is that we have a pandemic of misinformed doctors and a misinformed and unwittingly harmed public. Coercively mandating these COVID-19 vaccinations (most certainly not an evidence-based policy) has been a particularly egregious mis-step, especially in the light of clear indicators suggesting that the use of these pharmaceutical interventions – especially in younger age groups – should have been suspended. Such policies continue to undermine the principles of ethical evidence-based medical practice and informed consent, to the detriment of optimising patient outcomes.

In his 2017 paper, 'How to survive the medical misinformation mess', Professor John Ioannidis and colleagues highlight that:

> [M]ost clinical trial results may be misleading or not useful for patients. Most guidelines (which many clinicians rely on to guide treatment decisions) do not fully acknowledge the poor quality of data on which they are based. Most medical stories in mass media do not meet criteria for accuracy, and many stories exaggerate benefit and minimise the harms.[1] (p. 1)

A senior doctor in regular contact with the United Kingdom's (UKs) Chief Medical Officer Professor Chris Whitty recently expressed concerns to me that he felt most of his colleagues in

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leadership positions influencing health policy may not be critically appraising the evidence and instead are relying on media stories on COVID-19 and the vaccine. This is consistent with the admission of Rochelle Walensky, the former chair of the Centers of Disease Control (CDC), whose optimism in the efficacy of Pfizer's COVID-19 vaccine came from reading a CNN news story, which was an almost verbatim reproduction of Pfizer's own press release.[2]

Has the UKs Chief Medical Officer Professor Chris Whitty critically appraised the evidence? Recently, he publicly shared a letter[3] outlining the importance of healthcare staff to become vaccinated against COVID-19, which was neither comprehensive nor consistent with the totality of the evidence: 'The COVID-19 vaccines are safe and effective'. It would have been more accurate to state that 'the vaccine is not completely safe and not anywhere close to being as effective as we'd hoped for. Not even in the same ball park when compared to the efficacy and safety of traditional vaccines'.

Professor Chirs Witty stated:

> Our professional responsibility is to get the covid vaccines as recommended to protect our patients'.[5]

He should have said as far as omicron is concerned, 'the vaccine offers little to no protection against infection. Data on the delta variant also revealed that once infected there is no significant difference in transmission rates between the vaccinated and unvaccinated individuals.

Professor Whitty's statements are especially surprising given that the CEO of Pfizer has stated that in realtion to omicron 'We know that the two doses of a vaccine offer very limited pretection, if any'.[5]

Could it be that Professor Whitty is also a victim of the medical misinformation mess?

There are four key drivers and seven sins that are at the root of the medical misinformation mess:

- Drivers:
  - Much published medical research is not reliable or is of uncertain reliability, offers no benefit to patients or is not useful for decision makers;
  - Most healthcare professionals are not aware of this problem;
  - Even if they are aware of this problem, most healthcare professionals lack the skills necessary to evaluate the reliability and usefulness of medical evidence; and
  - Patients and families frequently lack relevant, accurate medical evidence and skilled guidance at the time of medical decision making.[1]
- Sins:
  - Biased funding of research (that's research that's funded because it's likely to be profitable, not beneficial for patients)
  - Biased reporting in medical journals
  - Biased reporting in the media
  - Biased patient pamphlets
  - Commercial conflicts of interest
  - Defensive medicine
  - An inability of doctors to understand and communicate health statistics.[6]

Ioannidis and colleagues highlight that:

> 'Ignorance of this problem, even at the highest levels of academic and clinical leadership, is profound'[1]

Compounded over several decades, these upstream and downstream risk factors for misinformation have had a devastating effect in the healthcare environment we find ourselves in today. Over-prescription of drugs is considered such a public health threat that two leading medical journals in the past 10 years (the *BMJ* and *JAMA Internal Medicine*) have launched campaigns to reduce the harms of too much medical intervention. According to the cofounder of the Cochrane Collaboration, Peter Gøtzsche, prescribed medications are the third most common cause of death globally after heart disease and cancer.[7] This is not surprising when one understands that most published research is misleading specifically where benefits from drug trials are exaggerated, and harms downplayed (Box 1[8]).

If a doctor is making clinical decisions on biased information, it will lead (at best) to suboptimal outcomes and (more concerningly) harm to patients.

Shortcomings of the medical profession

According to Professor Carl Heneghan and urgent care General Practitioner, the director of the University of Oxford's Centre of Evidence-Based Medicine: 'with every intervention you do as a doctor you must ask yourself two questions: how much difference does it make? How do I know this?'[9]

Building on the Academy of Medical Royal Colleges Choosing Wisely campaign,[10]it is instructive to note that the

BOX 1: Major limitations in the interpretation, external validity and usefulness of drug industry-sponsored clinical trials.

1.	Trials are conducted of a study drug against a treatment known to be inferior
2.	Use multiple endpoints in the trial and select for publication those that give favourable results
3.	Do multicentre trials and select for publication results from centres that are favourable
4.	Conduct subgroup analyses and select for publication those that are favourable
5.	Present results that exaggerate the benefit – for example, use of relative risks as opposed to absolute risks
6.	Conduct trials on subjects that are unrepresentative of the patient population
7.	Conflate primary and secondary endpoints in the published report
8.	Conceal unblinded patients and include them in efficacy analyses for publication
9.	Exclude placebo responders in the wash-out phase of the trial
10.	Delay publication of negative trial results until positive trial results are published
11.	Conceal negative trial results whilst publishing only positive trial results
12.	Conceal serious adverse events
13.	Fail to distinguish clinical from statistical significance

Source: Adapted from Jureidini J, McHenry L. The illusion of evidence based medicine. Adelaide: Wakefield Press; 2020

General Medical Council in 2020 issued guidance on the duty of doctors to engage in Shared Decision Making with patients, underpinned by informed consent.[11]

There are six components essential to informed decision making: (1) description of the nature of the decision; (2) discussion of alternatives; (3) discussion of risks and benefits (in absolute terms); (4) discussion of related uncertainties; (5) assessment of the patient's understanding; and (6) elicitation of the patient's preference.

If the administration of the vaccine did not adhere to these principles (which is likely widespread, consistent with historical evidence[12]), then it is also a significant breach of General Medical Council duties of a doctor to 'give patients the information they want or need in a way that they can understand'.[13]

It is instructive to note that the greater the financial interests in a given field, the less likely the research findings are to be true.[14] As has been already demonstrated in Part 1[15] of this article, mandating a novel emergency use authorisation vaccine to non-vulnerable people has little to no effect on preventing infection and serious illness, therefore does not have any scientific validity, and therefore breaches the principles of informed consent. It does, however, dramatically enhance the profits of the manufacturer. By expanding the uptake of the mRNA vaccine to the majority of the population that are very low risk of serious complications from COVID-19 but are more likely to suffer serious and/or life-threatening adverse events such as myocarditis or sudden cardiac death, Pfizer has generated tens of billion dollars in revenues to date, making it one it one of the most lucrative products in history. If policymakers had focussed more on protecting the vulnerable – and doctors had been given the opportunity to practice shared decision making with patients using transparent communication of risk and benefit – patient outcomes would likely have been significantly improved,[16] but the drug companies' profits would likely have been a tiny fraction of what they actually generated. As former Editor of the *New England Journal of Medicine* Dr Marcia Angell has previously pointed out 'the real battle in healthcare is one of truth versus money'.[17]

Institutional corruption and erosion of public trust

Institutional corruption is defined as an institution's deviation from a baseline of integrity.[16] There is a long-documented history (both through studies and lawsuits) of the strategies in which drug companies hide, ignore or misrepresent evidence about new drugs. Distortion of medical literature and misrepresentation of data by companies keen to expand the marketplace for their product may result in overprescribing with predictable consequences of millions of patients suffering from avoidable adverse reactions.

Prior to 2020 there already existed gross shortcomings in the medical–industrial complex – there has been too much pharmaceutical industry influence on clinical decision making. This has not gone unnoticed, resulting in a growing crisis of trust in medical research: a report by the Academy of Medical Sciences in 2017 revealed that 82% of GPs and 63% of the public did not believe the results of pharmaceutical industry-sponsored research to be unbiased.[19] Similarly, only 37% of the public trust medical research compared to 65% who trust the experience of their friends and family.[20]

This growing lack of trust – most recently exacerbated by coercion, vaccine passports and little mainstream media coverage of an unprecedented scale of reported vaccine harms in the population – has been most recently exemplified by 8 million people in the UK refusing to take the COVID-19 booster shot. In addition, with all the attention on COVID-19 (which poses almost zero risk to children in its current omicron form), diverts attention away from, and even worse raises the suspicion of, more efficacious and safe interventions such as the measles, mumps, rubella (MMR) vaccine. Indeed, in the UK MMR vaccination rates have hit their lowest for 10 years.

Failure of regulation and research misconduct

Authorities want the public to 'trust the science', but vaccine manufacturers have successfully negotiated deals with several major governments globally that indemnify them against any financial liability in the event of vaccine-related harm. Interestingly, India, the world's largest democracy, refused to grant Pfizer indemnity from harms for its vaccine. An Indian government source told Reuters that:

> [T]he whole problem with Pfizer is the indemnity bond. Why should we sign it? If something happens, a patient dies, we will not be able to question them [*Pfizer*]. If somebody challenges in a court of law, the central government will be responsible for everything, not the company.[21] (p. 1)

Pfizer walked away from the Indian market rather than undertake a local safety and immunogenicity study.[22]

It is important to first understand that drug companies have a fiduciary obligation to deliver profits to their shareholders, not any legal responsibility to provide you with the best treatment. At a talk at the Centre of Evidence-Based Medicine in Oxford in 2014, Peter Wilmshurst said the real scandal is that many of those with a responsibility to patients and scientific integrity (doctors, academic institutions and medical journals) often collude with industry for financial gain.[23] It is this very industry that has been found guilty of the most egregious corporate crimes: between 2003 and 2016 the top 11 pharmaceutical companies paid $28.8 billion in fines just within the United States (US),[24] much of it for criminal activity such as the illegal marketing of drugs, manipulation of results and hiding data on harms. As pointed out in the *BMJ*, since then no systemic changes have been made to mitigate these harms.[9]

In an international survey of respondents from higher education institutions, 14% admitted to knowing a colleague who fabricated, falsified and modified data, and 34% of scientists report questionable research practices that included selective reporting of clinical outcomes in published research and concealing conflicts of interest.[25] An egregious documented case of research misconduct involved a prominent Dutch physician whose work influenced the European Society of Cardiology guidelines on the use of beta blocker drugs in non-cardiac surgery. He was dismissed from Erasmus University for 'violations in academic integrity', including using 'fictitious data' in research. It's estimated that these guidelines increased patient mortality by 27% resulting in 800 000 excess deaths across Europe over an 8-year period.[26]

In evidence submitted to the UK parliamentary science and technology review into research integrity committee in 2017 (Chaired by Sir Norman Lamb), Dr Peter Wilmshurst lists a number of risk factors that drive research misconduct in British institutions (see Box 2[27]). His solution, which I agree with, would be to ensure that serious forms of research misconduct are made into criminal offences with meaningful sanctions and that allegations of such activity should be investigated by an independent body with legal powers.[27]

BOX 2: Written evidence from Dr Peter Wilmshurst to UK Parliamentary Science and Technology Research Integrity Committee (June 2018).

Academic institutions bear responsibility for the pressure to publish for career advancement that can result in research misconduct

A record of prominent publication is likely to attract future funding, which institutions demand, and good publicity, which institutions desire.

Other pressures for misconduct come from the association of academic institution with industry, such as when investigators or their institutions hold patents or shares, or they receive payments from industry, so that there is financial pressure to publish research that will be profitable for the company and to suppress 'negative' findings.

Some publications are simply organised criminal activities, which may be at the behest of sponsors, when prominent academics are paid large sums of money to publish false data by industry, or a sponsor may be one of the victims, when payments for conducting research are made to 'investigators', who simply fabricate data.

Medical journals have financial pressures to publish positive findings of research on drugs and medical devices, because their manufacturers buy reprints of the papers for distribution to doctors and they pay for advertisements linked to articles favourable to their product.

Academic institutions and journals depend on the public belief in the integrity of science, so they are unwilling to admit the seriousness and frequency of research misconduct.

To protect their reputations academic institutions conceal research misconduct, destroy evidence and silence whistle-blowers.

Journals are reluctant to admit that they published flawed research, so they commonly refuse to publish failures to replicate.

Fear of a libel action contributes to the failure to expose research misconduct

Investigation of research misconduct may be difficult because there may be international collaboration between investigators, many of whom do not see the full data, and the resulting publications may be in journals that are published in countries where none of the investigators work.

The bodies that investigate research misconduct in the UK (such as the GMC and UKRIO) are hampered by a desire to play down the problem, by lack of proper forensic skills when investigating, by inconsistent interpretation of rules and by inadequate powers to compel the cooperation of academic institutions and journals.

Because lenient sanctions are imposed, institutions believe that the misconduct is not very serious, and potential research fraudsters are not deterred.

Source: Wilmshurst P. Written evidence [homepage on the Internet]. 2017 [cited 2022 Jun 5]. Available from: http://data.parliament.uk/writtenevidence/committeeevidence.svc/evidencedocument/science-and-technology-committee/research-integrity/written/68813.html

GMC, General Medical Council; UKRIO, United Kingdom Research Integrity Office.

One researcher at a prestigious UK institution contacted me to inform me that in his cardiology department a group of academics were deliberately suppressing research that revealed that the mRNA vaccine was shown to significantly increase coronary risk as determined by cardiac imaging as compared to the unvaccinated. The chair of the group expressed concerns that publishing the data may result in loss of funding from the pharmaceutical industry.[28] After I had alluded to this on GB News, the whistle-blower informed me that non-disclosure agreement letters were sent to all members of the team involved in this particular area of research.

Evidence-based medicine and COVID-19 vaccine roll-out

Neither the drug regulators nor the vaccine manufacturers have yet to share all the raw data from the pivotal trials for the COVID-19 vaccines.[29] The raw data from clinical trials comprise thousands of pages that have yet to be released for independent scrutiny. This is important because historically when independent researchers have on occasion gained access to this data then it can completely overturn the conclusions of the published trials: A case in point is Tamiflu.[30] Getting access to clinical case reports for Tamiflu ultimately revealed that the drug was no more effective than paracetamol for influenza and also came with small but significant harms. The UK government had spent half a billion dollars stockpiling a drug that in effect proved to be useless despite claims by the manufacturers (Roche, Basil, Switzerland) that it shortened the duration and severity of the illness. The independent researchers who were able to analyse the data concluded that all industry-sponsored research should be considered marketing until proven otherwise.

It is against this backdrop that transparency advocates sued the Food and Drug Administration (FDA) to gain access to the data upon which the Pfizer (BNT162b2) vaccine was granted emergency use authorisation.[31] The FDA wanted a US Federal court judge to allow the agency 55 years to release this data.[32] Why would the FDA – 'which is responsible for the oversight of more than $2.7 trillion in consumption of food, medical products, and tobacco'[33] – do this? Secrecy should never surround any public health intervention. The lawyer acting on behalf of the plaintiff Aaron Siri reported that:

> [T]he government also sought to delay full release of the data it relied upon to license this product until almost every American alive today is dead. That form of governance is destructive to liberty and antithetical to the openness required in a democratic society.[31]

Instead, the judge ordered the FDA to release the data over a period of eight months after all commercially sensitive information has been redacted.

A major risk factor for failure to protect the public from such harms is lack of independence of the regulator. The FDA's

Centre for Drug Evaluation Research (CDER) receives 65% of its funding from the pharmaceutical industry (mainly in the form of user fees).[34] For example, as part of the approval process for its COVID-19 vaccine, Pfizer made a wire transfer to the FDA of $2875842 million in May 2021[35] under the *Prescription Drug User Fee Act* of 1992.[36] Full FDA approval for Pfizer's COVID-19 injection duly followed in August 2021[37] despite recent evidence emerging that the original RCT data suggested a greater risk of serious adverse events from the vaccine than from hospitalisation because of COVID-19.

Separate analyses have revealed the overwhelming majority of new drugs that have been approved by the FDA in the past few decades have later been shown to be just copies of old ones, which is not surprising when one understands that drug companies spend 19 times more on marketing than they do on researching new molecular entities, which all contributes to considerable waste. Between 2000 and 2008 of the 667 drugs approved by the FDA, only 11% were found to be truly innovative. In the US it's estimated that 30% – 50% of healthcare activity brings no benefit to patients. Extraordinarily, a survey of FDA scientists revealed 70% of them did not feel the FDA had the resources to perform effectively in its mission in 'protecting public health … and helping the public get accurate science-based information to use medicines and foods to improve their health'.[38]

An analysis of every new drug product approved in France between 2002 and 2011 revealed only 8% offered some advantages and double that amount – at 15.6% – were found to be more harmful than beneficial with the majority of other new drugs being essentially copies of old ones contributing to a colossal waste of public money.[16] Similar conclusions have been drawn in Canada and Holland. In my opinion the evidence is overwhelming that the overall net effect of the pharmaceutical industry in the last few decades on society and population health has been a hugely negative one.

COVID-19 vaccination in lower risk individuals

Irrespective of the merits of inoculating higher risk groups where a small but significant benefit may exist against the original Wuhan strain, vaccinating lower risk children in the name of preventing asymptomatic transmission has no strong scientific validity and therefore exposes them to possible harm.

In the UK the Office for National Statistics has revealed an as yet unexplained significant increase in deaths over the 5-year average in 15- to 19-year-old children since May 2021. Given what we now know of potential harms especially in relation to myocarditis, myocardial infarction and sudden cardiac death (even in 16- to 39-year-olds) has the COVID-19 vaccine been excluded as a possible cause?[39]

In September 2021, the Joint Committee on Vaccination and Immunisation (JCVI) made a controversial recommendation that the Pfizer/BioNTech vaccine is marginally beneficial for 12- to 15-year-old children.[40] The Medicines and Healthcare products Regulatory Agency (MHRA, the UK's equivalent of the FDA) had previously stated that:

> [T]hey have carefully reviewed clinical trial data for Pfizer/BioNtech vaccine in over 2000 children aged 12–15 years of age and have concluded that the benefits of this vaccine outweigh any risk and that it is effective and acceptably safe in this age group … No new side effects were identified and the safety data in children was comparable to that seen in young adults. As in the young adult age group, the majority of adverse events were mild to moderate, relating to reactogenicity (e.g. sore arm and tiredness).[41] (p. 1)

Is this in keeping with the totality of the evidence?

Award winning investigative science journalist Maryanne Demasi published the harrowing story of one of those trial participants, 12-year-old Maddie De Garay. After experiencing severe abdominal pain followed by seizures she was admitted to hospital and is now left permanently disabled, wheelchair bound and fed through a nasogastric tube. In Pfizer's trial they reported her adverse effect as mild: stomach upset.[42]

It is important to emphasise that the risk of death from COVID-19 in a 12- to 15-year-old is close to zero at 1 in 76 000. In keeping with the principles of ethical evidence-based medical practice through shared decision making, parents need to be told that there is no high-quality data in children that the vaccine will prevent infection, transmission, serious illness or death but may come with serious side effects of myocarditis – particularly in young males where it occurs in up to 1 in 2700[43] – and serious disability as a general principle of transparent communication of risk and informed consent: without understanding the numbers involved the public is vulnerable to their hopes and anxieties being exploited by political and commercial interests.

Could financial interests be biasing the recommendations?

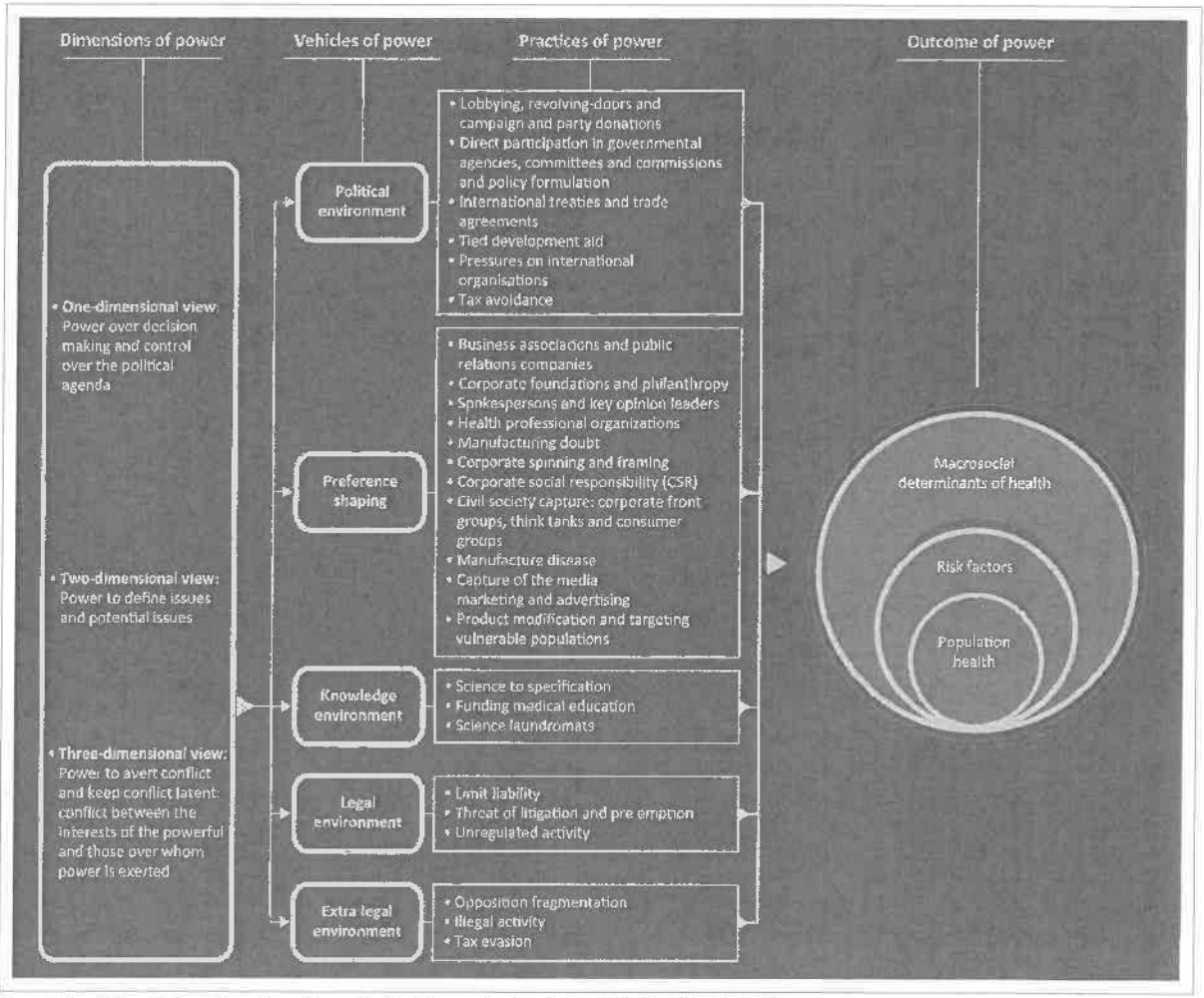
On its website the MHRA declares that the majority of its funding comes from the pharmaceutical industry and £3 million (UK pounds) from the Bill and Melinda Gates Foundation (BMGF). Are policymakers and the public aware that the foundation's corporate stock endowment is heavily invested in food (including McDonald's and Coca-Cola) and pharmaceutical companies, directly and indirectly? As pointed out in a 2009 *Lancet* paper, the funders' priorities are often driven by personal interests, not the health priority interests of the recipient country.[44] 'The BMGF's portfolio of pharmaceutical companies calls for attention given Mr Gates' personal belief in the role of patents as motors for innovation in medicines and medical technology'.[45]

Obesity researcher Dr Zoe Harcombe has also investigated the financial ties that could potentially be biasing the view of the joint committee for vaccines and immunisation and discovered that the subcommittee members work for organisations that receive in total $1bn from the BMGF.[46] It is

also worth noting that Professor Wei Shen Lim, chairman of the JCVI vaccine subcommittee, has direct responsibility for material levels of funding received by his department from Pfizer.[47] This is not in any way suggesting that the JCVI have acted in an improper way, but when confidence in an organisation such as the JCVI is imperative it's essential that there should be no perceptions of conflicts of interest. The systems of selection of panellists, the scrutiny of evidence and the methodology and openness of their recommendations need to be beyond reproach.

The most proximate cause of detrimental health outcomes: Corporate power and the commercial determinants of health

The commercial determinants of health are best defined by 'strategies and approaches adopted by the private sector to promote products and choices that are detrimental to health'.[48] Corporations exert their power by a combination of factors including intellectual exploitation. This includes the ability to define the dominant narrative: set the rules and procedures by which society is governed; determine the rights, living and working conditions of ordinary people; and take ownership of knowledge and ideas[49] (see Figure 1[45]). It appears that in the case of the mRNA vaccine, Pfizer has at least to some degree taken advantage of this corporate framework strategy by shaping the knowledge environment (Pfizer was responsible for the design and conduct of the trial, data collection, data analysis, data interpretation and the writing of the manuscript), the political environment (lobbying), preference shaping (corporate foundations and philanthropy, spokespersons and key opinion leaders, capture of the media), the legal environment (limit liability) and the extra-legal environment (opposition fragmentation by de-platforming critics of the current dominant narrative that the vaccine is safe and effective).[45] Consequently, it has made tens of billions of dollars in revenue from a product that in comparison with time-tested traditional vaccines and most other drugs has extremely poor efficacy and unprecedented reports of serious harms.



Source: Madureira Lima J, Galea S. Corporate practices and health: A framework and mechanisms. Global Health. 2018;14(1):21

FIGURE 1: Diagram of dimensions, vehicles, practices and outcomes of power.

Optimal metabolic health is having all five, and the metabolic syndrome (METS) is defined as failing to achieve at least three of the following:

- Blood pressure (systolic < 120 mmHg and diastolic < 80 mmHg)
- HbA1c < 5.7%
- Waist circumference < 102 cm for a man < 88 cm for a woman (for south Asians it's < 90 cm for a man and < 85 cm for woman)
- Blood triglycerides < 1.7 mmol/L (< 150 mg/dL)
- HDL-C > 1 mmol/L (> 40/50 mg/dL for men/women)

Source: Araujo J, Cai J, Stevens J. Prevalence of optimal metabolic health in American adults: National Health and Nutrition Examination Survey 2009–2016. Metab Syndr Relat Disord. 2019;17(1):46–52. https://doi.org/10.1089/met.2018.0105

HDL-C, high density lipoprotein cholesterol.

FIGURE 2: Markers of metabolic health.

Biased reporting in the media and censorship of legitimate scientific debate

Corporations are able to shape preferences and frame the dominant narratives on the determinants of health, through unchecked invisible power. One pathway is through the ownership of mass media. The global media market is dominated by seven corporations and chains that own 80% of the newspapers in the US.[50] The grants paid to global media companies by the BMGF are notable – for example, The Guardian Media Group has been in receipt of over $12m in grants from the BMGF over the last 12 years. Control over advertising in print and broadcast media also has an influence over editorial decisions. Most health journalists (including a number I have spoken to) are generally unaware that the information they obtain for stories has been deliberately shaped by the private interests of manufacturers and 'research' universities.

The BBC, though seemingly not directly influenced by industry interests, has traditionally been seen by some as the UK's most trusted media source. Its coverage of issues surrounding COVID-19 has in my view (possibly through additional government pressure) been extremely poor and – specifically on issues surrounding the vaccine – grossly negligent. During a recent report on tennis player Novak Djokovic explaining his decision to not take the vaccine until he has more information on its benefits and harms, a reporter asked the question 'how much more information does he need?'. The reporter failed to mention the fact that Djokovic has had COVID-19 and that evidence suggests that natural immunity offers *significant* protection against reinfection and severe disease, and that systemic side effects are almost threefold more likely in those with natural immunity who subsequently get vaccinated. Furthermore, the BBC falsely framed a guest on popular podcast host Joe Rogan, Dr Robert Malone, as a 'known anti-vaxxer, who is against vaccinating kids', failing to mention that Dr Malone is a co-inventor of the very technology that led to the vaccine, has spent 20 years in vaccine development at US government level and was one the first to actually receive two shots of the Moderna jab. The BBC also strangely failed to cover perhaps one of the most significant stories of the pandemic published in one of the most respected and influential medical journals in the world: An investigation by the *BMJ* revealed evidence of poor practices at a contract research company involved in Pfizer's pivotal COVID-19 vaccine trial. A regional director employed at one of the trial sites in Texas, US, documented evidence that Pfizer falsified data, unblinded patients, employed inadequately controlled vaccinators and was slow to follow up on adverse events. The very same day that she emailed her complaint to the FDA she was fired from her position.[51] She subsequently commenced litigation under whistle-blower legislation for fraud against Pfizer on behalf of the American Government (and the people of the US). Pfizer's motion to dismiss the case (which apparently did not sway the judge) was based on the fact that the FDA had not acted on her (or any other) complaints, hence the allegations were not material to the Government.

In the US, Senator Ron Johnson, who conducted hearings with healthcare professionals who were presenting data on clear, substantial and very common adverse effects from the mRNA jabs, which deserved widespread public attention, said 'the mainstream media are co-conspirators in this political dirty trick. Will they be held accountable for their role in this deception'?[52]

Social media platforms continue to be guilty of spreading misinformation. Their business model that focusses on increasing engagement at any cost makes society increasingly lose access to the truth and worsens our capacity for empathy as individuals, sowing even greater division and hostility. The so-called 'fact checkers' have censored anything that challenges the prevailing mainstream narrative (the establishment is trustworthy, and the vaccines are completely safe). They even labelled the *BMJ*'s investigation into potential fraud in Pfizer's pivotal trial as misinformation and stopped users sharing the story on their platform. A letter from the journal's current and former editor in chief to Mark Zuckerberg calls into question the integrity of Facebook's fact checkers:

> [R]ather than investing a proportion of Meta's substantial profits to help ensure the accuracy of medical information shared through social media, you apparently delegated responsibility to people incompetent in carrying out this crucial task.[53] (p. 1)

It has also come to light that Facebook has partnered with drug company Merck in deciding what content should be censored on its platform in relation to COVID-19 and the vaccine.[54] Is Facebook aware that Merck paid one of the largest fines in US history for being found guilty of fraud in relation to their pain killer Vioxx?[55] Not only did an investigation reveal that the drug did not reduce gastric bleeds (their original key selling point) in comparison with ibuprofen, but it significantly increased the risk of heart attacks and strokes, estimated to have caused excess deaths of between 40 000 and 60 000 Americans over a 5-year period.[56]

Improving metabolic health

Failure of public health messaging and policies to help individuals to improve their lifestyles during the pandemic represents a missed opportunity to mitigate harms from respiratory diseases such as COVID-19. After age, the biggest risk factor for worse COVID-19 outcomes has been obesity and

conditions related to excess body fat. More than 90% of the deaths from COVID-19 occurred in countries where more than 50% of the population is overweight or obese. The United Kingdom's biobank data during the first wave revealed a more than fourfold higher risk in hospitalisation from COVID-19 depending on lifestyle factors. For example, a non-smoking adult in their mid-fifties with a normal body mass index (BMI) and obtaining adequate physical activity levels had a 1 in 1521 chance of being admitted to hospital after contracting COVID-19, whereas an obese, smoking, sedentary person's risk was 1 in 327.[57]

Postulated pathophysiological mechanisms of risk and complications from infection include an array of markers that have insulin resistance and chronic inflammation at the root.

Even a single high blood glucose reading in non-diabetics (a marker of insulin resistance) admitted to hospital has been shown to be associated with worse outcomes.[58] It has also recently emerged in the UK that of the 175256 deaths associated with COVID-19 (2020–2021 inclusive) less than 10% (17371) had COVID-19 as the only cause on the death certificate suggesting that the risk to those individuals with optimal metabolic health from COVID-19 (Figure 2[59]) was significantly smaller, as per the results of the aforementioned UK biobank study.[60]

The government and medical authorities should have made it a priority to emphasise the importance of eliminating ultra-processed foods and low-quality carbohydrates to reduce risk. They could have made the public aware that reversal of metabolic syndrome has been shown to occur in up to 50% of patients – independent of weight loss – within four weeks of dietary changes alone.[61]

The coronavirus disease 2019 was a momentary crisis that exploited a slow pandemic of poor metabolic health (see Figure 2[59]), which is also the predominant root cause behind the major chronic diseases that have been putting healthcare systems around the world under increasing strain for decades. It is estimated that healthier lifestyles would (in absolute terms) *potentially* eliminate 40% of cancers and 75% of cardiovascular disease and type 2 diabetes.[63]

Optimising metabolic health would not just improve immune resilience but also reduce the burden of heart disease, type 2 diabetes, cancer and dementia. Learning lessons from tobacco control, policy changes that target the availability, acceptability and affordability of ultra-processed food and drink and low-quality carbohydrates would significantly reduce the burden of obesity, related metabolic diseases and likely optimise immune resilience in populations within a few years (see Box 3[62]).

The solutions

There was never any evidence justifying any COVID-19 vaccine mandates, passports or any of the other coercive measures adopted by various governments worldwide. Every patient who was offered any COVID-19 vaccine should have been made aware of what their risk from COVID-19 is according to age and risk factors. In keeping with ethical medical practice, doctors should have informed patients of their absolute risk reduction for infection from previous more lethal variant being approximately 0.84% or 1 in 119 (based on non-transparent data) and that this level of protection only lasts for a few months. They should also have provided more precise and robust data on what the actual absolute individual risk reduction of COVID-19 death from the vaccine is, what the true rates of serious adverse events (such as permanent disability, hospitalisation or death) are.

BOX 3: Policies to curb obesity and lifestyle-related disease.

1. Taxation of all ultra-processed foods and drinks needs to be enforced with the money gained going directly to subsidise whole and minimally processed foods such as fruit and vegetables
2. All medical students and doctors need to have adequate training in nutrition and lifestyle medicine
3. Every doctor should be measuring the metabolic health of their patients and making lifestyle prescriptions specifically linked to diet, physical activity and stress reduction to improve those health markers as their first-line intervention before the use of medication
4. Compulsory nutrition education and cooking skills introduced into all school curriculums
5. All hospital chief executives need to be made accountable for allowing the sale of ultra-processed food on hospital grounds, as it continues to harm the health of staff and patients and legitimises the acceptability of such food consumption to the wider public
6. A ban on advertising of all ultra-processed food and drink on television and online demand services
7. A public education campaign is needed to help consumers understand what ultra-processed food is and the harm it causes
8. A complete ban and dissociation of ultra-processed food and drink sponsorship of sports teams and sporting events
9. Local authorities should encourage active travel and protect and increase green spaces in urban areas to make the healthy option the easy option
10. Medical staff, including doctors, nurses and dietitians, should themselves be assessed on their metabolic health and encouraged and helped to improve it, not just to set an example to patients but to optimise their own health and performance.

Source: Malhotra A. The 21-day immunity plan. United Kingdom: Yellow Kite; 2021.

BOX 4: Defining real evidence-based medicine and actions to deliver it.

1. Is the application of individual clinical expertise with best available evidence and taking into consideration patient preferences and values in order to improve patient outcomes (relieve suffering and pain, treat illness and address risks to health)
2. Makes the ethical care of the patient it's top priority
3. Demands individualised evidence in a format that clinicians and patients can understand
4. Is characterised by expert judgement rather than mechanical rule following
5. Shares decisions with patients through meaningful conversations
6. Builds on a strong clinician–patient relationship and the human aspect of care
7. Applies these principles at community level for evidence-based public health

Actions to deliver real evidence-based medicine

1. Although the pharmaceutical industry plays an important role in developing new drugs, they should play no role in testing them
2. All results of all trials that involve humans must be made publicly available
3. Regulators such as the FDA and MHRA must be publicly funded, and not receive any money from the pharmaceutical industry
4. Independent researchers must increasingly shape the production, synthesis and dissemination of high-quality clinical and public health evidence
5. Medical education should not be funded or sponsored by the pharmaceutical industry
6. Patients must demand better evidence, better presented (using absolute and not relative risk), better explained and applied in a more personalised way

Source: Adapted from Greenhalgh T, Howick J, Maskrey N. Evidence based medicine Renaissance Group. Evidence based medicine: A movement in crisis? *BMJ*. 2014;348:g3725. https://doi.org/10.1136/bmj.g3725

It is only when doctors and patients have all this information that they can then be empowered to have frank decision making conversations on whether any treatment – including this vaccine – is right for them.

The profession must explain that optimising metabolic health will give patients the best chance for ensuring they are not just resilient to infection but reducing their risk of chronic disease including heart disease, cancer and dementia.

The time has come to stop misleading evidence flowing downstream into media reporting and clinical decision making and resulting in unethical and unscientific policy decisions. It's time for real evidence-based medicine (Box 4[66]).

There is also a strong scientific, ethical and moral case to be made that the current mRNA vaccine administration must stop until Pfizer releases all the raw data for independent scrutiny.[30] This will allow a more accurate understanding of which groups are more likely to potentially benefit from the vaccine versus those who are more likely to be harmed.

Given all the recent well-documented aforementioned shortcomings in medical research integrity (including that possibly half the published medical literature 'may simply be untrue'), the editor of the *Lancet* Richard Horton wrote in 2015 that science has taken a turn towards darkness and asked who was going to take the first step in cleaning up the system.[65] The unprecedented roll-out of an emergency use authorisation vaccine without access to the raw data, with increasing evidence of significant harms, compounded by mandates that appear to serve no purpose other than to bolster profits of the drug industry, have highlighted modern medicine's worst failings on an epic scale, with additional catastrophic harms to trust in public health.

We must use this as an opportunity to transform the system to produce better doctors, better decision making, healthier patients and restore trust in medicine and public health. Until all the raw data on the mRNA COVID-19 vaccines have been independently analysed, any claims purporting that they confer a net benefit to humankind cannot be considered to be evidence-based.

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Disclaimer

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Covid-19 vaccines and treatments: we must have raw data, now

Data should be fully and immediately available for public scrutiny

Peter Doshi, Fiona Godlee, Kamran Abbasi

In the pages of *The BMJ* a decade ago, in the middle of a different pandemic, it came to light that governments around the world had spent billions stockpiling antivirals for influenza that had not been shown to reduce the risk of complications, hospital admissions, or death. The majority of trials that underpinned regulatory approval and government stockpiling of oseltamivir (Tamiflu) were sponsored by the manufacturer; most were unpublished, those that were published were ghostwritten by writers paid by the manufacturer, the people listed as principal authors lacked access to the raw data, and academics who requested access to the data for independent analysis were denied.[1-4]

The Tamiflu saga heralded a decade of unprecedented attention to the importance of sharing clinical trial data.[5,6] Public battles for drug company data,[7,8] transparency campaigns with thousands of signatures,[9,10] strengthened journal data sharing requirements,[11,12] explicit commitments from companies to share data,[13] new data access website portals,[8] and landmark transparency policies from medicines regulators[14,15] all promised a new era in data transparency.

Progress was made, but clearly not enough. The errors of the last pandemic are being repeated. Memories are short. Today, despite the global rollout of covid-19 vaccines and treatments, the anonymised participant level data underlying the trials for these new products remain inaccessible to doctors, researchers, and the public—and are likely to remain that way for years to come.[16] This is morally indefensible for all trials, but especially for those involving major public health interventions.

Unacceptable delay

Pfizer's pivotal covid vaccine trial was funded by the company and designed, run, analysed, and authored by Pfizer employees. The company and the contract research organisations that carried out the trial hold all the data.[17] And Pfizer has indicated that it will not begin entertaining requests for trial data until May 2025, 24 months after the primary study completion date, which is listed on ClinicalTrials.gov as 15 May 2023 (NCT04368728).

The lack of access to data is consistent across vaccine manufacturers.[16] Moderna says data "may be available ... with publication of the final study results in 2022."[18] Datasets will be available "upon request and subject to review once the trial is complete," which has an estimated primary completion date of 27 October 2022 (NCT04470427).

As of 31 December 2021, AstraZeneca may be ready to entertain requests for data from several of its large phase III trials.[19] But actually obtaining data could be slow going. As its website explains, "timelines vary per request and can take up to a year upon full submission of the request."[20]

Underlying data for covid-19 therapeutics are similarly hard to find. Published reports of Regeneron's phase III trial of its monoclonal antibody therapy REGEN-COV flatly state that participant level data will not be made available to others.[21] Should the drug be approved (and not just emergency authorised), sharing "will be considered." For remdesivir, the US National Institutes of Health, which funded the trial, created a new portal to share data (https://accessclinicaldata.niaid.nih.gov/), but the dataset on offer is limited. An accompanying document explains: "The longitudinal data set only contains a small subset of the protocol and statistical analysis plan objectives."

We are left with publications but no access to the underlying data on reasonable request. This is worrying for trial participants, researchers, clinicians, journal editors, policy makers, and the public. The journals that have published these primary studies may argue that they faced an awkward dilemma, caught between making the summary findings available quickly and upholding the best ethical values that support timely access to underlying data. In our view, there is no dilemma; the anonymised individual participant data from clinical trials must be made available for independent scrutiny.

Journal editors, systematic reviewers, and the writers of clinical practice guideline generally obtain little beyond a journal publication, but regulatory agencies receive far more granular data as part of the regulatory review process. In the words of the European Medicine Agency's former executive director and senior medical officer, "relying solely on the publications of clinical trials in scientific journals as the basis of healthcare decisions is not a good idea ... Drug regulators have been aware of this limitation for a long time and routinely obtain and assess the full documentation (rather than just publications)."[22]

Among regulators, the US Food and Drug Administration is believed to receive the most raw data but does not proactively release them. After a freedom of information request to the agency for Pfizer's vaccine data, the FDA offered to release 500 pages a month, a process that would take decades to complete, arguing in court that publicly releasing data was slow owing to the need to first redact sensitive information.[23] This month, however, a judge rejected the FDA's offer and ordered the data be released at a rate of 55 000 pages a month. The data are to be made available on the requesting organisation's website (https://phmpt.org/).

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In releasing thousands of pages of clinical trial documents, Health Canada and the EMA have also provided a degree of transparency that deserves acknowledgment.[24 25] Until recently, however, the data remained of limited utility, with copious redactions aimed at protecting trial blinding. But study reports with fewer redactions have been available since September 2021,[24 25] and missing appendices may be accessible through freedom of information requests.

Even so, anyone looking for participant level datasets may be disappointed because Health Canada and the EMA do not receive or analyse these data, and it remains to be seen how the FDA responds to the court order. Moreover, the FDA is producing data only for Pfizer's vaccine; other manufacturers' data cannot be requested until the vaccines are approved, which the Moderna and Johnson & Johnson vaccines are not. Industry, which holds the raw data, is not legally required to honour requests for access from independent researchers.

Like the FDA, and unlike its Canadian and European counterparts, the UK's regulator—the Medicines and Healthcare Products Regulatory Agency—does not proactively release clinical trial documents, and it has also become delayed in posting information released in response to freedom of information requests on its website.[26]

Transparency and trust

As well as access to the underlying data, transparent decision making is essential. Regulators and public health bodies could release details[27] such as why vaccine trials were not designed to test efficacy against infection and spread of SARS-CoV-2.[28] Had regulators insisted on this outcome, countries would have learnt sooner about the effect of vaccines on transmission and been able to plan accordingly.[29]

Big pharma is the least trusted industry.[30] At least three of the many companies making covid-19 vaccines have past criminal and civil settlements costing them billions of dollars.[31] One pleaded guilty to fraud.[31] Other companies have no pre-covid track record. Now the covid pandemic has minted many new pharma billionaires, and vaccine manufacturers have reported tens of billions in revenue.[32]

The BMJ supports vaccination policies based on sound evidence. As the global vaccine rollout continues, it cannot be justifiable or in the best interests of patients and the public that we are left to just trust "in the system," with the distant hope that the underlying data may become available for independent scrutiny at some point in the future. The same applies to treatments for covid-19. Transparency is the key to building trust and an important route to answering people's legitimate questions about the efficacy and safety of vaccines and treatments and the clinical and public health policies established for their use.

Twelve years ago we called for the immediate release of raw data from clinical trials.[1] We reiterate that call now. Data must be available when trial results are announced, published, or used to justify regulatory decisions. There is no place for wholesale exemptions from good practice during a pandemic. The public has paid for covid-19 vaccines through vast public funding of research, and it is the public that takes on the balance of benefits and harms that accompany vaccination. The public, therefore, has a right and entitlement to those data, as well as to the interrogation of those data by experts.

Pharmaceutical companies are reaping vast profits without adequate independent scrutiny of their scientific claims.[33] The purpose of regulators is not to dance to the tune of rich global corporations and enrich them further; it is to protect the health of their populations. We need complete data transparency for all studies, we need it in the public interest, and we need it now.

Competing interests: We have read and understood BMJ policy on declaration of interests and declare that *The BMJ* is a co-founder of the AllTrials campaign. PD was one of the Cochrane reviewers studying influenza antivirals beginning in 2009, who campaigned for access to data. He also helped organise the Coalition Advocating for Adequately Licensed Medicines (CAALM), which formally petitioned the FDA to refrain from fully approving any covid-19 vaccine this year (docket FDA-2021-P-0786). PD is also a member of Public Health and Medical Professionals for Transparency, which has sued the FDA to obtain the Pfizer covid-19 vaccine data. The views and opinions do not necessarily reflect the official policy or position of the University of Maryland.

Provenance and peer review: Commissioned; externally peer reviewed.

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"HE20"

Pfizer and BioNTech Conclude Phase 3 Study of COVID-19 Vaccine Candidate, Meeting All Primary Efficacy Endpoints

Wednesday, November 18, 2020 - 06:59am

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Primary efficacy analysis demonstrates BNT162b2 to be 95% effective against COVID-19 beginning 28 days after the first dose; 170 confirmed cases of COVID-19 were evaluated, with 162 observed in the placebo group versus 8 in the vaccine group Efficacy was consistent across age, gender, race and ethnicity demographics; observed efficacy in adults over 65 years of age was over 94% Safety data milestone required by U.S. Food and Drug Administration (FDA) for Emergency Use Authorization (EUA) has been achieved Data demonstrate vaccine was well tolerated across all populations with over 43,000 participants enrolled; no serious safety concerns observed; the only Grade 3 adverse event greater than 2% in frequency was fatigue at 3.8% and headache at 2.0% Companies plan to submit within days to the FDA for EUA and share data with other regulatory agencies around the globe The companies expect to produce globally up to 50 million vaccine doses in 2020 and up to 1.3 billion doses by the end of 2021 Pfizer is confident in its vast experience, expertise and existing cold-chain infrastructure to distribute the vaccine around the world

NEW YORK & MAINZ, Germany--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) and BioNTech SE (Nasdaq: BNTX) today announced that, after conducting the final efficacy analysis in their ongoing Phase 3 study, their mRNA-based COVID-19 vaccine candidate, BNT162b2, met all of the study's primary efficacy endpoints. Analysis of the data indicates a vaccine efficacy rate of 95% ($p<0.0001$) in participants without prior SARS-CoV-2 infection (first primary objective) and also in participants with and without prior SARS-CoV-2 infection

(second primary objective), in each case measured from 7 days after the second dose. The first primary objective analysis is based on 170 cases of COVID-19, as specified in the study protocol, of which 162 cases of COVID-19 were observed in the placebo group versus 8 cases in the BNT162b2 group. Efficacy was consistent across age, gender, race and ethnicity demographics. The observed efficacy in adults over 65 years of age was over 94%.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20201118005595/en/

There were 10 severe cases of COVID-19 observed in the trial, with nine of the cases occurring in the placebo group and one in the BNT162b2 vaccinated group.

To date, the Data Monitoring Committee for the study has not reported any serious safety concerns related to the vaccine. A review of unblinded reactogenicity data from the final analysis which consisted of a randomized subset of at least 8,000 participants 18 years and older in the phase 2/3 study demonstrates that the vaccine was well tolerated, with most solicited adverse events resolving shortly after vaccination. The only Grade 3 (severe) solicited adverse events greater than or equal to 2% in frequency after the first or second dose was fatigue at 3.8% and headache at 2.0% following dose 2. Consistent with earlier shared results, older adults tended to report fewer and milder solicited adverse events following vaccination.

In addition, the companies announced that the safety milestone required by the U.S. Food and Drug Administration (FDA) for Emergency Use Authorization (EUA) has been achieved. Pfizer and BioNTech plan to submit a request within days to the FDA for an EUA based on the totality of safety and efficacy data collected to date, as well as manufacturing data relating to the quality and consistency of the vaccine. These data also will be submitted to other regulatory agencies around the world.

"The study results mark an important step in this historic eight-month journey to bring forward a vaccine capable of helping to end this devastating pandemic. We continue to move at the speed of science to compile all the data collected thus far and share with regulators around the world," said Dr. Albert Bourla, Pfizer Chairman and CEO. "With hundreds of thousands of people around the globe infected every day, we urgently need to get a safe and effective vaccine to the world."

"We are grateful that the first global trial to reach the final efficacy analysis mark indicates that a high rate of protection against COVID-19 can be achieved very fast after the first 30 μg dose, underscoring the power of BNT162 in providing early protection,"

said Ugur Sahin, M.D., CEO and Co-founder of BioNTech. "These achievements highlight the potential of mRNA as a new drug class. Our objective from the very beginning was to design and develop a vaccine that would generate rapid and potent protection against COVID-19 with a benign tolerability profile across all ages. We believe we have achieved this with our vaccine candidate BNT162b2 in all age groups studied so far and look forward to sharing further details with the regulatory authorities. I want to thank all the devoted women and men who contributed to this historically unprecedented achievement. We will continue to work with our partners and governments around the world to prepare for global distribution in 2020 and beyond."

The Phase 3 clinical trial of BNT162b2 began on July 27 and has enrolled 43,661 participants to date, 41,135 of whom have received a second dose of the vaccine candidate as of November 13, 2020. Approximately 42% of global participants and 30% of U.S. participants have racially and ethnically diverse backgrounds, and 41% of global and 45% of U.S. participants are 56-85 years of age. A breakdown of the diversity of clinical trial participants can be found here from approximately 150 clinical trials sites in United States, Germany, Turkey, South Africa, Brazil and Argentina. The trial will continue to collect efficacy and safety data in participants for an additional two years.

Based on current projections, the companies expect to produce globally up to 50 million vaccine doses in 2020 and up to 1.3 billion doses by the end of 2021. Four of Pfizer's facilities are part of the manufacturing and supply chain; St. Louis, MO; Andover, MA; and Kalamazoo, MI in the U.S.; and Puurs in Belgium. BioNTech's German sites will also be leveraged for global supply.

Pfizer is confident in its vast experience, expertise and existing cold-chain infrastructure to distribute the vaccine around the world. The companies have developed specially designed, temperature-controlled thermal shippers utilizing dry ice to maintain temperature conditions of -70°C±10°C. They can be used be as temporary storage units for 15 days by refilling with dry ice. Each shipper contains a GPS-enabled thermal sensor to track the location and temperature of each vaccine shipment across their pre-set routes leveraging Pfizer's broad distribution network.

Pfizer and BioNTech plan to submit the efficacy and safety data from the study for peer-review in a scientific journal once analysis of the data is completed.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality,

safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on Twitter at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Pfizer Disclosure Notice

The information contained in this release is as of November 18, 2020. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer's efforts to combat COVID-19, the collaboration between BioNTech and Pfizer to develop a potential COVID-19 vaccine, the BNT162 mRNA vaccine program, and modRNA candidate BNT162b2 (including qualitative assessments of available data, potential benefits, expectations for clinical trials, anticipated timing of regulatory submissions and anticipated manufacturing, distribution and supply), that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as risks associated with clinical data (including the Phase 3 data that is the subject of this release), including the possibility of unfavorable new preclinical or clinical trial data and further analyses of existing preclinical or clinical trial data; the ability to produce comparable clinical or other results, including the rate of vaccine effectiveness and safety and tolerability profile observed to date, in additional analyses of the Phase 3 trial or in larger, more diverse populations upon commercialization; the risk that clinical trial data are subject to differing interpretations and assessments, including during the peer review/publication process, in the scientific community generally, and by regulatory authorities; whether and when data from the BNT162 mRNA vaccine program will be published in scientific journal publications and, if so, when and with what modifications;

whether regulatory authorities will be satisfied with the design of and results from these and any future preclinical and clinical studies; whether and when any biologics license and/or emergency use authorization applications may be filed in any jurisdictions for BNT162b2 or any other potential vaccine candidates; whether and when any such applications may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the vaccine candidate's benefits outweigh its known risks and determination of the vaccine candidate's efficacy and, if approved, whether it will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of a vaccine, including development of products or therapies by other companies; disruptions in the relationships between us and our collaboration partners or third-party suppliers; risks related to the availability of raw materials to manufacture a vaccine; challenges related to our vaccine candidate's ultra-low temperature formulation and attendant storage, distribution and administration requirements, including risks related to handling after delivery by Pfizer; the risk that we may not be able to successfully develop non-frozen formulations; the risk that we may not be able to create or scale up manufacturing capacity on a timely basis or have access to logistics or supply channels commensurate with global demand for any potential approved vaccine, which would negatively impact our ability to supply the estimated numbers of doses of our vaccine candidate within the projected time periods indicated; whether and when additional supply agreements will be reached; uncertainties regarding the ability to obtain recommendations from vaccine technical committees and other public health authorities and uncertainties regarding the commercial impact of any such recommendations; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

About BioNTech

Biopharmaceutical New Technologies is a next generation immunotherapy company pioneering novel therapies for cancer and other serious diseases. The Company exploits a wide array of computational discovery and therapeutic drug platforms for the rapid development of novel biopharmaceuticals. Its broad portfolio of oncology product

candidates includes individualized and off-the-shelf mRNA-based therapies, innovative chimeric antigen receptor T cells, bi-specific checkpoint immuno-modulators, targeted cancer antibodies and small molecules. Based on its deep expertise in mRNA vaccine development and in-house manufacturing capabilities, BioNTech and its collaborators are developing multiple mRNA vaccine candidates for a range of infectious diseases alongside its diverse oncology pipeline. BioNTech has established a broad set of relationships with multiple global pharmaceutical collaborators, including Genmab, Sanofi, Bayer Animal Health, Genentech, a member of the Roche Group, Regeneron, Genevant, Fosun Pharma, and Pfizer. For more information, please visit www.BioNTech.de.

BioNTech Forward-looking statements

This press release contains "forward-looking statements" of BioNTech within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements may include, but may not be limited to, statements concerning: BioNTech's efforts to combat COVID-19; the collaboration between BioNTech and Pfizer to develop a potential COVID-19 vaccine; our expectations regarding the potential characteristics of BNT162b2 in our Phase 2/3 trial and/or in commercial use based on data observations to date; the expected timepoint for additional readouts on efficacy data of BNT162b2 in our Phase 2/3 trial; the nature of the clinical data, which is subject to ongoing peer review, regulatory review and market interpretation; the timing for submission of data for, or receipt of, any potential Emergency Use Authorization; the timing for submission of manufacturing data to the FDA; and the ability of BioNTech to supply the quantities of BNT162 to support clinical development and, if approved, market demand, including our production estimates for 2020 and 2021. Any forward-looking statements in this press release are based on BioNTech current expectations and beliefs of future events, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: the ability to meet the pre-defined endpoints in clinical trials; competition to create a vaccine for COVID-19; the ability to produce comparable clinical or other results, including our stated rate of vaccine effectiveness and safety and tolerability profile observed to date, in the remainder of the trial or in larger, more diverse populations upon commercialization; the ability to effectively scale our productions capabilities; and other potential difficulties. For a discussion of these and other risks and uncertainties, see BioNTech's Annual Report on Form 20-F filed with the SEC on March 31, 2020, which is available on the SEC's website at www.sec.gov. All information in this press release is as of the date of the release, and

BioNTech undertakes no duty to update this information unless required by law.

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Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

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ABSTRACT

BACKGROUND

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the resulting coronavirus disease 2019 (Covid-19) have afflicted tens of millions of people in a worldwide pandemic. Safe and effective vaccines are needed urgently.

METHODS

In an ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 μg per dose). BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full-length spike protein. The primary end points were efficacy of the vaccine against laboratory-confirmed Covid-19 and safety.

RESULTS

A total of 43,548 participants underwent randomization, of whom 43,448 received injections: 21,720 with BNT162b2 and 21,728 with placebo. There were 8 cases of Covid-19 with onset at least 7 days after the second dose among participants assigned to receive BNT162b2 and 162 cases among those assigned to placebo; BNT162b2 was 95% effective in preventing Covid-19 (95% credible interval, 90.3 to 97.6). Similar vaccine efficacy (generally 90 to 100%) was observed across subgroups defined by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions. Among 10 cases of severe Covid-19 with onset after the first dose, 9 occurred in placebo recipients and 1 in a BNT162b2 recipient. The safety profile of BNT162b2 was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache. The incidence of serious adverse events was low and was similar in the vaccine and placebo groups.

CONCLUSIONS

A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older. Safety over a median of 2 months was similar to that of other viral vaccines. (Funded by BioNTech and Pfizer; ClinicalTrials.gov number, NCT04368728.)

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*A complete list of investigators in the C4591001 Clinical Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Polack and Thomas contributed equally to this article.

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Coronavirus disease 2019 (COVID-19) has affected tens of millions of people globally[1] since it was declared a pandemic by the World Health Organization on March 11, 2020.[2] Older adults, persons with certain coexisting conditions, and front-line workers are at highest risk for Covid-19 and its complications. Recent data show increasing rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and Covid-19 in other populations, including younger adults.[3] Safe and effective prophylactic vaccines are urgently needed to contain the pandemic, which has had devastating medical, economic, and social consequences.

We previously reported phase 1 safety and immunogenicity results from clinical trials of the vaccine candidate BNT162b2,[4] a lipid nanoparticle–formulated,[5] nucleoside-modified RNA (modRNA)[6] encoding the SARS-CoV-2 full-length spike, modified by two proline mutations to lock it in the prefusion conformation.[7] Findings from studies conducted in the United States and Germany among healthy men and women showed that two 30-μg doses of BNT162b2 elicited high SARS-CoV-2 neutralizing antibody titers and robust antigen-specific CD8+ and Th1-type CD4+ T-cell responses.[8] The 50% neutralizing geometric mean titers elicited by 30 μg of BNT162b2 in older and younger adults exceeded the geometric mean titer measured in a human convalescent serum panel, despite a lower neutralizing response in older adults than in younger adults. In addition, the reactogenicity profile of BNT162b2 represented mainly short-term local (i.e., injection site) and systemic responses. These findings supported progression of the BNT162b2 vaccine candidate into phase 3.

Here, we report safety and efficacy findings from the phase 2/3 part of a global phase 1/2/3 trial evaluating the safety, immunogenicity, and efficacy of 30 μg of BNT162b2 in preventing Covid-19 in persons 16 years of age or older. This data set and these trial results are the basis for an application for emergency use authorization.[9] Collection of phase 2/3 data on vaccine immunogenicity and the durability of the immune response to immunization is ongoing, and those data are not reported here.

METHODS

TRIAL OBJECTIVES, PARTICIPANTS AND OVERSIGHT

We assessed the safety and efficacy of two 30-μg doses of BNT162b2, administered intramuscularly 21 days apart, as compared with placebo. Adults 16 years of age or older who were healthy or had stable chronic medical conditions, including but not limited to human immunodeficiency virus (HIV), hepatitis B virus, or hepatitis C virus infection, were eligible for participation in the trial. Key exclusion criteria included a medical history of Covid-19, treatment with immunosuppressive therapy, or diagnosis with an immunocompromising condition.

Pfizer was responsible for the design and conduct of the trial, data collection, data analysis, data interpretation, and the writing of the manuscript. BioNTech was the sponsor of the trial, manufactured the BNT162b2 clinical trial material, and contributed to the interpretation of the data and the writing of the manuscript. All the trial data were available to all the authors, who vouch for its accuracy and completeness and for adherence of the trial to the protocol, which is available with the full text of this article at NEJM.org. An independent data and safety monitoring board reviewed efficacy and unblinded safety data.

TRIAL PROCEDURES

With the use of an interactive Web-based system, participants in the trial were randomly assigned in a 1:1 ratio to receive 30 μg of BNT162b2 (0.3 ml volume per dose) or saline placebo. Participants received two injections, 21 days apart, of either BNT162b2 or placebo, delivered in the deltoid muscle. Site staff who were responsible for safety evaluation and were unaware of group assignments observed participants for 30 minutes after vaccination for any acute reactions.

SAFETY

The primary end points of this trial were solicited, specific local or systemic adverse events and use of antipyretic or pain medication within 7 days after the receipt of each dose of vaccine or placebo, as prompted by and recorded in an electronic diary in a subset of participants (the reactogenicity subset), and unsolicited adverse events (those reported by the participants without prompts from the electronic diary) through 1 month after the second dose and unsolicited serious adverse events through 6 months after the second dose. Adverse event data through approximately 14 weeks after the second dose are included in this report. In this report, safety

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data are reported for all participants who provided informed consent and received at least one dose of vaccine or placebo. Per protocol, safety results for participants infected with HIV (196 patients) will be analyzed separately and are not included here.

During the phase 2/3 portion of the study, a stopping rule for the theoretical concern of vaccine-enhanced disease was to be triggered if the one-sided probability of observing the same or a more unfavorable adverse severe case split (a split with a greater proportion of severe cases in vaccine recipients) was 5% or less, given the same true incidence for vaccine and placebo recipients. Alert criteria were to be triggered if this probability was less than 11%.

EFFICACY

The first primary end point was the efficacy of BNT162b2 against confirmed Covid-19 with onset at least 7 days after the second dose in participants who had been without serologic or virologic evidence of SARS-CoV-2 infection up to 7 days after the second dose; the second primary end point was efficacy in participants with and participants without evidence of prior infection. Confirmed Covid-19 was defined according to the Food and Drug Administration (FDA) criteria as the presence of at least one of the following symptoms: fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhea, or vomiting, combined with a respiratory specimen obtained during the symptomatic period or within 4 days before or after it that was positive for SARS-CoV-2 by nucleic acid amplification–based testing, either at the central laboratory or at a local testing facility (using a protocol-defined acceptable test).

Major secondary end points included the efficacy of BNT162b2 against severe Covid-19. Severe Covid-19 is defined by the FDA as confirmed Covid-19 with one of the following additional features: clinical signs at rest that are indicative of severe systemic illness; respiratory failure; evidence of shock; significant acute renal, hepatic, or neurologic dysfunction; admission to an intensive care unit; or death. Details are provided in the protocol.

An explanation of the various denominator values for use in assessing the results of the trial is provided in Table S1 in the Supplementary Appendix, available at NEJM.org. In brief, the safety population includes persons 16 years of age or older; a total of 43,448 participants constituted the population of enrolled persons injected with the vaccine or placebo. The main safety subset as defined by the FDA, with a median of 2 months of follow-up as of October 9, 2020, consisted of 37,706 persons, and the reactogenicity subset consisted of 8183 persons. The modified intention-to-treat (mITT) efficacy population includes all age groups 12 years of age or older (43,355 persons; 100 participants who were 12 to 15 years of age contributed to person-time years but included no cases). The number of persons who could be evaluated for efficacy 7 days after the second dose and who had no evidence of prior infection was 36,523, and the number of persons who could be evaluated 7 days after the second dose with or without evidence of prior infection was 40,137.

STATISTICAL ANALYSIS

The safety analyses included all participants who received at least one dose of BNT162b2 or placebo. The findings are descriptive in nature and not based on formal statistical hypothesis testing. Safety analyses are presented as counts, percentages, and associated Clopper–Pearson 95% confidence intervals for local reactions, systemic events, and any adverse events after vaccination, according to terms in the *Medical Dictionary for Regulatory Activities* (MedDRA), version 23.1, for each vaccine group.

Analysis of the first primary efficacy end point included participants who received the vaccine or placebo as randomly assigned, had no evidence of infection within 7 days after the second dose, and had no major protocol deviations (the population that could be evaluated). Vaccine efficacy was estimated by $100 \times (1-\mathrm{IRR})$, where IRR is the calculated ratio of confirmed cases of Covid-19 illness per 1000 person-years of follow-up in the active vaccine group to the corresponding illness rate in the placebo group. The 95.0% credible interval for vaccine efficacy and the probability of vaccine efficacy greater than 30% were calculated with the use of a Bayesian beta-binomial model. The final analysis uses a success boundary of 98.6% for probability of vaccine efficacy greater than 30% to compensate for the interim analysis and to control the overall type 1 error rate at 2.5%. Moreover, primary and secondary efficacy end points are evaluated sequentially to control the

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familywise type 1 error rate at 2.5%. Descriptive analyses (estimates of vaccine efficacy and 95% confidence intervals) are provided for key subgroups.

RESULTS

PARTICIPANTS

Between July 27, 2020, and November 14, 2020, a total of 44,820 persons were screened, and 43,548 persons 16 years of age or older underwent randomization at 152 sites worldwide (United States, 130 sites; Argentina, 1; Brazil, 2; South Africa, 4; Germany, 6; and Turkey, 9) in the phase 2/3 portion of the trial. A total of 43,448 participants received injections: 21,720 received BNT162b2 and 21,728 received placebo (Fig. 1). At the data cut-off date of October 9, a total of 37,706 participants had a median of at least 2 months of safety data available after the second dose and contributed to the main safety data set. Among these 37,706 participants, 49% were female, 83% were White, 9% were Black or African American, 28% were Hispanic or Latinx, 35% were obese (body mass index [the weight in kilograms divided by the square of the height in meters] of at least 30.0), and 21% had at least one coexisting condition. The median age was 52 years, and 42% of participants were older than 55 years of age (Table 1 and Table S2).

SAFETY

Local Reactogenicity

The reactogenicity subset included 8183 participants. Overall, BNT162b2 recipients reported more local reactions than placebo recipients. Among BNT162b2 recipients, mild-to-moderate pain at the injection site within 7 days after an injection was the most commonly reported local reaction, with less than 1% of participants across all age groups reporting severe pain (Fig. 2). Pain was reported less frequently among participants older than 55 years of age (71% reported pain after the first dose; 66% after the second dose) than among younger participants (83% after the first dose; 78% after the second dose). A noticeably lower percentage of participants reported injection-site redness or swelling. The proportion of participants reporting local reactions did not increase after the second dose (Fig. 2A), and no participant reported a grade 4 local reaction. In general, local reactions were mostly mild-to-moderate in severity and resolved within 1 to 2 days.

Figure 1 (facing page). Enrollment and Randomization.
The diagram represents all enrolled participants through November 14, 2020. The safety subset (those with a median of 2 months of follow-up, in accordance with application requirements for Emergency Use Authorization) is based on an October 9, 2020, data cut-off date. The further procedures that one participant in the placebo group declined after dose 2 (lower right corner of the diagram) were those involving collection of blood and nasal swab samples.

Systemic Reactogenicity

Systemic events were reported more often by younger vaccine recipients (16 to 55 years of age) than by older vaccine recipients (more than 55 years of age) in the reactogenicity subset and more often after dose 2 than dose 1 (Fig. 2B). The most commonly reported systemic events were fatigue and headache (59% and 52%, respectively, after the second dose, among younger vaccine recipients; 51% and 39% among older recipients), although fatigue and headache were also reported by many placebo recipients (23% and 24%, respectively, after the second dose, among younger vaccine recipients; 17% and 14% among older recipients). The frequency of any severe systemic event after the first dose was 0.9% or less. Severe systemic events were reported in less than 2% of vaccine recipients after either dose, except for fatigue (in 3.8%) and headache (in 2.0%) after the second dose.

Fever (temperature, ≥38°C) was reported after the second dose by 16% of younger vaccine recipients and by 11% of older recipients. Only 0.2% of vaccine recipients and 0.1% of placebo recipients reported fever (temperature, 38.9 to 40°C) after the first dose, as compared with 0.8% and 0.1%, respectively, after the second dose. Two participants each in the vaccine and placebo groups reported temperatures above 40.0°C. Younger vaccine recipients were more likely to use antipyretic or pain medication (28% after dose 1; 45% after dose 2) than older vaccine recipients (20% after dose 1; 38% after dose 2), and placebo recipients were less likely (10 to 14%) than vaccine recipients to use the medications,

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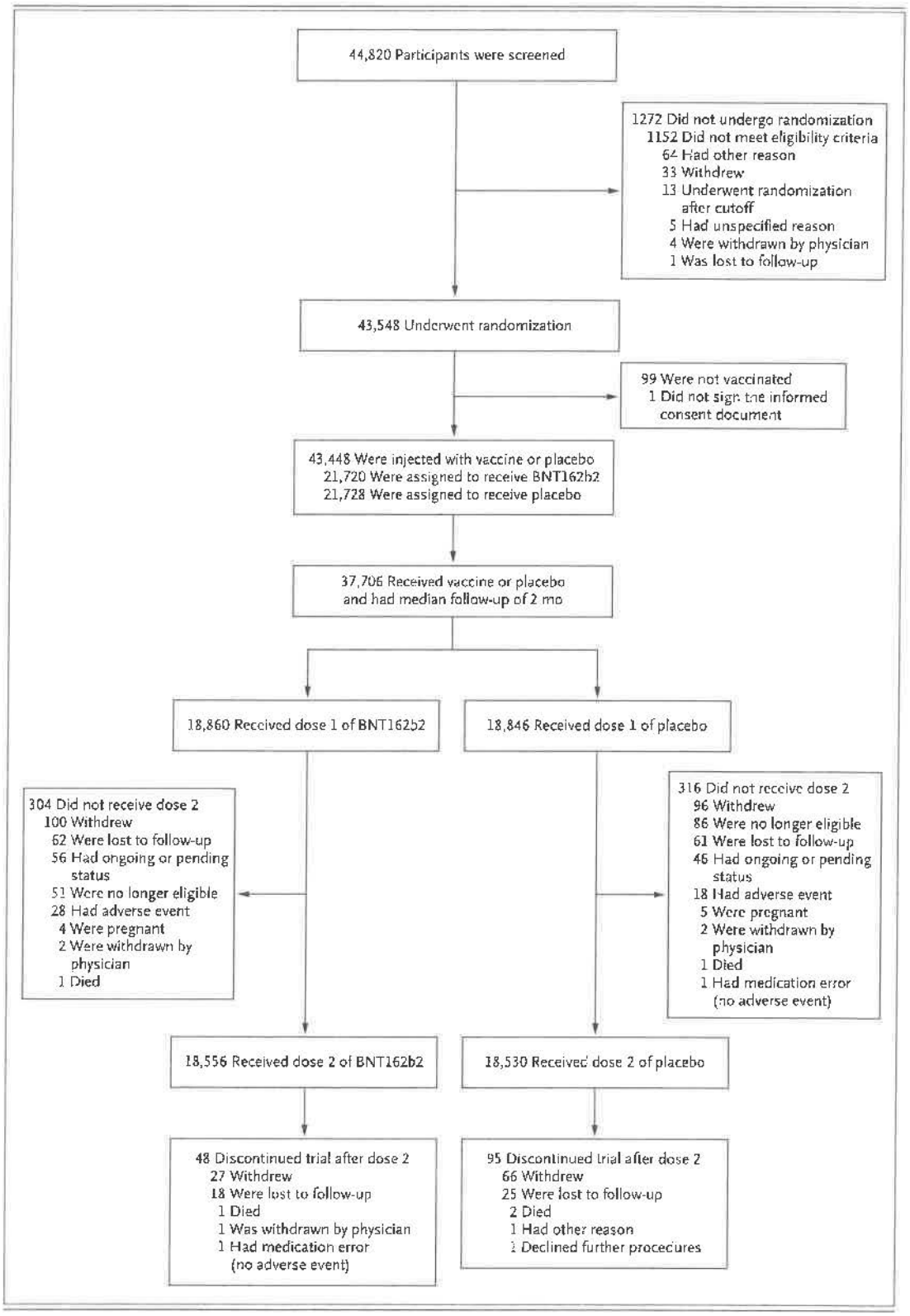

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Table 1. Demographic Characteristics of the Participants in the Main Safety Population.*

Characteristic	BNT162b2 (N=18,860)	Placebo (N=18,846)	Total (N=37,706)
Sex — no. (%)			
Male	9,639 (51.1)	9,436 (50.1)	19,075 (50.6)
Female	9,221 (48.9)	9,410 (49.9)	18,631 (49.4)
Race or ethnic group — no. (%)†			
White	15,636 (82.9)	15,630 (82.9)	31,266 (82.9)
Black or African American	1,729 (9.2)	1,763 (9.4)	3,492 (9.3)
Asian	801 (4.2)	807 (4.3)	1,608 (4.3)
Native American or Alaska Native	102 (0.5)	99 (0.5)	201 (0.5)
Native Hawaiian or other Pacific Islander	50 (0.3)	26 (0.1)	76 (0.2)
Multiracial	449 (2.4)	406 (2.2)	855 (2.3)
Not reported	93 (0.5)	115 (0.6)	208 (0.6)
Hispanic or Latinx	5,266 (27.9)	5,277 (28.0)	10,543 (28.0)
Country — no. (%)			
Argentina	2,883 (15.3)	2,881 (15.3)	5,764 (15.3)
Brazil	1,145 (6.1)	1,139 (6.0)	2,284 (6.1)
South Africa	372 (2.0)	372 (2.0)	744 (2.0)
United States	14,460 (76.7)	14,454 (76.7)	28,914 (76.7)
Age group — no. (%)			
16–55 yr	10,889 (57.7)	10,896 (57.8)	21,785 (57.8)
>55 yr	7,971 (42.3)	7,950 (42.2)	15,921 (42.2)
Age at vaccination — yr			
Median	52.0	52.0	52.0
Range	16–89	16–91	16–91
Body-mass index‡			
≥30.0; obese	6,556 (34.8)	6,662 (35.3)	13,218 (35.1)

* Percentages may not total 100 because of rounding.
† Race or ethnic group was reported by the participants.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

regardless of age or dose. Systemic events including fever and chills were observed within the first 1 to 2 days after vaccination and resolved shortly thereafter.

Daily use of the electronic diary ranged from 90 to 93% for each day after the first dose and from 75 to 83% for each day after the second dose. No difference was noted between the BNT162b2 group and the placebo group.

ADVERSE EVENTS

Adverse event analyses are provided for all enrolled 43,252 participants, with variable follow-up time after dose 1 (Table S3). More BNT162b2 recipients than placebo recipients reported any adverse event (27% and 12%, respectively) or a related adverse event (21% and 5%). This distribution largely reflects the inclusion of transient reactogenicity events, which were reported as adverse events more commonly by vaccine recipients than by placebo recipients. Sixty-four vaccine recipients (0.3%) and 6 placebo recipients (<0.1%) reported lymphadenopathy. Few participants in either group had severe adverse events, serious adverse events, or adverse events leading to withdrawal from the trial. Four related serious adverse events were reported among BNT162b2 recipients (shoulder injury related to vaccine administration, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, and right leg

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paresthesia). Two BNT162b2 recipients died (one from arteriosclerosis, one from cardiac arrest), as did four placebo recipients (two from unknown causes, one from hemorrhagic stroke, and one from myocardial infarction). No deaths were considered by the investigators to be related to the vaccine or placebo. No Covid-19–associated deaths were observed. No stopping rules were met during the reporting period. Safety monitoring will continue for 2 years after administration of the second dose of vaccine.

EFFICACY

Among 36,523 participants who had no evidence of existing or prior SARS-CoV-2 infection, 8 cases of Covid-19 with onset at least 7 days after the second dose were observed among vaccine recipients and 162 among placebo recipients. This case split corresponds to 95.0% vaccine efficacy (95% confidence interval [CI], 90.3 to 97.6; Table 2). Among participants with and those without evidence of prior SARS CoV-2 infection, 9 cases of Covid-19 at least 7 days after the second dose were observed among vaccine recipients and 169 among placebo recipients, corresponding to 94.6% vaccine efficacy (95% CI, 89.9 to 97.3). Supplemental analyses indicated that vaccine efficacy among subgroups defined by age, sex, race, ethnicity, obesity, and presence of a coexisting condition was generally consistent with that observed in the overall population (Table 3 and Table S4). Vaccine efficacy among participants with hypertension was analyzed separately but was consistent with the other subgroup analyses (vaccine efficacy, 94.6%; 95% CI, 68.7 to 99.9; case split: BNT162b2, 2 cases; placebo, 44 cases). Figure 3 shows cases of Covid-19 or severe Covid-19 with onset at any time after the first dose (mITT population) (additional data on severe Covid-19 are available in Table S5). Between the first dose and the second dose, 39 cases in the BNT162b2 group and 82 cases in the placebo group were observed, resulting in a vaccine efficacy of 52% (95% CI, 29.5 to 68.4) during this interval and indicating early protection by the vaccine, starting as soon as 12 days after the first dose.

DISCUSSION

A two-dose regimen of BNT162b2 (30 μg per dose, given 21 days apart) was found to be safe and 95% effective against Covid-19. The vaccine met both primary efficacy end points, with more than a 99.99% probability of a true vaccine efficacy greater than 30%. These results met our prespecified success criteria, which were to establish a probability above 98.6% of true vaccine efficacy being greater than 30%, and greatly exceeded the minimum FDA criteria for authorization.[9] Although the study was not powered to definitively assess efficacy by subgroup, the point estimates of efficacy for subgroups based on age, sex, race, ethnicity, body-mass index, or the presence of an underlying condition associated with a high risk of Covid-19 complications are also high. For all analyzed subgroups in which more than 10 cases of Covid-19 occurred, the lower limit of the 95% confidence interval for efficacy was more than 30%.

The cumulative incidence of Covid-19 cases over time among placebo and vaccine recipients begins to diverge by 12 days after the first dose, 7 days after the estimated median viral incubation period of 5 days,[10] indicating the early onset of a partially protective effect of immunization. The study was not designed to assess the efficacy of a single-dose regimen. Nevertheless, in the interval between the first and second doses, the observed vaccine efficacy against Covid-19 was 52%, and in the first 7 days after dose 2, it was 91%, reaching full efficacy against disease with onset at least 7 days after dose 2. Of the 10 cases of severe Covid-19 that were observed after the first dose, only 1 occurred in the vaccine group. This finding is consistent with overall high efficacy against all Covid-19 cases. The severe case split provides preliminary evidence of vaccine-mediated protection against severe disease, alleviating many of the theoretical concerns over vaccine-mediated disease enhancement.[11]

The favorable safety profile observed during phase 1 testing of BNT162b2[4,8] was confirmed in the phase 2/3 portion of the trial. As in phase 1, reactogenicity was generally mild or moderate, and reactions were less common and milder in older adults than in younger adults. Systemic reactogenicity was more common and severe after the second dose than after the first dose, although local reactogenicity was similar after the two doses. Severe fatigue was observed in approximately 4% of BNT162b2 recipients, which is higher than that observed in recipients of some vaccines recommended for older adults.[12] This rate of severe fatigue is also lower than that

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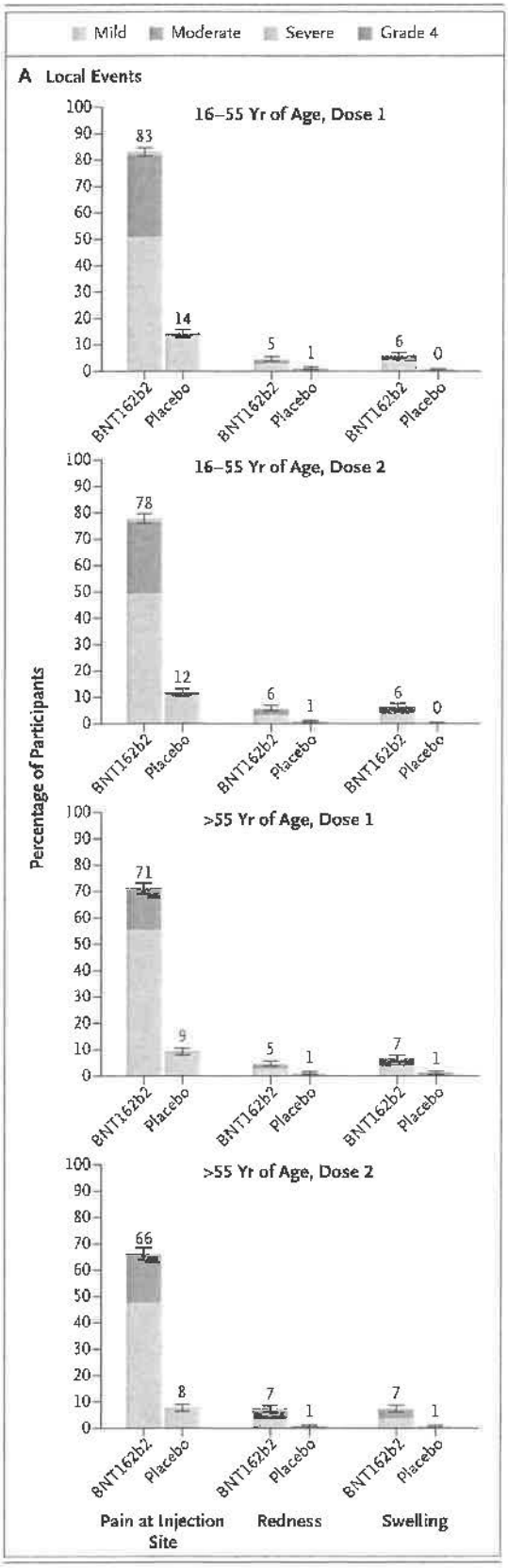
Figure 2. Local and Systemic Reactions Reported within 7 Days after Injection of BNT162b2 or Placebo, According to Age Group.

Data on local and systemic reactions and use of medication were collected with electronic diaries from participants in the reactogenicity subset (8,183 participants) for 7 days after each vaccination. Solicited injection-site (local) reactions are shown in Panel A. Pain at the injection site was assessed according to the following scale: mild, does not interfere with activity; moderate, interferes with activity; severe, prevents daily activity; and grade 4, emergency department visit or hospitalization. Redness and swelling were measured according to the following scale: mild, 2.0 to 5.0 cm in diameter; moderate, >5.0 to 10.0 cm in diameter; severe, >10.0 cm in diameter; and grade 4, necrosis or exfoliative dermatitis (for redness) and necrosis (for swelling). Systemic events and medication use are shown in Panel B. Fever categories are designated in the key; medication use was not graded. Additional scales were as follows: fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain (mild: does not interfere with activity; moderate: some interference with activity; or severe: prevents daily activity), vomiting (mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; or severe: requires intravenous hydration), and diarrhea (mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; or severe: 6 or more loose stools in 24 hours); grade 4 for all events indicated an emergency department visit or hospitalization. I bars represent 95% confidence intervals, and numbers above the I bars are the percentage of participants who reported the specified reaction.



observed in recipients of another approved viral vaccine for older adults.[13] Overall, reactogenicity events were transient and resolved within a couple of days after onset. Lymphadenopathy, which generally resolved within 10 days, is likely to have resulted from a robust vaccine-elicited immune response. The incidence of serious adverse events was similar in the vaccine and placebo groups (0.6% and 0.5%, respectively).

This trial and its preliminary report have several limitations. With approximately 19,000 participants per group in the subset of participants with a median follow-up time of 2 months after the second dose, the study has more than 83% probability of detecting at least one adverse event, if the true incidence is 0.01%, but it is not large enough to detect less common adverse events reliably. This report includes 2 months of follow-up after the second dose of vaccine for half the trial participants and up to 14 weeks' maximum follow-up for a smaller subset. Therefore, both

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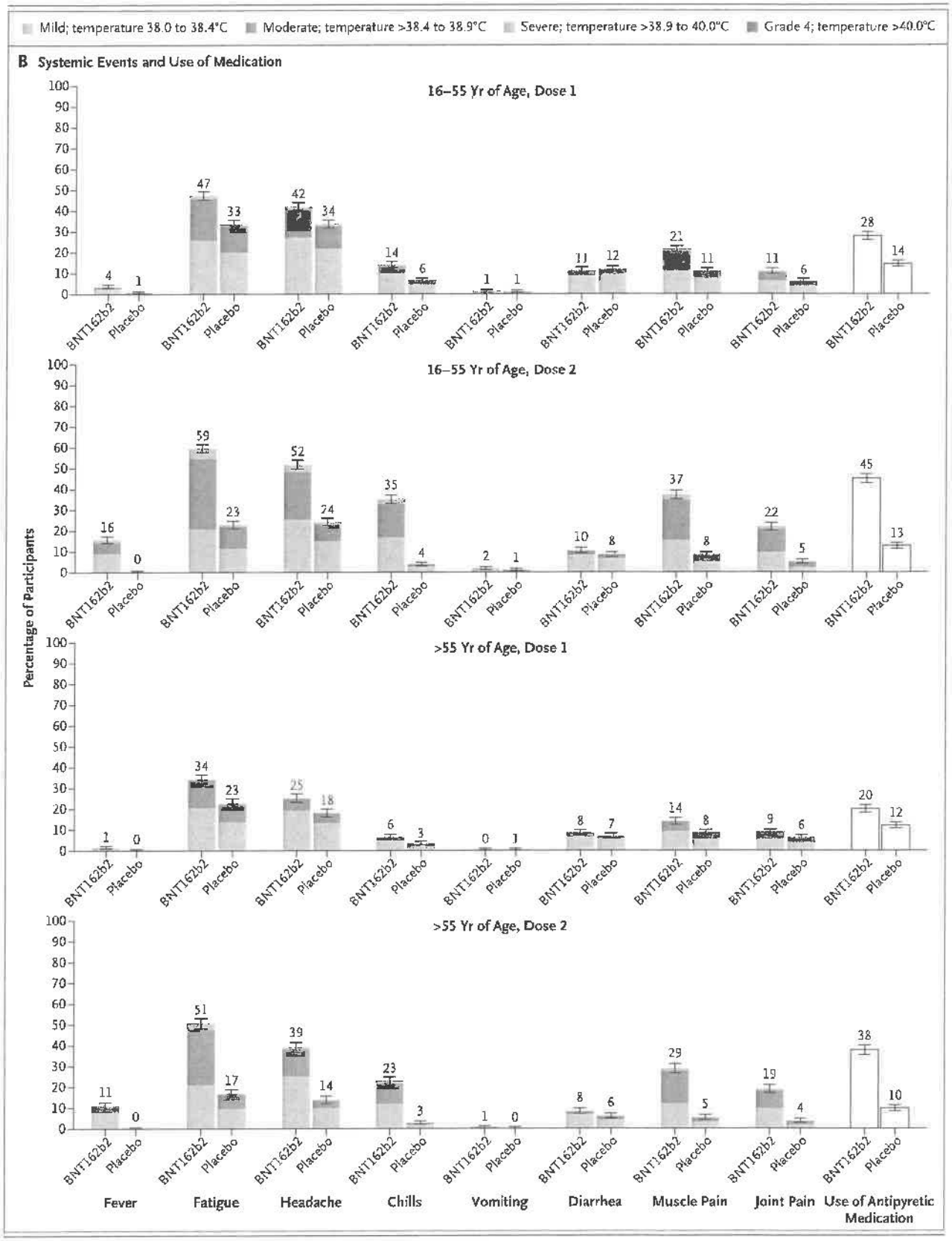

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Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2,214 (17,411)	162	2,222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2,332 (18,559)	169	2,345 (18,708)	94.6 (89.9–97.3)	>0.9999

* The total population without baseline infection was 36,523; total population including those with and those without prior evidence of infection was 40,137.

† The surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.

‡ The credible interval for vaccine efficacy was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.

§ Posterior probability was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.

the occurrence of adverse events more than 2 to 3.5 months after the second dose and more comprehensive information on the duration of protection remain to be determined. Although the study was designed to follow participants for safety and efficacy for 2 years after the second dose, given the high vaccine efficacy, ethical and practical barriers prevent following placebo recipients for 2 years without offering active immunization, once the vaccine is approved by regulators and recommended by public health authorities. Assessment of long-term safety and efficacy for this vaccine will occur, but it cannot be in the context of maintaining a placebo group for the planned follow-up period of 2 years after the second dose. These data do not address whether vaccination prevents asymptomatic infection; a serologic end point that can detect a history of infection regardless of whether symptoms were present (SARS-CoV-2 N-binding antibody) will be reported later. Furthermore, given the high vaccine efficacy and the low number of vaccine breakthrough cases, potential establishment of a correlate of protection has not been feasible at the time of this report.

This report does not address the prevention of Covid-19 in other populations, such as younger adolescents, children, and pregnant women. Safety and immune response data from this trial after immunization of adolescents 12 to 15 years of age will be reported subsequently, and additional studies are planned to evaluate BNT162b2 in pregnant women, children younger than 12 years, and those in special risk groups, such as immunocompromised persons. Although the vaccine can be stored for up to 5 days at standard refrigerator temperatures once ready for use, very cold temperatures are required for shipping and longer storage. The current cold storage requirement may be alleviated by ongoing stability studies and formulation optimization, which may also be described in subsequent reports.

The data presented in this report have significance beyond the performance of this vaccine candidate. The results demonstrate that Covid-19 can be prevented by immunization,

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Table 3. Vaccine Efficacy Overall and by Subgroup in Participants without Evidence of Infection before 7 Days after Dose 2.

Efficacy End-Point Subgroup	BNT162b2 (N=18,198)		Placebo (N=18,325)		Vaccine Efficacy, % (95% CI)†
	No. of Cases	Surveillance Time (No. at Risk)*	No. of Cases	Surveillance Time (No. at Risk)*	
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.0–97.9)
Age group					
16 to 55 yr	5	1.234 (9,897)	114	1.239 (9,955)	95.6 (89.4–98.6)
>55 yr	3	0.980 (7,500)	48	0.983 (7,543)	93.7 (80.6–98.8)
≥65 yr	1	0.508 (3,848)	19	0.511 (3,880)	94.7 (66.7–99.9)
≥75 yr	0	0.102 (774)	5	0.106 (785)	100.0 (–13.1–100.0)
Sex					
Male	3	1.124 (8,875)	81	1.108 (8,762)	96.4 (88.9–99.3)
Female	5	1.090 (8,536)	81	1.114 (8,749)	93.7 (84.7–98.0)
Race or ethnic group‡					
White	7	1.889 (14,504)	146	1.903 (14,670)	95.2 (89.8–98.1)
Black or African American	0	0.165 (1,502)	7	0.164 (1,486)	100.0 (31.2–100.0)
All others	1	0.160 (1,405)	9	0.155 (1,355)	89.3 (22.6–99.8)
Hispanic or Latinx	3	0.605 (4,764)	53	0.600 (4,746)	94.4 (82.7–98.9)
Non-Hispanic, non-Latinx	5	1.596 (12,548)	109	1.608 (12,661)	95.4 (88.9–98.5)
Country					
Argentina	1	0.351 (2,545)	35	0.346 (2,521)	97.2 (83.3–99.9)
Brazil	1	0.119 (1,129)	8	0.117 (1,121)	87.7 (8.1–99.7)
United States	6	1.732 (13,359)	119	1.747 (13,506)	94.9 (88.6–98.2)

* Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.
† The confidence interval (CI) for vaccine efficacy is derived according to the Clopper–Pearson method, adjusted for surveillance time.
‡ Race or ethnic group was reported by the participants. "All others" included the following categories: American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported.

provide proof of concept that RNA-based vaccines are a promising new approach for protecting humans against infectious diseases, and demonstrate the speed with which an RNA-based vaccine can be developed with a sufficient investment of resources. The development of BNT162b2 was initiated on January 10, 2020, when the SARS-CoV-2 genetic sequence was released by the Chinese Center for Disease Control and Prevention and disseminated globally by the GISAID (Global Initiative on Sharing All Influenza Data) initiative. This rigorous demonstration of safety and efficacy less than 11 months later provides a practical demonstration that RNA-based vaccines, which require only viral genetic sequence information to initiate development, are a major new tool to combat pandemics and other infectious disease outbreaks. The continuous phase 1/2/3 trial design may provide a model to reduce the protracted development timelines that have delayed the availability of vaccines against other infectious diseases of medical importance. In the context of the current, still expanding pandemic, the BNT162b2 vaccine, if approved, can contribute, together with other public health measures, to reducing the devastating loss of health,

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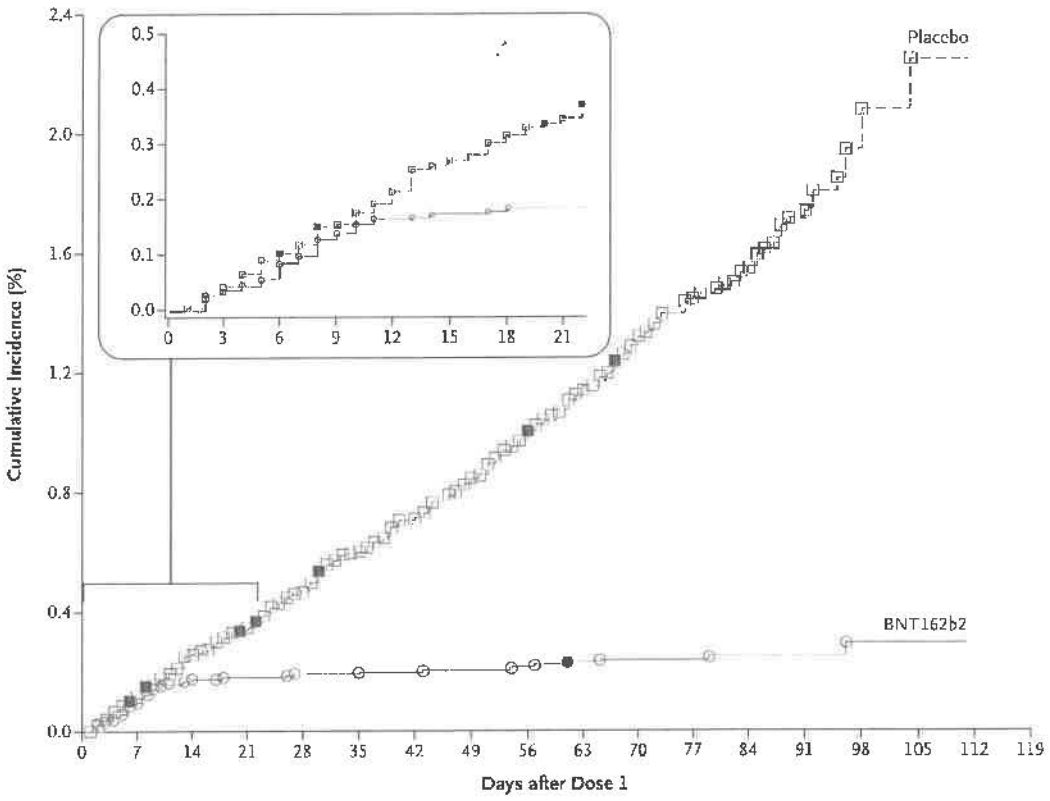

Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669)		Placebo (N=21,686)		VE (95% CI)
	No. of participants	Surveillance time *person-yr (no. at risk)*	No. of participants	Surveillance time *person-yr (no. at risk)*	*percent*
Covid-19 occurrence					
After dose 1	50	4,015 (21,314)	275	3,982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

Figure 3. Efficacy of BNT162b2 against Covid-19 after the First Dose.

Shown is the cumulative incidence of Covid-19 after the first dose (modified intention-to-treat population). Each symbol represents Covid-19 cases starting on a given day; filled symbols represent severe Covid-19 cases. Some symbols represent more than one case, owing to overlapping dates. The inset shows the same data on an enlarged y axis, through 21 days. Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from the first dose to the end of the surveillance period. The confidence interval (CI) for vaccine efficacy (VE) is derived according to the Clopper–Pearson method.

life, and economic and social well-being that has resulted from the global spread of Covid-19.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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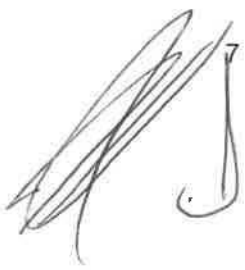
SARS-CoV-2 Testing Information

Testing for SARS-CoV-2 virus was conducted using the Cepheid Xpert Xpress SARS-CoV-2 PCR test.

Testing for SARS-CoV-2 antibodies was conducting using the Roche Elecsys® Anti-SARS-CoV-2 antibody test.

Figure/Table Number	Figure/Table Title	Population(s)/Sample Size	Explanation
Figure 1	Disposition of participants (CONSORT)	All enrolled population N=37,706 "main safety subset"	All randomized ≥16 years of age, N=43,548 • [minus 99 non-vaccinated, 1 no ICD] Vaccinated N=43,448 Main safety subset (N=37,706) needed to have been enrolled by October 9, 2020 for EUA application
Figure 2	Local and Systemic Reactions Reported within 7 Days after Receipt of 30 μg BNT162b2 or Placebo by Age Group	Reactogenicity subset of ≥16 years old N=8,183	Per protocol
Figure 3	Efficacy of BNT162b2 against COVID-19 Occurrence after Dose 1	N=43,355 (modified intention-to-treat)	All randomized >=12 years of age N= 43,651 • [minus 99 non-vaccinated, 1 no ICD] Vaccinated (dose 1 efficacy) N=43,551 • [minus 196 HIV+] All efficacy N=43,355
Table 1	Demographics	N=37,706 main safety subset	As above
Table 2	Vaccine Efficacy against COVID-19 from 7 Days after Dose 2 [Primary Endpoints]	1st primary efficacy endpoint: Includes those **without** evidence of prior infection (N=36,523) 2nd primary efficacy endpoint: Includes those **with and without** evidence of prior infection (N=40,137)	Evaluable population: • received 2 vaccinations as randomized • no major protocol deviations Excludes HIV+
Table 3	Vaccine Efficacy Overall and by Subgroup in Participants without Evidence of Infection Prior to 7 Days After Dose 2	N=36,523 (same as 1st primary endpoint)	
Table S2	Baseline Comorbidities	N=37,706 main safety subset	
Table S3	Participants Reporting at Least 1 Adverse Event From Dose 1 (All Enrolled Participants)	N=43,252	Vaccinated N=43,448 minus 196 HIV+
Table S4	Vaccine Efficacy from 7 Days After Dose 2 by Underlying Comorbidities among Participants without Evidence of Infection Prior to 7 Days after Dose 2	N=36,523 (same as 1st primary endpoint)	
Table S5	Vaccine Efficacy of Severe COVID-19 Occurrence after Dose 1 (Modified Intention-to-Treat)	N=43,355 (modified intention-to-treat)	See comments to Figure 3

Table S1 | Explanation of the Changes in Denominator Numbers in Various Analyses.



Charlson Comorbidity Index Category	BNT162b2 (30 µg) (N[a]=18860) n[b] (%)	Placebo (N[a]=18846) n[b] (%)	Total (N[a]=37706) n[b] (%)
Participants with any Charlson comorbidity	3934 (20.9)	3809 (20.2)	7743 (20.5)
AIDS/HIV	59 (0.3)	62 (0.3)	121 (0.3)
Any malignancy	733 (3.9)	662 (3.5)	1395 (3.7)
Cerebrovascular disease	195 (1.0)	166 (0.9)	361 (1.0)
Chronic pulmonary disease	1478 (7.8)	1453 (7.7)	2931 (7.8)
Congestive heart failure	88 (0.5)	83 (0.4)	171 (0.5)
Dementia	7 (0.0)	11 (0.1)	18 (0.0)
Diabetes with chronic complication	99 (0.5)	113 (0.6)	212 (0.6)
Diabetes without chronic complication	1473 (7.8)	1478 (7.8)	2951 (7.8)
Hemiplegia or paraplegia	13 (0.1)	21 (0.1)	34 (0.1)
Leukemia	12 (0.1)	10 (0.1)	22 (0.1)
Lymphoma	22 (0.1)	32 (0.2)	54 (0.1)
Metastatic solid tumor	4 (0.0)	3 (0.0)	7 (0.0)
Mild liver disease	125 (0.7)	89 (0.5)	214 (0.6)
Moderate or severe liver disease	1 (0.0)	2 (0.0)	3 (0.0)
Myocardial infarction	194 (1.0)	188 (1.0)	382 (1.0)
Peptic ulcer disease	52 (0.3)	71 (0.4)	123 (0.3)
Peripheral vascular disease	124 (0.7)	117 (0.6)	241 (0.6)
Renal disease	123 (0.7)	133 (0.7)	256 (0.7)
Rheumatic disease	62 (0.3)	56 (0.3)	118 (0.3)

Table S2 | Baseline Comorbidities. Baseline comorbid conditions are classified according to the Charlson Comorbidity Index (Charlson M, TP Szatrowski, J Peterson, J. Gold. Validation of a combined comorbidity index. J Clin Epidemiol 1994; 47:1245-51.). a. N = number of participants in the specified group. This value is the denominator for the percentage calculations. b. n = Number of participants with the specified characteristic. Participants with multiple occurrences within each category are counted only once. For 'Participants with any Charlson comorbidity', n = number of participants reporting at least 1 occurrence of any Charlson comorbidity.

	BNT162b2 (30 µg) (N[a]=21621)	Placebo (N[a]=21631)
Adverse Event	**n[b] (%)**	**n[b] (%)**
Any event	5770 (26.7)	2638 (12.2)
Related[c]	4484 (20.7)	1095 (5.1)
Severe	240 (1.1)	139 (0.6)
Life-threatening	21 (0.1)	24 (0.1)
Any serious adverse event	126 (0.6)	111 (0.5)
Related[c]	4 (0.0)	0
Severe	71 (0.3)	68 (0.3)
Life-threatening	21 (0.1)	23 (0.1)
Any adverse event leading to withdrawal	37 (0.2)	30 (0.1)
Related[c]	16 (0.1)	9 (0.0)
Severe	13 (0.1)	9 (0.0)
Life-threatening	3 (0.0)	6 (0.0)
Death	2 (0.0)	4 (0.0)

Table S3 | Participants Reporting at Least 1 Adverse Event from Dose 1 (All Enrolled Participants). The 'all enrolled' population included all participants who received at least 1 dose of vaccine irrespective of follow-up time. a. N = number of participants in the specified group. This value is the denominator for the percentage calculations. b. n = Number of participants reporting at least 1 occurrence of the specified event category. For 'any event', n = the number of participants reporting at least 1 occurrence of any event. c. Assessed by the investigator as related to investigational product.

Efficacy Endpoint Subgroup	BNT162b2 (30 µg) (N[a]=18198) n1[b]	Surveillance Time[c] (n2[d])	Placebo (N[a]=18325) n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Overall	8	2.214 (17411)	162	2.222 (17511)	95.0	(90.0, 97.9)
At risk[f]						
Yes	4	1.025 (8030)	86	1.025 (8029)	95.3	(87.7, 98.8)
No	4	1.189 (9381)	76	1.197 (9482)	94.7	(85.9, 98.6)
Age group (years) and at risk						
16–64 and not at risk	4	0.962 (7671)	69	0.964 (7701)	94.2	(84.4, 98.5)
16–64 and at risk	3	0.744 (5878)	74	0.746 (5917)	95.9	(87.6, 99.2)
≥65 and not at risk	0	0.227 (1701)	7	0.233 (1771)	100.0	(29.0, 100.0)
≥65 and at risk	1	0.281 (2147)	12	0.279 (2109)	91.7	(44.2, 99.8)
Obese[g]						
Yes	3	0.763 (6000)	67	0.782 (6103)	95.4	(86.0, 99.1)
No	5	1.451 (11406)	95	1.439 (11404)	94.8	(87.4, 98.3)
Age group (years) and obese						
16–64 and not obese	4	1.107 (8811)	83	1.101 (8825)	95.2	(87.3, 98.7)
16–64 and obese	3	0.598 (4734)	60	0.609 (4789)	94.9	(84.4, 99.0)
≥65 and not obese	1	0.343 (2582)	12	0.338 (2567)	91.8	(44.5, 99.8)
≥65 and obese	0	0.165 (1265)	7	0.173 (1313)	100.0	(27.1, 100.0)

Table S4 | Vaccine Efficacy from 7 Days after Dose 2 by Underlying Comorbidities among Participants without Evidence of Infection Prior to 7 Days after Dose 2. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period. a. N = number of participants in the specified group. b. n1 = Number of participants meeting the endpoint definition. c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period. d. n2 = Number of participants at risk for the endpoint. e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time. f. At risk is defined as having at least one of the Charlson Comorbidity Index categories or obesity (body mass index [BMI] ≥30 kg/m^2). g. Obese is defined as BMI ≥30 kg/m^2.

Efficacy Endpoint Subgroup	BNT162b2 (30 µg) (N[a]=21669) n1[b]	Surveillance Time[c] (n2[d])	Placebo (N[a]=21686) n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Severe COVID-19 occurrence after Dose 1	1	4.021 (21314)	9	4.006 (21259)	88.9	(20.1, 99.7)
After Dose 1 to before Dose 2	0		4		100.0	(-51.5, 100.0)
Dose 2 to 7 days after Dose 2	0		1		100.0	(-3800.0, 100.0)
≥7 Days after Dose 2	1		4		75.0	(-152.6, 99.5)

Table S5 | Vaccine Efficacy of Severe COVID-19 Occurrence after Dose 1 (Modified Intention-to-Treat). a. N = number of participants in the specified group. b. n1 = Number of participants meeting the endpoint definition. c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
d. n2 = Number of participants at risk for the endpoint. e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method (adjusted for surveillance time for overall row).

"HE22"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF HEALTH	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: LIMPOPO DEPARTMENT OF HEALTH	Twelfth Respondent

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MPUMALANGA DEPARTMENT OF HEALTH	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: MPUMALANGA DEPARTMENT OF HEALTH	Fourteenth Respondent
NORTHERN CAPE DEPARTMENT OF HEALTH	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTHERN CAPE DEPARTMENT OF HEALTH	Sixteenth Respondent
NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

CONFIRMATORY AND SUPPORTING AFFIDAVIT

I, the undersigned

DR STEPHEN SCHMIDT

do hereby make oath and state that:-

1. I am an adult male specialist physician and gastroenterologist, and an expert drug trialist, domiciled at 77 Linkside, Mosselbay, 6500.

2. The facts in this affidavit are, to the best of my knowledge, both true and correct, and, unless the contrary appears from the context of this document, they fall within my personal knowledge.

3. I am a specialist physician and gastroenterologist, and an expert drug trialist. I have been involved in drug trials for over thirty (30) years and have completed trials for the following manufacturing companies: Pfizer, Astra Zeneca, Janssen Cilag, Novavax, Gilead, Johnson and Johnson, Glaxo Smith, Adcock-Ingram, and the US Defence Force. I hold an MBChB and MMed(Int) from the University of Stellenbosch. From 1990 to 2022 I was part of, or was the responsible principal investigator in, fifty-seven (57) clinical drug trials. My experience as a training trialist and eventual Principal Investigator taught me every skill needed to conduct clinical trials, including the complete administrative management of the trial site, logistics, pharmacy control, dispensing and drug accountability, blood and tissue sampling and shipping, writing of- and updating 72 standard operative procedures detailing every action at the trial site, assessing and understanding novel drug protocols, continuous training of staff and refresher courses in Good Clinical Practice every 2 years, attending international trial commencement meetings, receiving clinical trial monitors and auditors, assessing and management of adverse events of any type, acting as first responder to safety signals observed at the site. I acted as national investigator in several studies and was audited by sponsors' auditors, CRO auditors, the Medical Control Council, SAHPRA and the FDA. Neither of my trial sites ever received a negative audit report. My conduct as

a Principal Investigator was based on the ethical principles of national and international institutions. I conducted my trial work in South Africa following the strict ethical guidelines of SA-GCP (South African Good Clinical Practice), the DOH research guidelines and the Constitution of South Africa. My full curriculum vitae is annexed as "**SS1**".

4. I have read the founding affidavit deposed to by Dr Herman Edeling. In his affidavit, Dr Edeling makes three references to me, my expertise and my conclusions. I confirm the content and correctness of those references. Specifically, I confirm that:

4.1. The Pfizer trial design was flawed from commencement. The problem is that the trial compared the vaccine arm (injected with the vaccine candidate, BNT162b2) to a saline placebo. The trial should have compared the vaccine intervention to, at the very least, other interventions against Covid-19 and/or natural immunity – not a saline placebo. But, as set out in the Pfizer trial protocol, they didn't do this. Instead, trial subjects who had been treated with medicines intended to prevent infection, and those with previous exposure to Covid-19 (and who therefore had natural immunity) were excluded.

4.2. There are multiple reasons why the vaccine arm should have been compared to other interventions against Covid-19 and/or natural immunity instead of a saline placebo:

4.2.1. First, it is the only way to preserve equipoise. Equipoise is a concept in clinical research that refers to a state of genuine uncertainty about the

relative effectiveness and safety of two or more interventions being compared in a clinical trial. In other words, equipoise is a state of genuine uncertainty that exists in the minds of researchers as to which of the interventions being compared is better, or whether there is no difference between them.

4.2.2. This state of uncertainty is important because it helps to ensure that the clinical trial is conducted in an ethical manner. If researchers have a clear preference for one intervention over another, or believe that one intervention is clearly superior, then it may not be ethical to subject some patients to the inferior intervention.

4.2.3. By maintaining equipoise, researchers can ensure that patients are randomized to different interventions in a fair and unbiased manner, and that the results of the trial will provide reliable information about the relative effectiveness and safety of the interventions being compared.

4.2.4. The problem is this: when equipoise is not maintained because the researchers believe that one product will be more efficacious/safe than the other, it can bias not only the collection of trial data but the analysis thereof. In the Pfizer trial, equipoise did not exist. The mere fact that the vaccine arm was trialled against a saline placebo meant that those conducting the trial commenced the trial with the bias that the vaccine would be more effective than the saline placebo. Had they used alternative Covid-19 treatments or natural immunity, they would not have had that certainty, and the bias would have been mitigated for.

4.2.5. Second, testing the vaccine arm against the saline placebo artificially inflated the efficacy profile. Obviously, a vaccine candidate appears highly effective when compared to nothing (saline placebo). The efficacy profiles would likely have been substantially lower if compared to other interventions or natural immunity.

4.2.6. Third, it is unethical in the midst of a global pandemic to give some patients a saline placebo if there is a known effective treatment available. In my view, it was unethical to withhold this standard of care from the control group. It seems as though this ethical violation was countenanced in pursuit of Pfizer's own ends – to artificially inflate the efficacy profiles.

4.2.7. Fourth, the saline placebo may not have accurately reflected the natural course of the disease or the effects of the experimental treatment. Comparing the experimental vaccine treatment to a natural immunity or another type of medication was more likely to provide a realistic and informative comparison.

4.3. I also confirm Dr Edeling's reasoning in his affidavit as it pertains to the unblinding and the cross-over.

4.3.1. In any phase three clinical randomised controlled trial (RCT), which is what the Pfizer trial purported to be, there must be an inoculated group

of trial subjects and an equivalent placebo group. Those groups must subsist until the end of the trial. It is the long-term comparison of the efficacy and safety profiles between the vaccinated trial arm and the placebo trial arm which allows for a proper assessment as to whether the product (in this case, Comirnaty) has acceptable efficacy and safety profiles. Without this data it is impossible to assess long term efficacy or safety.

4.3.2. Usually, vaccine trials are run for a period of ten to fifteen years. This time, because of the exigencies of the situation, the trial period was severely truncated to three years, due to terminate sometime in 2023. The vaccine arm and placebo arm should have been maintained until the culmination of the trial in order to secure decent efficacy and safety data sets.

4.3.3. But Pfizer sabotaged the entire comparative data collection process, thereby invalidating their trial.

4.3.4. After only 2 months, the trial groups were unblinded. "Unblinding" is a term used in the context of clinical trials to refer to the process of revealing the group assignment of a participant in a study – in other words, telling trial subjects whether they were part of the vaccine arm, or the placebo arm of the study. Following the unblinding, those in the placebo group were offered the vaccine.

4.3.5. As set out in Dr Edeling's affidavit, 88.8% of the trial subjects in the placebo group elected to take the vaccine and crossed over.

4.3.6. An 88.8% crossover is a calamity. It effectively annihilates any prosect of collecting reliable long-term efficacy and safety data about the vaccines. In all my years of conducting clinical trials, I have never seen an unblinding and cross-over of virtually the entire control group. In my view, the only plausible explanation is that Pfizer wanted to destroy the control group and the long-term collection of safety and efficacy data. Whether their motivation for this was to conceal what they knew would be problematic outcomes, I cannot say.

4.4. Lastly I confirm that a serious issue of concern in the Pfizer trial related to the conveniently and selectively chosen study population itself, and the blanket vaccine efficacy and safety claims made in the published summary of the trial data. In trials that test for efficacy, it is only possible to make efficacy claims for the population demographics and other circumstances that applied in the trial. For example, if you're trialing medicine X, and you test it in adults in the trial, you cannot then claim efficacy or safety for children. The reasons are self-evident.

4.5. In this trial, adolescents below the age of 16 years were excluded from the initial trial, pregnant women and women who were breastfeeding were excluded, and those who were sick with underlying health conditions were also excluded. The candidate vaccine intervention was only trialed on healthy individuals over the age of 16. The supposed 95%/91.3% efficacy claims and

the so-called favourbale safety profiles (which I dispute for all the reasons set out in Dr Edeling's affidavit) should have been limited to the population demographics in which the medicine was trialed (healthy individuals over the age of 16) – but instead it was marketed by Pfizer, regulatory authorities and governments as being safe and effective for all cohorts, including those in which it was never tested. Not only is this unethical but it is severely scientifically flawed.

DR STEPHEN SCHMIDT

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me at Mossel Bay on this the 13th day of March 2023, the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

COMMISSIONER OF OATHS

Name:
Address:
Position:

JOHAN CILLIERS
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"SS1"

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CURRICULUM VITAE

Dr Stephen John Schmidt

PERSONAL DETAIL

Title	Dr
Initials	SJ
Full Name	Stephen John
Surname	Schmidt
Date of Birth	13 September 1959
Nationality	South African
HPCSA Nr	MP0289450
Malpractice Insurance	Medical Protection Society Member Nr: 03/27947
Professional Body Membership	HPCS, SAGES, SAVIMS
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Dr S J Schmidt
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QUALIFICATIONS

Academic and Professional Qualifications	Year
MBChB. University of Stellenbosch	1984
MMed (Int). University of Stellenbosch	1995
Registered Gastroenterologist. University of Stellenbosch	1999

WORK EXPERIENCE AND CURRENT POSITION

Internship: Kimberley Hospital	1985
South African Defense Force: Rank Captain	1986 - 1988
Medical Officer Emergency Unit: Somerset Hospital	1989 - 1990
Registrar in training: Internal Medicine: Tygerberg Hospital and University of Stellenbosch	1990 - 1994
Consulting in training Department of Gastroenterology: Tygerberg Hospital and University of Stellenbosch	1995 - 1999
Consultant in General medicine and Gastroenterology: Tygerberg Hospital and University of Stellenbosch	1997 - 1999
Founder and principal Investigator: Quatro Clinical Trial Institute	2000 - 2009
Specialist Physician and Principal Investigator in private practice	2000 - 2022
Managing Director and Principal Investigator Endocare Clinics	2009 – 2022

CURRENT POSITION

CEO Endocare Clinics Pty Ltd: Integrative Health Initiatives and alternate Therapeutics

Icanfunction Health: Consulting Physician and member of management team

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TEACHING AND COURSES

Lecturer undergraduate medicine: Medical School University of Stellenbosch	1991- 1999
Continuing Medical education (GUT CLUB) to general practitioners	2000 - 2020
Pharmacy course: Dispensing License	2000-2002
International Training course Small Bowel endoscopy: GIVEN	2002
Certificate Course in Metabolic Diseases: Nutritional Network: Prof Tim Noakes	2019

SKILLS

CLINICAL

During training as a specialist physician, I rotated through the intensive care units and departments of Cardiology, Nephrology, Pulmonology, Neurology, Endocrinology, Psychiatry, Internal Medicine, Occupational Medicine.

In the period from 1995 to 2022 I specialized in practice as a Gastroenterologist and specialist Physician with special interest and expertise in stomach diseases, hepatology, small bowel diseases and colon diseases. I developed a special interest in metabolic syndrome, Diabetes and fatty liver disease applying innovative and novel concepts in life-style management to reverse chronic disease. I performed > 15000 endoscopies of the upper digestive tract, the colon and was an expert in assessing the small bowel with capsule endoscopy.

RESEARCH

I am a expert drug trialist. I started my training in 1990 at the University of Stellenbosch Medical School and Tygerberg Hospital. My mentors were the late Prof's Frans Maritz and Steven Hough, both Endocrinologist and Lipidologists. I trained as a trialist by performing all aspects of trial work.

1990 – 1999: Junior study coordinator, senior study coordinator, administrative clerk, data capturer, therapeutic pharmacist, intensive care pharmacist and sub-investigator.

I started Quatro Clinical trial Institute in 2000 and performed the duties of Principal Investigator from 2000 – 2009. In 2009 I founded Endocare Clinics as the Principal Investigator with a staff of 10 employees. From 1990 to 2022 I was part of or was the responsible principal investigator in 57 clinical drug trials. My experience as a training trialist and eventual Principal Investigator taught me every skill needed to conduct clinical trials. This entails the complete administrative management of the trial site, logistics, pharmacy control, dispensing and drug accountability, blood and tissue sampling and shipping, writing of- and updating 72 standard operative procedures detailing every action at the trial site, assessing and understanding novel drug protocols, continuous training to staff and refresher courses in

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Good Clinical Practice every 2 years, attending international trial commencement meetings, receiving clinical trial monitors and auditors, assessing and management of adverse events of any type, acting as first responder to safety signals observed at the site. I acted as national investigator in several studies and I was audited by sponsors auditors, CRO auditors, the Medical Control Council, SAHPRA and the FDA. Neither of my trial sites ever received a negative audit report.

My conduct as a Principal Investigator was based on national and international ethical bodies and principles. I conducted my trial work in South Africa following the strict ethical guidelines of SA-GCP, the DOH research guidelines and the Constitution of South Africa.

PARTICIPATION IN CLINICAL TRIALS:

GASTROENTEROLOGY

- An open label access trial to document the humanitarian use of oral R1 08512 1 to 4 mg in subjects with chronic constipation.
- A double- blind placebo- controlled dose-finding trial to evaluate the efficacy and safety of R149524 in diabetic subjects with symptoms of gastroparesis.
- An open label access trial to document the humanitarian use of oral R 08512 1 to 4 mg in subjects with chronic constipation.
- Maintenance treatment of patients with healed oesophagitis, comparing the remission rates during 6 months with esomeprazole 20 mg q.i.d. – a randomized, double- blind, multi centre study (METROPOLE)
- On demand versus continuous treatment of endoscopy negative subjects with gastroesophageal reflux disease (GERD) with esomeprazole 20mg O>D> over a 6-months long term treatment phase. An open, randomized, multi-center study (NEED)
- Efficacy of esomeprazole 40 mg once daily versus placebo and esomeprazole 20 mg daily versus placebo in treatment for relief of upper gastrointestinal symptoms associated with continuous use of NSAIDS including COX-2 selective NSAIDS (SPACE)
- Efficacy of esomeprazole 40 mg daily versus placebo and esomeprazole 20 mg daily versus placebo in prevention of upper gastrointestinal symptoms associated with continuous use of NSADS including COX-2 selective NSAIDS (SPACE 2)
- A comparative efficacy and safety study of esomeprazole delayed-release capsules (40 mg qd and 20 mg qd) versus placebo for the prevention of gastric ulcers associated with daily NSAID use in patients at risk (PLUTO)

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- A randomized, double-blind, multi-center Phase III study to evaluate safety of esomeprazole 40 mg give IV or orally o.d. for 1 week to subjects with erosive reflux oesophagitis, followed by 3 weeks open oral treatment with esomeprazole 40 mg o.d.

- Healing rates after the administration of 10 mg BY359 o.d. versus 5 mg b.i.d. over 28 days in patients suffering from gastroesophageal reflux disease.

- A Double-Blind, Placebo-Controlled, Randomized, Multinational study to investigate the Safety and Efficacy of 2 mg TID of Cilansetron Over 26 Weeks in Diarrhea-Predominant Irritable Bowel Syndrome Subjects

- An Open-Label, Multi-center study to investigate the safety of 2 mg TID of Cilansetron over one year in Diarrhea-Predominant Irritable Bowel Syndrome Subjects (Protocol nr : S241.3.008)

- Change of health-related quality of life (HRQoL) in patients suffering from endoscopically confirmed reflux oesophagitis after treatment with Pantoprazole 40 mg o.d. over 4 weeks

- PPI Comparator Study to compare the efficacy of healing and maintenance treatment with esomeprazole and pantoprazole in subjects with reflux oesophagitis – a multi-center, randomized. double-blind study (EXPO)

- A Clinical study investigating the effects of treatment with tegaserod in female patients with constipation-predominant irritable bowel syndrome (PHASE 4)

- A Clinical study investigating the effects of treatment with tegaserod in female patients with constipation-predominant irritable bowel syndrome (PHASE 3)

- A Clinical proof of concept study of the efficacy of oral xxxxxxx versus Azathioprine in Crohn's disease

- A Clinical study using a novel anti-TNF treatment in Crohn's disease.

- An eight-week, randomized, double blind Placebo-controlled, dose-ranging study to evaluate efficacy and safety of xxx in subjects with irritable bowel syndrome.

- A Study to assess the safety and maintenance of response of XXXXX versus placebo in patients with active Crohn's disease.

- Patients with mild to moderate ulcerative Colitis.

- The prevention of Ascites Recurrence due to cirrhosis of the liver

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CARDIOLOGY

- A Randomized, double blind study to investigate the safety and clinical efficacy of MK- 383 in patients with unstable angina/non-q-wave myocardial infarction. Protocol 011/097. 1994 – 1995, Principal Investigator
- The continuous infusion versus bolus administration of Alteplase (COBALT) study. Protocol ID 135.70. 1995 – 1996. Principal Investigator
- The Prism Plus Study. 1995 – 1996 Principal Investigator
- Safety assessment of single-bolus administration of TNK0-tissue-plasminogen adtivator in acute myocardial infarction. He assent-1trial. 1996. Principal investigator
- A randomized, double-blind, placebo-controlled trial comparing two drugs in subject with acute ST Elevation Myocardial Infarction (STEMI) treated with Fibrinolytic therapy Principal Investigator

DERMATOLOGY

- A Multi Centre, Double blind, Parallel-group study comparing Mupirocin Ointment 2% and Bactroban ® Ointment (mupirocin Ointment 2%) in the treatment of Impetigo. Principal Investigator
- A Multi-center, double-blind, Parallel-group, Placebo-controlled Study to compare the efficacy and safety of Mupirocin Ointment 2% and Bactroban ® Ointment (Mupirocin Ointment, 2%) in the treatment of Impetigo (MUP-0204) Principal Investigator
- A Randomized, observer-blind, multi-center, non-inferiority, comparative phase III study of the safety and efficacy of topical xxx ointment applied twice a day, for five days, versus topical xxx ointment applied three times daily for 7 days in the treatment of adult and pediatric subjects with Impetigo. Principal Investigator

NEUROLOGY

- A randomized, double-blind, parallel group, dose-response study to evaluate the efficacy and safety of two doses of topiramate compared to placebo and propranolol in the prophylaxis of migraine. Protocol Pri/TopInt47. Principal Investigator
-

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ONGOING RESEARCH / CLINICAL TRIALS:

- Ulcerative Colitis Study: To evaluate Clinical efficacy and safety of induction and maintenance Therapy of BMS 936557
- Preventative RSV disease in infants: Study to determine Immunogenicity and Safety of a RSV vaccine.

Schmidt

Dr SJ Schmidt **Date**

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S75.

"HE23"

A PHASE 1/2/3, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND, DOSE-FINDING STUDY TO EVALUATE THE SAFETY, TOLERABILITY, IMMUNOGENICITY, AND EFFICACY OF SARS-COV-2 RNA VACCINE CANDIDATES AGAINST COVID-19 IN HEALTHY INDIVIDUALS

Study Sponsor:	BioNTech
Study Conducted By:	Pfizer
Study Intervention Number:	PF-07302048
Study Intervention Name:	RNA-Based COVID-19 Vaccines
US IND Number:	19736
EudraCT Number:	2020-002641-42
Protocol Number:	C4591001
Phase:	1/2/3

Short Title: A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals

This document and accompanying materials contain confidential information belonging to Pfizer. Except as otherwise agreed to in writing, by accepting or reviewing these documents, you agree to hold this information in confidence and not copy or disclose it to others (except where required by applicable law) or use it for unauthorized purposes. In the event of any actual or suspected breach of this obligation, Pfizer must be promptly notified.

Type of Participant and Disease Characteristics:

2. Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures.

3. Healthy participants who are determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study.

   Note: Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, can be included. Specific criteria for Phase 3 participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV) can be found in Section 10.8.

4. **Phase 2/3 only:** Participants who, in the judgment of the investigator, are at higher risk for acquiring COVID-19 (including, but not limited to, use of mass transportation, relevant demographics, and frontline essential workers).

Informed Consent:

5. Capable of giving personal signed informed consent/have parent(s)/legal guardian capable of giving signed informed consent as described in Appendix 1, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol.

5.2. Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

Medical Conditions:

1. Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.

2. **Phases 1 and 2 only:** Known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV).

3. History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s).

4. Receipt of medications intended to prevent COVID-19.

5. Previous clinical (based on COVID-19 symptoms/signs alone, if a SARS-CoV-2 NAAT result was not available) or microbiological (based on COVID-19 symptoms/signs and a positive SARS-CoV-2 NAAT result) diagnosis of COVID-19.

"HE24"

MASTER PARTICIPANT INFORMATION AND INFORMED CONSENT FORM (ICF)

Study BNT162-17

Study title:	A Phase II trial to evaluate the safety and immunogenicity of SARS-CoV-2 monovalent and multivalent RNA-based vaccines in healthy subjects
Brief study title:	Safety and immunogenicity of RNA-based vaccines against SARS-CoV-2 variants in healthy participants
ICF version:	6.0 **Date:** 25 Aug 2022
Study protocol version/date:	6.0 / 04 Aug 2022
Study vaccines	Study Vaccine A is BNT162b2, Study Vaccine B is BNT162b2 (B.1.1.7), Study Vaccine C is BNT162b2 (B.1.617.2), Study Vaccine D is BNT162b2 (B.1.1.7 + B.1.617.2), and Study Vaccine E is BNT162b2 (B.1.1.529)
Study regulatory identifiers:	EudraCT no.: 2021-003458-22; US IND 19736
Study sponsor:	BioNTech SE An der Goldgrube 12, 55131 Mainz, Germany
Site name and identifier:	[redacted]
Study doctor name:	[redacted]
Participant number:	
Contact for information about the study: **Mon. – Fri., during the day:**	[redacted]
Evenings, nights, weekends, holidays:	[redacted]

Information on data privacy can be found in section "Confidentiality and data privacy".

INTRODUCTORY STATEMENT

Dear prospective participant,

Clinical studies (henceforth referred to as "study") are necessary to obtain or expand knowledge about the effectivity (here the immune response or "immunogenicity") and safety of vaccines. This is why laws require that new vaccines undergo clinical investigation before being approved for marketing or for use.

The study doctor is supporting a company called BioNTech SE (henceforth BioNTech) which is developing new vaccines. For this support, the study doctor will be paid by BioNTech.

An infection with the SARS-CoV-2 (Severe Acute Respiratory Syndrome – Coronavirus-2) virus can lead to coronavirus disease 2019 (COVID-19). More recently, new strains (variants) of the original SARS-CoV-2 virus, have been detected and have quickly spread worldwide.

This study sponsored by BioNTech will investigate the safety and effectivity of several investigational new vaccines against new strains of the original SARS-CoV-2 virus. These new vaccines are referred to collectively as "study vaccines".

You will be given a copy of this document, and may read it at your leisure. This document explains the study in more detail in the following sections. As required by law, the study has been approved by Pharma-Ethics Research Ethics Committee and authorities.

It is important that you understand that research is not the same as regular medical care. Research may involve risks that are not yet known. Also, you cannot assume that you will receive effective protection against SARS-CoV-2 - and thus against COVID-19 by participating in this study.

Please make sure that you understand why and how the study will be carried out and which examinations will be done. Please ask your study doctor if there is anything that you do not understand, or if you would like additional information. Your study doctor must answer your questions to your complete satisfaction. Feel free to discuss this study with anybody that you feel comfortable with. You will be given as much time as needed to decide whether you want to participate.

Your participation in this study is voluntary. Any refusal to participate in this study will have no bearing on your access to vaccination to protect against COVID-19 via your general practitioner or your health insurance. After agreeing to participate in this study, you may decide to withdraw from the study at any time without stating any reasons and without any penalty or loss of benefits.

The information in this document is intended to help you decide whether you want to participate in this study. For you to join this study, it is essential that you give consent to participate by signing and dating this document. By doing so, you confirm that you have understood why and how the study will be carried out, that you know what you must do, and that you know your rights.

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1 PARTICIPANT INFORMATION

1.1 What is the purpose of this study?

An infection with the SARS-CoV-2 virus can lead to COVID-19. An infection with SARS-CoV-2 can lead to symptoms such as fever and cough. Persons affected also report sniffles, shortness of breath, muscle and joint pain, sore throat and headaches, as well as nausea/vomiting and diarrhea, and also a decreased sense of smell and taste. The course of the disease may vary in severity, from courses without obvious symptoms to courses with severe lung inflammation (pneumonia) with pulmonary failure and death.

This study sponsored by BioNTech will investigate the safety and effectivity of several investigational new vaccines against new strains of the original SARS-CoV-2 virus.

1.1.1 What are the study vaccines?

The vaccines used in this study consist of large molecules, known as ribonucleic acids (RNA). In contrast to conventional vaccines in which the viruses are given in killed form, RNA vaccines contain the genetic information or parts of the virus. This genetic information is like a building plan for proteins.

The study vaccines in this study contain RNA with instructions for producing a part of the SARS-CoV-2 virus (a protein). Once in the body, the body uses these instructions to produce a SARS-CoV-2 protein specific to a strain of the original SARS-CoV-2 virus. As would happen in any natural infection, these proteins cause the body to produce antibodies against the SARS-CoV-2 virus, the "effect" or "immune response".

The study vaccines that will be used in this study are:

- Study Vaccine A fights the parent SARS-CoV-2 virus.
- Study Vaccine B is designed to fight the SARS-CoV-2 strain Alpha.
- Study Vaccine C is designed to fight the SARS-CoV-2 strain Delta.
- Study Vaccine D is a 1 to 1 mixture of Study Vaccines B and C designed to fight the SARS-CoV-2 strains Alpha and Delta.
- Study Vaccine E is designed to fight the SARS-CoV-2 strain Omicron.

Study Vaccine A (also referred to as "BNT162b2") has already been investigated in clinical studies and has been approved by Regulatory Authorities for use in numerous countries worldwide. Study Vaccine A is not approved for use in South Africa.

Post-approval administration of Study Vaccine A to hundreds of millions of individuals has confirmed its favorable safety and effectivity profile in individuals aged 12 years or older.

Study vaccines B, C, D and E are considered "investigational" because they have not been approved by any regulatory authority for use. These "investigational" study vaccines are very similar to Study Vaccine A.

1.1.2 What are the objectives of this study?

To understand the study objectives, please note that:

- "Pre-vaccinated participants" are participants who have previously received two 30 micrograms doses of Study Vaccine A and have no prior history of COVID-19 or infection with SARS-CoV-2 virus or

  Participants who have previously received two or three doses of any authorized COVID-19 RNA-based vaccine and have had a prior history of COVID-19 or infection with SARS-CoV-2 virus, from January 2022 onwards.

- "Vaccine-naïve participants" are participants who have had no previous vaccinations with Study Vaccine A and have no prior history of COVID-19 or infection with SARS-CoV-2 virus.

This study is separated into three parts, Part A, Part B and Part C. You are invited to participate in Part B. Part A and Part C is not applicable at this site, a summary is provided for your information only.

In Part A the safety and immune response of one or two or three doses of the Study Vaccine D will be studied on pre-vaccinated and vaccine-naïve participants; and it will be compared against data from participants receiving the Study Vaccines A, B and C.

After preliminary data from Part A is analyzed, Part B will start. In Part B the safety and immune response of one or three doses of Study Vaccine D will be further studied and also compared against data from participants who received Study Vaccine A in other research study (BNT162-02/C4591001). Part B, will also compare participants who received one dose of Study Vaccine C against data from participants who received Study Vaccine A in other research study (BNT162-02/C4591001).

Part C of the study will include participants who were previously vaccinated with two or three doses of any authorized COVID-19 RNA-based vaccine more than 4 months before starting participation in the study and were then diagnosed with a SARS-CoV-2 infection from January 2022 onwards. The latest SARS-CoV-2 infection should be at least 2 months before taking part in this study. In Part C, the safety and immune response of one dose of Study Vaccine E will be studied; and it will be compared against data from participants receiving one dose of Study Vaccine A. In addition, Part C will evaluate the immune response after infection with the SARS-CoV-2 strain Omicron.

1.2 Who might benefit from this study?

A beneficial effect of the study vaccines cannot be guaranteed. About 110 of the approximate 1,470 participants in this study will receive the approved Study Vaccine A.

By participating in this study, you may help BioNTech to develop safe and effective new vaccines that protect against new virus strains that may lead to COVID-19.

1.3 Do I have to take part?

Your participation in the study is purely voluntary and entirely up to you. There may be reasons why you would not want to participate in this study, such as the risk of side-effects and/or health damage, the inconvenience linked to the study restrictions and visits.

If you have not already been vaccinated to prevent COVID-19, your refusal to participate in this study will have no bearing on your access to vaccination to prevent COVID-19. Vaccination to prevent COVID-19 may be available via government vaccination programs; this may include vaccination with the already approved BioNTech Study Vaccine A. You can discuss alternative ways for vaccination to prevent COVID-19 with the study doctor.

1.4 Can I withdraw from the study, or can anyone else stop or end the study earlier than planned?

You have the right to withdraw from the study at any time, without giving a reason and without prejudice. For your own safety, it is recommended that you tell the study doctor about the reasons for your decision, especially if it is because of a side-effect.

If any of the following happens, you will not receive any further dose of study vaccine, if applicable, but you may be asked to continue with the study visit schedule for your safety:

- Any serious event warranting discontinuation.
- Any other study-related safety concerns, e.g., if your health worsens.
- If you become pregnant.
- Any request from you or your study doctor, e.g., if you do not follow instructions.
- If you receive any SARS-CoV-2 vaccine apart from the study vaccine during your participation in this study.

If your participation in the study is stopped, for your own safety you should undergo all assessments planned for the "early stop" visit as described in the following pages.

The study may also be stopped at any time by BioNTech, relevant independent ethics committees such as Pharma-Ethics Research Ethics Committee, or the responsible authority (such as the Food and Drug Administration [FDA] for study sites in the US) or the South African Health Products Regulatory Authority (SAHPRA) in South Africa. If for any reason your participation in the study is stopped, the reason will be explained to you.

1.5 How many people will take part in this study

In total, approximately 1,470 participants in approximately 37 sites worldwide will take part in this study. In South Africa approximately 436 participants from 12 sites will participate.

1.6 How long would I be in this study?

Depending on which study group you are assigned to, your participation in this study may last up to approximately 61 weeks. "Study groups" are groups of participants who receive the same study vaccine and undergo the same assessments.

[redacted]

1.7 What will happen during the study

1.7.1 The study vaccines and the study groups

Study vaccines and administration

All of the study vaccines are "real" vaccines, i.e., vaccines containing active substance. They will be given by injection into the upper arm and will only be administered by medically qualified personnel. You will be observed for 30 minutes after each injection.

The study groups

You will be assigned to Part B, to one of the following groups:

Pre-vaccinated participants will be selected from individuals who received their prior vaccines in the BNT162-02 / C4591001 trial. They will have one in two (50%) chances to be assigned to either of the following groups:

- Group 1: One 30 micrograms dose of Study Vaccine D.
- Group 4: One 30 micrograms dose of Study Vaccine C.

Vaccine-naïve participants will be assigned to the following group:

- Group 6: Three 30 micrograms doses of Study Vaccine D, with the first and second dose given 3 weeks apart and the third dose given about 6 months after the second dose.

1.7.2 What visits does the study involve?

Depending on the study group you are assigned to, there will be five to ten site visits. The study site staff will tell you when to come in for your site visits, i.e., give you an exact visit schedule which reflects the chronological and organizational course of the study. For the planned site visits and assessments, see the study schedules (Table 1 to Table 2).

1.7.2.1 Screening - Visit 0 (within the 7 days prior to Visit 1)

Visit 0 will be used to check whether you are eligible (i.e., meet the entry requirements) to participate in this study. During this time, the study doctor will:

- Document your gender, age, and ethnic background.
- Ask you about your medical history including your past medication use, past vaccination, your current medication use, and your contraception use. You cannot participate in Part B of this study if you had COVID-19 in the past.
- Perform various standard medical assessments, e.g., a comprehensive physical examination, body weight, height, oral body temperature, heart rate, blood pressure, an electrocardiogram (ECG, a recording of your heart function), and collect blood and urine for standard laboratory tests to check your general health status. ECG recordings may be sent to central laboratory for central reading. For reporting and surveillance purposes, all ECGs may be forwarded to a central vendor for assessment.
- Perform oral swab-based test to determine if you are infected with SARS-CoV-2.

- Perform urine pregnancy test (for women who can become pregnant).

Once all results from these assessments are available, you will be informed if you can continue in this study and receive the study vaccine.

If you do not meet the entry requirements, you may be rescreened later, upon Medical Monitor approval, and at discretion of the study doctor. In this case, you will be asked to provide consent again.

1.7.2.2 Treatment and post-treatment Follow-up – (4 to 9 visits spread over up to 1 year after the last dose of study vaccine)

You will be assigned to one of the study groups detailed above. Assignment to a study group will depend on your vaccination status (pre-vaccinated or vaccine-naïve), but will otherwise be done by chance.

Depending on your study group, you will receive one or three doses of study vaccine.

At the visits, you will also be questioned about your wellbeing, your use of non-study medication, and any pregnancies (of you or your partner). Blood will also be collected at each visit for study assessments. Electrocardiograms (ECGs) will be recorded before, 7 days after each injection of study vaccine and at any time point later if considered necessary by your study doctor. Likewise, oral swabs will be collected for assessment of your SARS-CoV-2 status, and, if you test positive, other oral swabs collected will be used to identify the virus strain.

At the visit 1 (vaccination day) you will be provided with an electronic diary, which can also be downloaded as an app on your own electronic device (e.g. cellular phone) for use at home daily. You will be asked to report any injection site reactions (e.g., pain, tenderness, redness, swelling) and any flu-like symptoms (e.g., vomiting, diarrhea, headache, fatigue/tiredness, oral body temperatures, chills, nausea, new or worsened muscle pain, new or worsening joint pain) until 7 days following study vaccination. If you are in a group that receives 1 or 3 doses of the vaccine you will be asked to report these items in your eDiary again from the time of the 1st, 2nd and 3rd (if applicable) injection until 7 days following study vaccination.

You will also be provided with a thermometer or device to measure your oral body temperature daily and report it in the electronic diary.

You will also be asked to tell the study doctor or site staff about any changes in your health. If there are any symptoms of COVID-19, such as any respiratory problems (breathing shortness of breath) and/or flu-like symptoms.

The reporting of any symptoms of illness using the electronic diary or by direct contact may trigger additional unplanned visits and diagnostic tests.

1.7.2.3 Study assessments

The following study assessments will be performed using biological samples (or biosamples) collected from you:

- Blood will be used for assessing your body's immune response, e.g., has vaccination caused your body to produce antibodies against the SARS-CoV-2 virus.
- For some participants of Part B in preselected sites, blood will be collected and used to further assess your immune response including genetic analyses. If you are a participant at one of the preselected sites and in Part B of the study, you may be asked to sign a separate consent for this optional additional blood draws and genetic testing.
- Oral swabs will be used to test if you are infected with SARS-CoV-2, and if you are infected, to identify which SARS-CoV-2 strain.
  {Note: In the event of a confirmed suspicion of SARS-CoV-2, a positive result on an oral swab of an active COVID-19 infection, or positive antibody detection prior to the start of treatment or in the course of the study, a report identifying you by name must be made to the health authorities and you must quarantine in accordance with the stipulations from the health authorities.}

If you give consent, the following will also be done:

- It is assumed that all of the material (biosamples, such as blood or serum) collected from you during the course of the study will be used up within the scope of the study and for the purposes of the study, however, any leftover biosamples (blood or serum) during the study or at the end of the study, may also be used for future unspecified (exploratory) research relating to vaccines against COVID-19 and/or immune therapy research, which research will be conducted in terms of other studies that have undergone the necessary ethics review.
- Biosamples will be used for optional genetic testing. For participants in Part B, Group 6 at one of the preselected sites, you will be provided a separate consent that contains further information on this optional genetic testing.
- To give effect to these purposes, the Sponsor will be required to share your personal data and biomaterial samples (or biosamples) with third parties, including affiliate companies, service providers (e.g., laboratories, statistics experts) and other collaboration partners of the Sponsor (e.g., universities, pharmaceutical companies, research institutions). Where the Sponsor shares your personal information and/or biomaterial samples with any such third parties for research purposes, the Sponsor will ensure that your personal data is provided to such third parties as coded personal data (pseudonymised) and that such third parties undertake to only process such personal information and biomaterial samples for research purposes.

The biosamples for these assessments, and all data generated using the biosamples, will be handled in accordance with applicable laws and regulations; this includes requirements applicable for data privacy (for additional details, see the following pages).

Participation in the study is in no way contingent on you consenting to the use of biosamples collected from you during the course of the study for these further purposes. You can decide to give/not give us your consent to this extent.

1.7.2.4 Blood collection

The total volume of blood collected and number of visits with blood collection depends on which study group you are assigned to. Throughout the study, depending on the study group, between 6 and 19 blood samples will be taken from you for safety monitoring and to measure the effect of study vaccines. Intravenous needle insertion will be required once per site visit for this blood collection. Depending on the planned assessments, the samples collected will each be between 15 mL and 135 mL (approximately 1 to 9 tablespoons). Depending on the study group, the total blood volume drawn during the entire study will be between 115 mL (approximately half a can of coke) and 1110 mL (approximately 3.5 cans of coke). Additional blood samples may be taken, e.g., for safety tests or if you attend additional unplanned visit due to COVID-19 illness.

For all study groups, this collection of blood will take place over approximately 1 year, and will remain less than 550 mL for any 46-day period. For comparison: in the case of a blood donation, 500 mL is generally drawn at a time and up to four (women) to six (men) full blood donations are allowed per year.

1.7.3 Visit schedules

The planned study visits are summarized in the following visit schedules. The study doctor may schedule unplanned visits in order to perform medical assessments for your safety.

When reading the visit schedules, please note the "Visit schedule footnotes" as well.

Table 1: Schedule of events for study groups 1 and 4 in Part B

Activity	Visit 0	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5 / Study end	Early stop
Visit description	Screening	Pre-Vax	1 week Post-Vax	1 month Post-Vax	6 month Post-Vax	1 year Post-Vax	(if needed)
Report your age, gender, ethnic background, and medical history	X	X					
Standard medical assessment [a]	X	X	X [b]	X [b]			
Electrocardiogram	X	X [a]	X				
Urine pregnancy test (women who can become pregnant)	X	X					
Receive study vaccine		X					
Have oral body temperature measured daily at home		→					
Collect (incl. train), return e-diary		Collect	Return				Return
Daily report of oral body temperature and any injection site reactions or flu-like symptoms for 7 days after dosing in the e-diary		Start after Vax	End				End
Report any medication use, pregnancies or side effects	X	X	X	X	X	X	X
Provide oral swabs for SARS-CoV-2 testing and (if needed) for identification of the virus [c]	X	X	X	X	X	X	X
Provide blood for study-specific assessments [d]		X	X	X	X	X	X

Table 2: Schedule of events for study group 6 in Part B

Activity	Visit 0	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9 / Study end	Early stop
Visit description	Screening	Vax 1	1 week Post-Vax 1	Vax 2	1 week Post-Vax 2	1 month Post-Vax 2	6 month Post-Vax 2/ Pre-Vax 3	1 week Post-Vax 3	1 month Post-Vax 3	1 year Post-Vax 2/6 months Post-Vax 3	(if needed)
Report your age, gender, ethnic background, and medical history	X	X									
Standard medical assessment [a]	X	X	X [b]	X	X [b]	X [b]	X	X [b]	X [b]		
Electrocardiogram	X	X [b]	X	X	X		X	X			
Urine pregnancy test (women who can become pregnant)	X	X		X			X				
Receive study vaccine		X		X			X				
Have oral body temperature measured daily at home		→		→			→				
Collect (incl. train), return e-diary		Collect			Return		Collect	Return			Return
Daily report of oral body temperature and any injection site reactions or flu-like symptoms for 7 days after each dose in the e-diary		Start after Vax 1	End	Start after Vax 2	End		Start after Vax 3	End			End
Report prior/concomitant medication, pregnancies, or side-effects	X	X	X	X	X	X	X	X	X	X	X
Provide oral swabs for SARS-CoV-2 for testing and (if required) for identification of the virus [c]	X	X	X	X	X	X	X	X	X	X	X
Provide blood for study-specific assessments [d]		X	X	X	X	X	X	X	X	X	X
Pre-selected sites: Blood for further immune response assessments [f]		X		X	X [e]	X	X	X	X	X	

Visit schedule footnotes:

a. At Visit 0: complete physical examination including body weight, height, record vital signs (oral body temperature, heart rate, blood pressure), and collect blood and urine for standard laboratory tests to check your general health status.

   Short physical examination will be performed:

   - At Visit 1
   - At Visit 3 and 6 for study group 6

b. Only oral body temperature will be measured.

c. All Swabs will be used to assess the identification of the coronavirus strain, even if no COVID-19 symptoms are shown.

d. Blood/Serum samples will be stored and may be analyzed retrospectively for additional clinical parameters (troponin, cytokine) after recommendation from the Safety Review Committee.

e. The 12-lead ECG at Visit 1 can be skipped if the 12-lead ECG from Visit 0 was performed within 24 hours prior to the planned vaccine dose.

f. For approximately 15 participants at preselected sites in Part B group 6 only.

g. 5 ml of blood will be taken from this sample for genetic testing (human leukocyte antigen typing)

h. Visit 7 and 8 for Part B group 6 are only planned for participants who receive the third vaccination.

Abbreviations: e-diary = electronic diary provided by the study site; Vax = vaccination.

1.8 What must I be aware of if I participate?

If you decide to participate, you will be asked to sign and date a consent form and you will receive a copy of this "Participant Information and Informed Consent Form". During your participation in this study (participation begins with your signature and date on the consent form), you may not enroll in any other study involving investigational medicines.

1.8.1 General considerations

During the study, you will be required to adhere to the following:

- To always carry the study card (which identifies you as a study participant) with you.
- To follow any instructions that you are given.
- To complete the e-diary as instructed by the study team.
- To follow COVID-19 prevention guidance as per your health authorities (mask wearing, social distancing, etc.).
- To come to the study site for your visits and to allow the planned procedures.
- To provide accurate and complete answers to questions, e.g., regarding information about your medical history and your present health.
- To tell the study doctor or site staff about any changes in your health, even if you think they are not related to the study vaccine.

- To tell the study doctor or site staff if you take new medications or alter your normal medication when in the study.
- To not take or receive any other medications or vaccinations during the study that have not been discussed with your study doctor. You should not receive any SARS-CoV-2 vaccine apart from the study vaccine during your participation in this study.
- To inform and consult with your study doctor before consulting with a non-study doctor, taking any other medication, or undergoing any other medical treatment. This rule does not apply if there is a medical emergency, but your study doctor must be informed immediately if you receive any emergency treatment. If, for any reason, you consult with another doctor during the study, you should tell the non-study doctor that you are taking part in a study and show him/her your study card. This may be important for diagnosing and treating your complaints. You must tell your study doctor immediately, if anything affecting your health occurs.
- To drink plenty of liquids, at least 0.5 to 1 L water, before each visit and again within the 2 hours after vaccine injection.
- To avoid strenuous exercise for the 7 days following injections
- To not smoke or to drink alcohol when at the study site.
- To not take part in another study at the same time as this one.

1.8.2 Prevention of pregnancy

It is not yet known whether the use of the study vaccines in a parent could be harmful to an unborn baby or an infant. Therefore, please read the information below regarding contraception. If you have questions about reliable contraception, the study doctors are happy to answer any questions.

With the exception of complete abstinence (no sexual intercourse), no method of birth control offers 100% reliable prevention of pregnancy. Most pregnancies occur due to improper or irregular use of a contraceptive method.

For women

You must not participate in the study if you are planning to become pregnant or if you are pregnant, or you are breast-feeding. For this reason, all women who can become pregnant must undergo a pregnancy test at the start of the study. However, pregnancy tests only confirm pregnancy reliably a few days after conception. Only women in menopause (at least 1 year after the permanent absence of menstrual periods) or those who have been surgically sterilized (ligature/dissection of the Fallopian tubes, removal of the uterus), do not have to do a pregnancy test.

If you participate in the study and can become pregnant, you must use a highly effective method of contraception (that is, with a failure rate of less than 1% per year) in the time from Visit 0 and continuously until 28 days after the last study vaccine injection in this study. Your study doctor will discuss your birth control method options with you.

The following birth control method options apply:

- Hormonal contraceptives which prevent ovulation (tablets – "the pill" –, patches, vaginal ring, three-month injectable contraceptives, contraceptive implants)
- Copper or hormonal intrauterine devices

Under the following conditions, it may be sufficient that the male sexual partner of the female participant is sterilized:

- the success of the sterilization has been verified (by means of semen testing).
- a corresponding medical certificate is available, and there are no other sexual partners.

Abstinence from heterosexual intercourse is also a suitable method of contraception for this study. Please speak to the study doctors at the study site about this, if necessary.

If you become pregnant or think that you might be pregnant in the time from Visit 0 until you withdraw or complete participation in this study, you must inform the study doctor immediately. Further injection of study vaccine (if planned) will be stopped immediately. You will be asked to continue with the study procedures. You will be asked to allow the study doctor to receive regular updates about the course of the pregnancy, the delivery, and the health of your child. In such cases, you will receive a separate information and consent form for this purpose on which you can give consent.

If you can become pregnant, you must agree not to donate eggs in the time from Visit 0 and continuously until 28 days after the last study vaccine injection in this study.

For men

If you are a fertile man with a female partner who can become pregnant and if you participate in this study, you must agree to use a highly effective method of contraception with your partner (that is, from Visit 0 and continuously until 28 days after the last study vaccine injection). You are not considered to be fertile if you have been successfully sterilized (e.g., have had a vasectomy).

Under the following conditions, it may be sufficient that the male participant is sterilized:

- the success of the sterilization has been verified (by means of semen testing)
- there is a corresponding medical certificate available

Abstinence from heterosexual intercourse may also be a suitable method of contraception for this study. Please speak to the study doctors at the study site about this, if necessary.

If your partner becomes pregnant after you have received the study vaccine, but before you have come off the study, you must immediately notify one of the study doctors at the study site about this pregnancy. In such cases your partner will receive a separate information and consent form. If she gives consent, she will be asked to allow the study doctor to receive regular updates about the course of the pregnancy, the delivery, and the health of your child.

You must refrain from sperm donations in the time from Visit 0 and continuously until 28 days after the last study vaccine injection in this study.

1.9 What are the risks and possible discomforts when in this study?

General information about risks

Due to administration in the muscle, there may be locally limited and mild reactions at the injection site – for example, reddening of the skin, itching, pain, touch sensitivity, and/or swelling.

Because of their effects on the immune system, all vaccinations can cause unwanted effects. These effects (side-effects) may be fever, headaches, fatigue or a loss of appetite, as in the case of any vaccination. They may be mild or serious. These symptoms are – as in the case of other vaccinations – transient. You might have side-effects specific to the study vaccines. In some cases, these side-effects might be long lasting, or permanent, and may even be life threatening. Because the effects the study vaccines could have on you are not fully known, the study team will be monitoring you while you are in this study.

The study is being conducted in research sites whose medical personnel is trained to detect any possible side-effects from study vaccines.

If any side-effects or injuries occur during the study, you must inform your study doctor; in the event of severe side-effects or injuries (e.g., leading to an unexpected admission to the hospital) you must inform your study doctor immediately, e.g., by telephone (see phone number given in Point of Contact section below). You should seek medical help right away if you think you have any of the following symptoms of:

- Serious allergic reaction: trouble breathing, or swelling of the face, mouth, lips, gums, tongue or neck.
- Other symptoms of an allergic reaction may include rash, hives, or blisters.

It is important that you tell the study doctor about any adverse changes in your health (also called "adverse reactions" or "side-effects") as soon as they occur, whether or not you think they are caused by the study medicine. Should you experience any side-effects during the study, the study team will assess them, and may give you medicines to treat the side-effects.

The study vaccines are not expected to influence your ability to drive and use machines. However, some of the effects mentioned in the "Risks related to the study vaccines" section may temporarily affect your ability to drive or use machines. You should not drive or use machines if you feel drowsy or dizzy, or if you have impaired vision after taking the study vaccines. Please ask your study doctor if you are able to drive and use machines as the ability to drive has to be examined on an individual basis.

1.9.1 Risks related to the study vaccines

The safety and effect of the study vaccines has not been fully tested in humans. There may be some side-effects that are not known yet.

Study Vaccines B, C, and D are very similar to Study Vaccine A, and so their safety and effectivity profile is expected to be similar to that for Study Vaccine A. The risks related to the Study Vaccine A are summarized below:

Up until September 2021, the safety of Vaccine A BNT162b2 has been studied in clinical trials that have included more than 49,000 people aged 12 years and above who have received at least one dose of the vaccine. Additionally, the safety of BNT162b2 has been studied in clinical trials including about 3100 children (ages 5 to <12 years) who have received at least one dose of the vaccine. Since the vaccine has been approved for emergency use or received a full or conditional marketing authorization in many countries across the world, by the end of September 2021 about 1.7 billion doses have been distributed and it is estimated that around 80% of those (around 1.3 billion doses) have been administered.

Based on the clinical trial results, and information gathered during general use, the following risks have been determined to be caused by the BNT162b2 vaccine:

Very common (occurring in more than 1 in 10 people): injection site pain, injection site swelling, fatigue (tiredness), increased body temperature (fever, more common after the second dose), chills, headache, diarrhea, joint aches, and muscle aches.

Common (between 1 in 10 and 1 in 100 people): feeling sick (nausea), being sick (vomiting), and injection site redness.

Uncommon (between 1 in 100 and 1 in 1,000 people): enlarged lymph glands, allergic reactions (symptoms may include rash, itching [not reported in adolescents], hives), decreased appetite (not reported in adolescents), lethargy (not reported in children or adolescents), sweating and night sweats (not reported in children or adolescents), pain in arm, and feeling weak (not reported in children or adolescents) or unwell.

Rare (between 1 in 1,000 and 1 in 10,000 people): swelling of the face or lips (not reported in children or adolescents).

Frequency that cannot be estimated from available data: severe allergic reaction (anaphylaxis).

The safety of an additional (third, booster) dose of Vaccine A BNT162b2 has also been studied in 306 people aged 18-55 years and the following risk (more frequent than listed above) has been determined to be caused by BNT162b2 vaccine following an additional third dose:

Common (between 1 in 10 and 1 in 100 people): enlarged lymph glands.

It was also determined that following an additional (third, booster) dose of Vaccine A BNT162b2 the following risks were not reported:

Hives, itching, lethargy, sweating and night sweats, feeling weak or unwell, swelling of the face or lips.

Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have occurred in some people who have received Vaccine A

BNT162b2. Cases have mainly been reported in males under 30 years of age and following the second vaccination, however, there have been some cases reported in older males and females as well as following the first vaccination. The chance of having this occur is very low and, in most of these people, symptoms began within a few days to a week following vaccination.
As a precaution, you should seek medical attention right away if you have any of the following symptoms after receiving the vaccine:

- Chest pain
- Shortness of breath
- Feelings of having a fast-beating, fluttering, or pounding heart

Please also notify study staff, if you have any of these symptoms.

Whilst some severe cases have been reported, most cases have been associated with full resolution of symptoms in the short term, however, long-term follow-up is limited. It is not known whether the risk of myocarditis or pericarditis is increased following additional doses of the vaccine, e.g. following a booster dose.

If you have had myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining outside the heart) previously, please tell your study doctor.

As in all research studies, the COVID-19 vaccine may involve risks that might be expected based on results from studies of similar vaccines, as well as risks that are currently unknown.

Therefore, it is important that you report all symptoms and side effects that you experience as soon as they occur, whether or not you think they are caused by the study vaccine.

Due to the way in which the study vaccines are made, they cannot cause COVID-19 disease.

If I catch COVID-19 disease, could the vaccine make it worse?

For some other vaccines tested in animals against similar viruses (but not the coronavirus that causes COVID-19), there have been reports of the illness being more severe in the animals that received the vaccine than in those that did not. So far this has not been seen with Vaccine A BNT162b2. It remains important for you to contact your study doctor if you develop symptoms that might be caused by COVID-19 (for example, fever, cough, shortness of breath).

1.9.2 Risks related to study procedures and assessments

This risks related to study procedures and assessments are linked to the collection of a blood samples and to pregnancy.

Risks of blood collection/intravenous needle insertion

The collection of a blood sample may cause some discomfort. Obtaining blood may cause pain/discomfort at the site where blood is collected, bruising, bleeding, occasional lightheadedness, and, rarely, infection or fainting. Nerve injuries may occur.

The total volume of blood collected and the number of visits with blood collect depend on the study group. Intravenous needle insertion will be required once per site visit for blood collection; this needle will be used for collecting blood for different assessments.

Pregnancy-related risks

The effects of the study vaccines on sperm, an unborn baby, or a breastfed child are unknown. Since the risks relating to pregnancy are unforeseeable, it is important that men and women able to bear children and fertile men use the birth control methods that are recommended by the study doctor from Visit 0 continuously until 28 days after the last dose of study vaccine as explained before.

You must tell your study doctor immediately, if you or your partner become pregnant while you are participating in the study.

1.10 How will I be informed in the event of new information?

Sometimes during the course of a study, new information becomes available about a study medicine or a vaccine. If this happens, your study doctor will inform you about it in a timely manner and discuss with you whether you want to continue in the study. You can then consider whether you want to continue taking part in this study on that basis.

1.11 Will there be any costs if I participate, e.g., travel expenses?

There are no costs for you, your medical scheme or your healthcare provider if you take part. You will receive the study vaccines and any study-related procedures and tests free of charge.

The sponsor has made provision to reimburse you for out-of-pocket expenses such as travelling to and from the study site and compensate you for other miscellaneous costs, such as time spent at the site and inconvenience, because of study participation.

You will receive a minimum amount of **R400** per visit. If the study calls for more invasive or strenuous procedures which are over and above standard inconvenience, and/or your study-related expenses exceed the specified amount and you have proof of such expenses, you may qualify for additional reimbursement.

1.12 What if I have an injury during the study?

1.12.1 Study participant insurance

It is not expected that you will suffer damage to your health due to your participation in this study. If you do suffer side-effects, please also inform your study doctor, they will provide medical treatment or refer you for appropriate treatment.

All study participants are insured during the study according to applicable laws. The scope of the insurance coverage can be found in the insurance documents which were given to you by the study doctor.

If you do suffer any health damage (e.g., physical injury) as a direct result of taking part in the study, you must inform the study doctor and the insurance company, using the following details, Policy No: SYD21033304A, Policyholder: BioNTech SE, An der Goldgrupe 12, 55131 Mainz, Germany, Local Contact: Carla Vieira, el: +27 11 505 0000, Carla.Vieira@lioyds.com, with the help of your study doctor if necessary in order to maintain your insurance cover. If you notify the insurance company directly, please also inform your study doctor.

If you do suffer any health damage, you must cooperate with the investigation into the cause or extent of damage, and do everything you can to avoid and minimize the health damage.

BioNTech will pay for the reasonable costs of medical treatment required for injuries of an enduring and disabling nature and arising directly from your participation in the study in accordance with local laws and general guidelines. BioNTech has insurance to cover these costs.

The insurance protection covers study-related injuries and treatment of study-related injuries, where the injury is of an enduring and disabling character requiring medical treatment (including exacerbation of an existing condition) (is not temporary) and/or compensation for death, according to this insurance. The insurance coverage is up to 500,000.00 € per person. The total coverage for the study is limited to 50 million €.

BioNTech will provide compensation for reasonable medical costs required to treat your bodily injury, in accordance with the SA Good Clinical Practice Guidelines (2006 or latest version), which are based on the Association of the British Pharmaceutical Industry Guidelines. You may request a copy of these guidelines from the study doctor.

There is no requirement to prove that the research was responsible for your bodily injury.

The insurance will not cover and neither will BioNTech pay for harm if, during the study you:

- Use medicines or substances that are not allowed
- Do not follow the study doctor's instructions
- Do not tell the study doctor that you have a bad side effect from the study medicine
- Suffer an injury arising from negligence on your part or do not take reasonable care of yourself and your study medicine.
- Medical treatment of other injuries or illnesses not related to administration of the study medication or study
- Injury caused by non-observance of the protocol by both study doctor and/or the participant

If you are harmed and the insurer or BioNTech pays for the necessary medical costs, usually you will be asked to accept that payment as full settlement of the claim for medical costs. However, accepting this offer of insurance cover does not mean you give up your right to make a separate claim for other losses based on negligence, in a South African court.

If you belong to a private medical scheme, you should inform them that you are participating in a research study. You must notify the study doctor immediately if you believe you have suffered any injury through participation in this study.

1.13 Confidentiality and data privacy

1.13.1 Consent

The study information will be recorded in your medical notes and on study forms. The collection and use of your information is based on your written consent and applicable laws and regulations, for example, on clinical studies and protecting study participant safety. By consenting to participate in the study, you acknowledge that certain personal data (information which is capable of identifying you), in particular health data and other data, which may be sensitive, such as year of birth, age, gender, race and ethnic background will be collected and processed electronically, used, and/or disclosed for research purposes in connection with this study. This consent is valid until the end of the study.

1.13.2 Medical records

The records identifying you, including your medical records, remain at the study site and will be kept confidential up to 20 years by those reviewing them, except as described in this consent form.

In certain circumstances, it may be necessary to provide direct access to the records identifying you (including your original medical records) to authorized personnel of BioNTech (e.g., monitors), its agents (e.g., from the contract research organization [ICON]), and regulatory authorities, ethical committees, BioNTech collaborators, research partners, assignees or designees, or other persons required by law. This access is required to verify that the study is conducted appropriately and that the information collected for the study is correct and complete.

In exceptional circumstances, such access to your personal data may also be required if for example BioNTech and/or its research partners were subject to legal proceedings or a regulatory investigation. Any such processing of personal data will always be in accordance with applicable data protection law.

1.13.3 Study data

Study data will also be recorded on study forms, which will be provided to the sponsor, BioNTech, as well as its affiliates, collaborators, and research partners. Any personal data, which is capable of identifying you, will be replaced on the study forms with a unique code referred to as a Participant Identification number (PID). All data collected about you for this study including all data collected about you at the study site and data obtained from your tests and samples will be identified using this PID number and this means that your personal identifying information, such as your name and address, will be removed and replaced with your PID number before your information leaves the study site. Your personal data is coded in this way to protect your privacy. We refer to this coded information as study data. Your name and identifying information will remain within the study site and will remain confidential at all times otherwise than in exceptional circumstances as set out above.

Your study doctor is responsible for keeping a code list, which makes it possible to link your PID to your name. This will be kept in a safe place to ensure that in case of an emergency you can be identified and contacted. BioNTech will act as responsible party in relation to your study data.

You will not receive results of tests/assessments, which are completed only for study purposes. You may receive results of routine tests/assessments completed as part of the study if the study doctor determines the results are important for your care.

The results of this study will be published, though you will not be identified in any report or publication. Your study doctor will be given a copy of the report or publication at the time of publication.

All your study data will be protected in accordance with applicable laws. BioNTech is responsible for protecting your data and will take reasonable steps to maintain the confidentiality of your personal information in accordance with all applicable data protection laws.

A description of this study will be available on http://www.clinicaltrials.gov. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

A description of this study will be also available on https://www.clinicaltrialsregister.eu/ and on https://sanctr.samrc.ac.za/, as required by South African law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

1.13.4 Your data protection rights

You have the right to refuse to consent to the use and disclosure of your personal data (which includes the use of biosamples collected from you during this study) for purposes of this study. However, if you do not consent to such use and disclosure, you will not be able to participate in this study. You also have the right to refuse to consent to the use and disclosure of your personal data for any additional purposes, such as future storage of your biosamples and further research.

Medical and personal information will be obtained from you ("personal data") as part of the study and be recorded at the study site in your individual record or stored electronically. Personal data also includes any biosamples collected from you during the study, such as blood and oral samples, and any derivative products.

Personal data will be processed by the study doctor(s), the Sponsor, and various third parties (including affiliate companies, service providers (e.g., laboratories, statistics experts) and other collaboration partners of the Sponsor (e.g., universities, pharmaceutical companies, research institutions) for the following purposes:

(i) the research purposes of this study;

(ii) analysis, now or in future (but not more than five years after the termination of this study); and

(iii) future research.

This personal data will only be provided in a pseudonymized (= coded) form to the study sponsor, the examining and approving authorities, or a site commissioned by it for scientific assessment. Pseudonymized means that no information such as names or initials are used, but instead only a number and/or letter code, in this study your PID. It is possible to allocate this personal data back to you personally only with the aid of this code. Decoded data, which enable you to be personally identified, are available only at the study site. The data are protected against unauthorized access.

Under South Africa data protection law ***"Protection of Personal Information Act 2013"*** your study site and the sponsor will each be responsible as a 'controller' to ensure that your information is safeguarded. Your data might be transferred to a country that may not have the same level or personal data protection as South Africa. If your data is transferred outside South Africa the sponsor is responsible for protecting your data.

Should you wish to contact BioNTech data privacy team: Stefanie Kirchner, data.privacy@biontech.de, +49 (0) 6131 9084 0, An der Goldgrube 12, 55131 Mainz, Germany.

In addition, if you are of the opinion that your study data is being used in violation of applicable data protection laws, you have the right to bring a complaint to the Information Regulator at:

Information Regulator (South Africa)
Address: JD House, 27 Stiemens Street, Braamfontein, Johannesburg, 2001
P.O.Box: P.O Box 31533, Braamfontein, Johannesburg, 2017
Email: **complaints.IR@justice.gov.za**

1.13.5 Your right to withdraw consent

After agreeing to participate in this study, you may decide to withdraw from the study at any time without stating any reasons and without any penalty or loss of benefits.

You can discuss this further with your study doctor, who will be your primary contact person for your rights, or you can contact the data protection officer of the study doctor's institution for further information.

How to withdraw consent

If you wish to withdraw your consent to participate in the study, please inform your study doctor verbally or (preferably) in writing using the contact information provided on the first page of this document.

Effects of withdrawing consent on study data

If you withdraw your consent, you will also stop your participation in this study. No new study data will be collected, but the study data that have already been collected will continue to be used and processed to maintain the integrity of the study in accordance with applicable data protection law.

If you stop participation in the study, the study site may contact you for follow-up activities, for example to obtain some more information about your health if you were experiencing a health problem at the time you decided to leave the study.

Effects of withdrawing consent on biosamples collected during the study

If you withdraw your consent, you will also stop your participation in this study. No new biosamples (for example blood) will be collected.

If you stop participation in the study you may request that any already collected but not analyzed biosamples (including any derivatives of biosamples such as serum) or any biosample leftover after analysis, are destroyed to prevent further analysis.

If you stop participation in the study, and you originally gave consent for biosample use (including storage for use up to 5 years after the end of the study) for research purposes, you will be asked what should happen to these biosamples. You may request that these biosamples are destroyed to prevent further analysis.

If you request that any of the biosamples collected in this study are to be destroyed at any time. If you so request, the study doctor may provide you with written confirmation that your samples have been destroyed. However, data already obtained from your samples will continue to be kept and used for the purposes described in this document. If you do not ask for your samples to be destroyed, they will continue to be used for the purposes described in this document.

Retention

BioNTech and the study doctor will retain your study data in accordance with applicable laws. The retention time may be longer if your study data is included in filings used to obtain approval of medicines and vaccines.

1.13.6 What will happen with the biosamples that are collected?

Your biosamples (blood, derivatives thereof such as serum, and urine) will only be used for the purposes described in this consent document.

a) Your blood and urine samples will undergo standard laboratory testing and will be sent to your local laboratory for analysis for procedures stated under section 1.7.
b) Your blood samples taken for assessing your immune response against SARS-CoV-2 virus will be sent to ICON Laboratory Services Dublin (ICON Clinical Research Ltd) for analysis.
c) For a subgroup of participants in Part B group 6 in pre-selected sites: Your blood samples for further assessing immune response against SARS-CoV-2 virus will be sent to Spencer Lister Building, NHLS Complex Corner Hospital and De Korte Street Johannesburg, South Africa and BioNTech SE, An der Goldgrube 12, 55131 Mainz, Germany for analysis.
d) Your oral swabs for SARS-CoV-2 testing will be tested at the study site local laboratory.

e) If the testing for b) and/or d) are positive, your oral swabs will be sent to ICON Laboratory Services Dublin for characterization of the specific SARS-CoV-2 virus strain.

If you consent, the sponsor may store any leftover biosamples or explorative research biosamples that you provided for future unspecified exploratory research relating to vaccines against COVID-19 and/or immune therapy research in accordance with the provisions of data protection laws, and use such biosamples for any such purpose. Your blood samples for explorative research using leftover samples will be sent to NHLS Lab for analysis following to Brooks for storage. The use of your biosamples in any such future exploratory or immune therapy research studies shall be contingent on any such studies being subject to prior ethical review.

All biosamples shall not be retained by the sponsor or any third parties to whom the sponsor provides access to your biosamples during this study or thereafter (as permitted) for longer than permitted under data protection laws. All biosamples will be stored in accordance with all legal requirements.

The Sponsor may share the coded personal data and biomaterial samples from this study for research purposes with affiliate companies, service providers (e.g., laboratories, statistics experts) and other collaboration partners of the Sponsor (e.g., universities, pharmaceutical companies, research institutions) during the term of the study and for a reasonable period after the termination of the study, provided that at no time will the Sponsor or any person retain such personal data and biomaterial samples for longer than permitted under date protection laws. The Sponsor will ensure that all persons with whom it shares your personal data and biomaterial samples in terms of this provision, are bound by the same security measures as it as a 'responsible party' under the applicable data protection laws, and that at no time will any reports published or derived from such research present or display any of your identifiable personal information. You hereby consent to the publication of any results derived from such research in any reports and on any platforms.

The biosamples and all data generated using the biosamples, will be handled in accordance with applicable laws and regulations; this includes requirements applicable for data privacy (for additional details see the following pages).

BioNTech and laboratories involved in this study will keep your information confidential. The tube with the biosample will be labeled with a participant identification number (PID) (optionally also with a bar code); the tube label will not include information that could be used to identify the participant. Only the study doctor will have access to a list that can link your name with the PID. This list will be kept in a secure location, but could be accessed in case of an emergency.

These biosamples may be used or shared with third parties. If not used up within 5 years of the end of the study, all biosamples will be destroyed.

By signing this document, you consent to the study doctor sharing and disclosing your personal information and records containing your personal information biometric information with the Sponsor, SAHPRA, the National Health Research Ethics Committee, Pharma-Ethics Research Ethics Committee and/or other regulatory authorities and/or you consent to the Sponsor disclosing such information to the aforesaid persons as may be required from time to time.

Information and inventions derived from your participation in the study, including information derived from your biological samples are the property of the BioNTech and its collaborators. You will not receive any compensation from commercial profit derived from this study.

1.14 Point of contact

In urgent cases, e.g., in the event of study-related injury, contact:

Name:	[redacted]
Address:	[redacted]
24-hour emergency phone number:	[redacted]

For further information regarding this study and your rights as study participant, contact:

Name:	Pharma-Ethics Research Ethics Committee Marzelle Haskins
Address:	PO Box 786, Irene, 0062
Phone number:	012 664 8690
E-Mail:	marzelle@pharma-ethics.co.za

Sponsor's point of contact for the participant:

Name:	BioNTech SE
Address:	An der Goldgrube 12, 55131 Mainz, Germany
Phone number:	During work days and working hours in Germany (09:00 to 17:00) the sponsor of this study, BioNTech, is available under the following phone number: +49 (0) 6131 9084 0

If you have any general questions about your rights as a study participant, or would like to obtain information from, offer suggestions to, or speak with someone not directly involved in the study, you may contact Pharma-Ethics Research Ethics Committee listed below

Address: PO Box 786, Irene, 0062
Phone number: 012 664 8690
E-Mail: marzelle@pharma-ethics.co.za

If you have questions about this trial, you should first discuss them with the study doctor or with Pharma-Ethics Research Ethics Committee. If you do not receive answers that are to your satisfaction, you should write to the South African Health Products Regulatory Authority (SAHPRA) or National Health Research Ethics Council (NHREC) at:

Dr. Boitumelo Semete-Makokotlela, CEO **South African Health Products Regulatory Authority (SAHPRA)** Department of Health Private Bag X828 PRETORIA 0001 Physical address: Building A Loftus Park 2nd Floor 402 Kirkness Street Arcadia 0083 Tel: (012) 501 0410 E-mail:Boitumelo.Semete@sahpra.org.za	The Chair **National Health Research Ethics Council** E-mail: nhrec@health.gov.za Tel: (012) 395 8113 Fax: (012) 3958467

2 CONSENT STATEMENT

By signing below, I agree that:

Initial Blocks

- I have read or had read to me the information sheet and consent form, for this study.
- I understand that this trial is investigational and what is means.
- The purpose, treatment and procedures of this trial have been explained to me and I understand them.
- I understand my responsibilities as a trial participant.
- I understand that participation in the trial is voluntary and that I can refuse to participate or withdraw at any time, without it affecting my ongoing care.

- I have been informed of the possible risks, harm and inconvenience of participating.
- For women: I am not pregnant, breastfeeding or trying to fall pregnant and will use acceptable birth control during the trial.
- I have been informed of the expected benefits of the trial.

- I have been informed of the alternative treatment, including its potential risks and benefits that may be available to me if I do not participate in this trial.
- I have been informed of the compensation and treatment that would be available to me in the event of a trial-related injury.
- I have been informed of any payment or reimbursement I may receive, as well as any anticipated expenses that I may incur while participating in the trial.
- I have had sufficient time to ask questions and they were answered to my satisfaction.
- I have been given time to discuss the trial with others and to decide whether or not to take part.
- I am aware that the results of the trial, including personal details about me and my health information may be reasonably disclosed to the sponsor, regulatory authorities and research ethics committees, if required by law.
- I agree for my blood/tissue samples to be transferred to a secure central laboratory outside South Africa.
- I will receive a signed and dated copy of this informed consent form.

- I agree to participate in this trial.

Participant's name (first name and family name in block letters; handwritten by the participant)	Handwritten Signature	Date (DD MMM YYYY)

I consent to use of the biosamples leftover after an analysis during this study for future unspecified research now and in the future relating to vaccines against COVID-19 and/or immune therapy research. I consent to the publication of any derivative research in reports or whatsoever form. I am aware that this consent for this purpose is optional and that I can withdraw this consent at any time, without any disadvantages to me.

[redacted] Yes ☐ No

[redacted]	[redacted]	[redacted]
Participant's name (first name and family name in block letters; handwritten by the participant)	Handwritten signature	Date (DD MMM YYYY)

Study doctor or delegate conducting the information discussion

With my signature, I confirm that I conducted the informed consent and information discussion, handed out the participant informed consent form, and answered any questions which arose about the nature, significance and implications of the study BNT162-17 and have given the participant the opportunity to ask questions and ample time to decide whether to participate. I obtained consent from the participant.

[redacted]	[redacted]	[redacted]
Job title /function, designee's name (block letters)	Handwritten signature	Date (DD MMM YYYY)

[redacted]

2.1 Declaration of participant consent with regard to data privacy

I am aware that in this study, personal data, in particular medical findings about me and biosamples (in the form of biometric data), are to be collected, stored, processed and analyzed. The data regarding my health is used according to legal regulations and this use requires the following voluntarily granted declaration of consent prior to participation in the study, that is, without the following consent, I cannot participate in the study.

My questions have been answered to my satisfaction.

I agree that:

- My personal data can be collected and recorded during this study, in particular regarding my health status, age, gender, and ethnic background.
- My personal data can be processed for purposes of this study, as well as the additional purposes set out in the ICF, including future research and storage of my biosamples beyond the term of this study, but in any event, for no longer than a period of five years after the termination of the study, unless the purpose for such storage or further processing of my personal data is not yet achieved.
- My personal data (including health data, and other data for the purposes of the study), can be passed on (shared), documented, stored in computers, and processed as long as I am only identified using a participant identification number and is processed for the purposes set out in this ICF.
- Authorized and confidentiality-bound representatives of the sponsor as well as the competent supervisory authorities to inspect my personal data will be granted direct access to my original medical records (i.e., the participant file that includes my personal details) to check that important data for scientific evaluation have been recorded completely and correctly to special report forms and to check that the study has been carried out properly.
- The results of the study can be published or sent to the responsible health authority in those countries where the vaccine is to be registered.
- If I stop participation in the study (following my own decision or otherwise), I agree not to restrict the use of the study data collected up to the moment of my withdrawal for purposes of the study.
- My data (without my name and address) can be passed on to BioNTech and other companies associated with BioNTech for scientific evaluation of the study and for use in further scientific evaluation.
- BioNTech may share the coded personal data and biomaterial samples from this study for research purposes with affiliate companies, service providers (e.g., laboratories, statistics experts) and other collaboration partners of BioNTech (e.g., universities, pharmaceutical companies, research institutions) during the term of this study and/or for a period of up to five years after the termination of the study.

- At all times when my personal data is shared with third parties for any of the purposes under this ICF, my personal data will be treated as confidential and processed in accordance with the provisions of applicable data protection laws and health laws.
- My data (without my name and address) may be sent outside South Africa { e.g., the EU}, including to countries with data protection laws that are not equivalent to or do not have equivalent protection to local data protection laws.
- I consent to my family doctor being informed about my participation in this study:

☐ YES, I want my personal/general doctor / specialist to be informed of my participation in this study.

☐ NO, I do not want my personal/general doctor / specialist to be informed of my participation in this study.

☐ I do not have a personal / general doctor /specialist

If the study doctor is not your family doctor, please enter the name and address (street, number, postal code, town, country) of your family doctor in the space provided below.

[redacted]	[redacted]	[redacted]
Participant's name (first name and family name in block letters; handwritten by the participant)	Signature	Date (DD MMM YYYY)

Family Doctor's Name: _____

Address: _____

_____

[redacted]

"HE25"

PFIZER-BIONTECH COVID-19 VACCINE

FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)

EMERGENCY USE AUTHORIZATION (EUA) OF THE PFIZER-BIONTECH COVID-19 VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

PRIMARY SERIES FOR 12 YEARS OF AGE AND OLDER
DILUTE BEFORE USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, Pfizer-BioNTech COVID-19 Vaccine, for active immunization to prevent COVID-19 in individuals 6 months of age and older.

There are 2 formulations of Pfizer-BioNTech COVID-19 Vaccine authorized for use in individuals 12 years of age and older:

The formulation supplied in a multiple dose vial with a purple cap MUST BE DILUTED PRIOR TO USE.
The formulation supplied in a multiple dose vial with a gray cap and label with a gray border IS NOT DILUTED PRIOR TO USE.

This Fact Sheet pertains only to Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with a purple cap, which is authorized for use in individuals 12 years of age and older and MUST BE DILUTED PRIOR TO USE.

Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with a purple cap is authorized for use to provide:

- **a 2-dose primary series to individuals 12 years of age and older; and**
- **a third primary series dose to individuals 12 years of age and older with certain kinds of immunocompromise.[1]**

COMIRNATY (COVID-19 Vaccine, mRNA) is an FDA-approved COVID-19 vaccine made by Pfizer for BioNTech that is indicated for active immunization to prevent COVID-19 in individuals 12 years of age and older. It is approved for use as a 2-dose primary series for the prevention of COVID-19 in individuals 12 years of age and older. It is also authorized for emergency use to provide a third primary series dose to individuals 12 years of age and older with certain kinds of immunocompromise.

The FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the EUA-authorized Pfizer-BioNTech COVID-19 Vaccine for individuals 12 years of age and older when prepared according to their respective instructions for use can be used interchangeably.[2]

COMIRNATY (COVID-19 Vaccine, mRNA) and the Pfizer-BioNTech COVID-19 Vaccine intended for individuals 12 years of age and older should not be used for individuals 6 months through 11 years of age because of the potential for vaccine administration errors, including dosing errors.[3]

SUMMARY OF INSTRUCTIONS FOR COVID-19 VACCINATION PROVIDERS

Vaccination providers enrolled in the federal COVID-19 Vaccination Program must report all vaccine administration errors, all serious adverse events, cases of myocarditis, cases of pericarditis, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of Pfizer-BioNTech COVID-19 Vaccine. See "MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION" for reporting requirements.

The Pfizer-BioNTech COVID-19 Vaccine is a suspension for intramuscular injection.

Primary Series

The Pfizer-BioNTech COVID-19 Vaccine is administered as a primary series of 2 doses (0.3 mL each) 3 weeks apart in individuals 12 years of age or older.

A third primary series dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 mL) at least 28 days following the second dose is authorized for administration to individuals at least 12 years of age with certain kinds of immunocompromise.

See this Fact Sheet for instructions for preparation and administration. This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.cvdvaccine.com.

For information on clinical trials that are testing the use of the Pfizer-BioNTech COVID-19 Vaccine for active immunization to prevent COVID-19, please see www.clinicaltrials.gov.

DESCRIPTION OF COVID-19

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that appeared in late 2019. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

DOSAGE AND ADMINISTRATION

The storage, preparation, and administration information in this Fact Sheet apply to the Pfizer-BioNTech COVID-19 Vaccine for individuals 12 years of age and older, which is supplied in a multiple dose vial with a purple cap and **MUST BE DILUTED** before use.

Pfizer-BioNTech COVID-19 Vaccine, Multiple Dose Vial with Purple Cap

Age Range	Dilution Information	Doses Per Vial After Dilution	Dose Volume
12 years and older	Dilute with 1.8 mL sterile 0.9% Sodium Chloride Injection, USP prior to use	6	0.3 mL

Storage and Handling

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of Pfizer-BioNTech COVID-19 Vaccine multiple dose vials with purple caps arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90°C to -60°C (-130°F to -76°F) until the expiry date printed on the label. This information in the package insert supersedes the storage conditions printed on the vial cartons.

Cartons and vials of Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with purple caps with an expiry date of December 2021 through December 2022 printed on the label may remain in use beyond the printed date until the updated expiry date shown below; as long as approved storage conditions have been maintained.

Printed Expiry Date		Updated Expiry Date
12/2021	→	31-Dec-2022
01/2022	→	31-Jan-2023
02/2022	→	28-Feb-2023
03/2022	→	31-Mar-2023
06/2022	→	31-Mar-2023
07/2022	→	30-Apr-2023
08/2022	→	31-May-2023
09/2022	→	30-Jun-2023
10/2022	→	31-July-2023
11/2022	→	31-Aug-2023
12/2022	→	30-Sep-2023

If not stored between -90°C to -60°C (-130°F to -76°F), vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned one time to the recommended storage condition of -90°C to -60°C (-130°F to -76°F). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which the Pfizer-BioNTech COVID-19 Vaccine arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90°C to -60°C (-130°F to -76°F). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned one time to the recommended storage condition of -90°C to -60°C (-130°F to -76°F).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2°C to 8°C (35°F to 46°F)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25°C (77°F)] for 30 minutes. Thawed vials can be handled in room light conditions. Vials must reach room temperature before dilution.

Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of one or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 48 hours.

Vials After Dilution

- After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution.
- During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.
- Any vaccine remaining in vials must be discarded after 6 hours.
- Do not refreeze.

Dosing and Schedule

Primary Series

The Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly as a primary series of 2 doses (0.3 mL each) 3 weeks apart to individuals 12 years of age and older.

A third primary series dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 mL) at least 28 days following the second dose is authorized for administration to individuals at least 12 years of age with certain kinds of immunocompromise.

Dose Preparation

Each vial **MUST BE DILUTED** before administering the vaccine.

Prior to Dilution

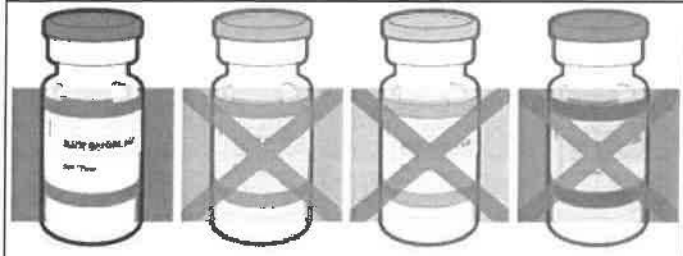
- The Pfizer-BioNTech COVID-19 Vaccine multiple dose vial with a purple cap contains a volume of 0.45 mL and is supplied as a frozen suspension that does not contain preservative.
- Each vial must be thawed before dilution.
    - Vials may be thawed in the refrigerator [2°C to 8°C (35°F to 46°F)] or at room temperature [up to 25°C (77°F)] *(see)*.
    - Refer to thawing instructions in the panels below.

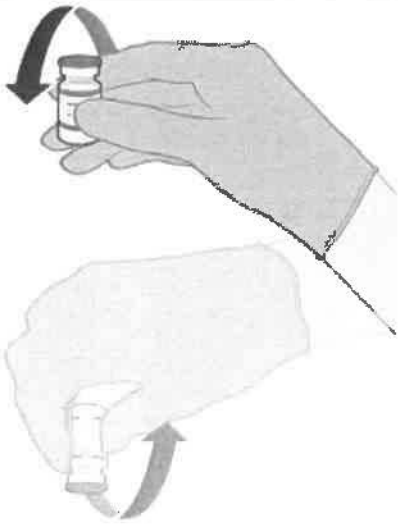
Dilution

Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine. ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not

packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent. Do not add more than 1.8 mL of diluent.

After dilution, 1 vial contains 6 doses of 0.3 mL.

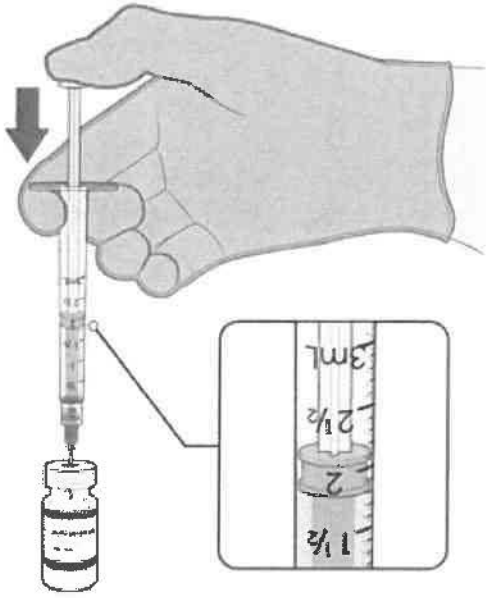
<table>
<tr><th colspan="2">Dilution and Preparation Instructions</th></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap –
VIAL VERIFICATION</td></tr>
<tr><td> 
✓ Purple plastic cap and purple label border.</td><td>Verify that the vial of Pfizer-BioNTech COVID-19 Vaccine has a purple plastic cap. Some vials also may have a purple label border.</td></tr>
<tr><td colspan="2">Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap –
THAWING PRIOR TO DILUTION</td></tr>
<tr><td> 
No more than 2 hours at room temperature (up to 25°C/77°F).</td><td>• Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by:
o Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month.
o Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes.
• Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.</td></tr>
</table>



Gently × 10

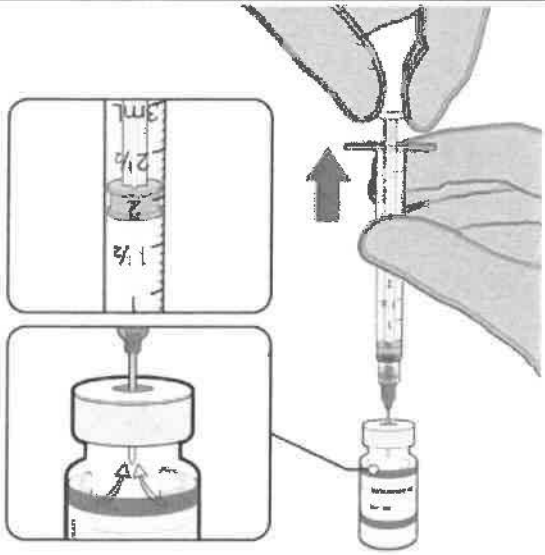
- Before dilution invert vaccine vial gently 10 times.
- Do not shake.
- Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles.
- Do not use if liquid is discolored or if other particles are observed.

Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – DILUTION



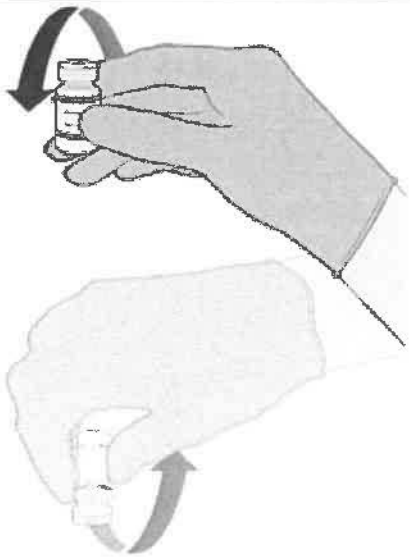
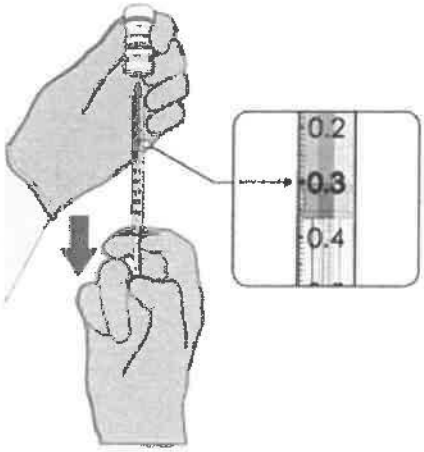
Add 1.8 mL of sterile 0.9% sodium chloride injection, USP.

- Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
- Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle).
- Cleanse the vaccine vial stopper with a single-use antiseptic swab.
- Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.



Pull back plunger to 1.8 mL to remove air from vial.

Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.

 **Gently × 10**	• Gently invert the vial containing the Pfizer-BioNTech COVID-19 Vaccine 10 times to mix. • Do not shake. • Inspect the vaccine in the vial. • The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.
 **Record the date and time of dilution.** **Use within 6 hours after dilution.**	• Record the date and time of dilution on the Pfizer-BioNTech COVID-19 Vaccine vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.
Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – WITHDRAWAL OF INDIVIDUAL 0.3 mL DOSES	
 **Withdraw 0.3 mL dose of vaccine.**	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of the Pfizer-BioNTech COVID-19 Vaccine preferentially using a low dead-volume syringe and/or needle. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

Administration

Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.

- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer the Pfizer-BioNTech COVID-19 Vaccine intramuscularly.

After dilution, vials of Pfizer-BioNTech COVID-19 Vaccine with purple caps contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract 6 doses from a single vial. Irrespective of the type of syringe and needle:

- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and content.
- Do not pool excess vaccine from multiple vials.

Contraindications

Do not administer Pfizer-BioNTech COVID-19 Vaccine to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 Vaccine *(see Full EUA Prescribing Information)*.

Warnings

Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Pfizer-BioNTech COVID-19 Vaccine.

Monitor Pfizer-BioNTech COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention (CDC) guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

Myocarditis and Pericarditis

Postmarketing data with Pfizer-BioNTech COVID-19 Vaccine demonstrate increased risks of myocarditis and pericarditis, particularly within the period 0 through 7 days following the second dose of the primary series. The observed risk is higher among adolescent males and adult males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting.

Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Pfizer-BioNTech COVID-19 Vaccine.

Limitation of Effectiveness

Pfizer-BioNTech COVID-19 Vaccine may not protect all vaccine recipients.

Adverse Reactions

Adverse Reactions in Clinical Trials

Adverse reactions following administration of the Pfizer-BioNTech COVID-19 Vaccine that have been reported in clinical trials include injection site pain, fatigue, headache, muscle pain, chills, joint pain, fever, injection site swelling, injection site redness, nausea, malaise, lymphadenopathy, decreased appetite, rash, and pain in extremity *(see Full EUA Prescribing Information)*.

Adverse Reactions Identified in Post Authorization Experience

Severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema), diarrhea, vomiting, pain in extremity (arm), syncope, and dizziness have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine.

Myocarditis and pericarditis have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine.

Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Pfizer-BioNTech COVID-19 Vaccine.

Use with Other Vaccines

There is no information on the co-administration of the Pfizer-BioNTech COVID-19 Vaccine with other vaccines.

INFORMATION TO PROVIDE TO VACCINE RECIPIENTS/CAREGIVERS

As the vaccination provider, you must communicate to the recipient or their caregiver, information consistent with the "Vaccine Information Fact Sheet for Recipients and Caregivers" (and provide a copy or direct the individual to the website www.cvdvaccine.com to obtain the Vaccine Information Fact Sheet for Recipients and Caregivers) prior to the individual receiving each dose of the Pfizer-BioNTech COVID-19 Vaccine, including:

- FDA has authorized the emergency use of the Pfizer-BioNTech COVID-19 Vaccine, which is not an FDA-approved vaccine.
- There is an option to accept or refuse Pfizer-BioNTech COVID-19 Vaccine.
- The significant known and potential risks and benefits of the Pfizer-BioNTech COVID-19 Vaccine, and the extent to which such risks and benefits are unknown.
- Information about available alternative vaccines and the risks and benefits of those alternatives.

For information on clinical trials that are testing the use of the Pfizer-BioNTech COVID-19 Vaccine to prevent COVID-19, please see www.clinicaltrials.gov.

Provide a vaccination card to the recipient or their caregiver with the date when the recipient needs to return for the second dose of Pfizer-BioNTech COVID-19 Vaccine.

Provide the v-safe information sheet to vaccine recipients/caregivers and encourage vaccine recipients to participate in v-safe. V-safe is a new voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. V-safe asks questions that help CDC monitor the safety of COVID-19 vaccines. V-safe also provides dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information, visit: www.cdc.gov/vsafe.

MANDATORY REQUIREMENTS FOR PFIZER-BIONTECH COVID-19 VACCINE ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION[4]

In order to mitigate the risks of using this unapproved product under EUA and to optimize the potential benefit of Pfizer-BioNTech COVID-19 Vaccine, the following items are required. Use of unapproved Pfizer-BioNTech COVID-19 Vaccine for active immunization to prevent COVID-19 under this EUA is limited to the following (all requirements **must** be met):

1. Pfizer-BioNTech COVID-19 Vaccine is authorized for use in individuals 6 months of age and older.
2. The vaccination provider must communicate to the individual receiving the Pfizer-BioNTech COVID-19 Vaccine or their caregiver, information consistent with the "Vaccine Information Fact Sheet for Recipients and Caregivers" prior to the individual receiving Pfizer-BioNTech COVID-19 Vaccine.
3. The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system.
4. The vaccination provider is responsible for mandatory reporting of the following to the Vaccine Adverse Event Reporting System (VAERS):Complete and submit reports to VAERS online at https://vaers.hhs.gov/reportevent.html. For further assistance with reporting to VAERS call 1-800-822-7967. The reports should include the words "Pfizer-BioNTech COVID-19 Vaccine EUA" in the description section of the report.

    - vaccine administration errors whether or not associated with an adverse event,
    - serious adverse events* (irrespective of attribution to vaccination),
    - cases of myocarditis,
    - cases of pericarditis,
    - cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and
    - cases of COVID-19 that result in hospitalization or death.

5.

The vaccination provider is responsible for responding to FDA requests for information about vaccine administration errors, adverse events, cases of myocarditis, cases of pericarditis, cases of MIS in adults and children, and cases of COVID-19 that result in hospitalization or death following administration of Pfizer-BioNTech COVID-19 Vaccine to recipients.

* Serious adverse events are defined as:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent 1 of the outcomes listed above.

OTHER ADVERSE EVENT REPORTING TO VAERS AND PFIZER INC.

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Pfizer Inc. using the contact information below or by providing a copy of the VAERS form to Pfizer Inc.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

ADDITIONAL INFORMATION

For general questions, visit the website or call the telephone number provided below.

To access the most recent Pfizer-BioNTech COVID-19 Vaccine Fact Sheets, please scan the QR code provided below.

Global website	Telephone number
www.cvdvaccine.com	1-877-829-2619 (1-877-VAX-CO19)

AVAILABLE ALTERNATIVES

COMIRNATY (COVID-19 Vaccine, mRNA) and SPIKEVAX (COVID-19 Vaccine, mRNA) are FDA-approved vaccines to prevent COVID-19 caused by SARS-CoV-2. There may be clinical trials or availability under EUA of other COVID-19 vaccines.

COMIRNATY (COVID-19 Vaccine, mRNA) and the Pfizer-BioNTech COVID-19 Vaccine intended for individuals 12 years of age and older should not be used for individuals 6 months through 11 years of age because of the potential for vaccine administration errors, including dosing errors.

FEDERAL COVID-19 VACCINATION PROGRAM

This vaccine is being made available for emergency use exclusively through the CDC COVID-19 Vaccination Program (the Vaccination Program). Healthcare providers must enroll as providers in the Vaccination Program and comply with the provider requirements. Vaccination providers may not charge any fee for the vaccine and may not charge the vaccine recipient any out-of-pocket charge for administration. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, Health Resources & Services Administration [HRSA] COVID-19 Uninsured Program for non-insured recipients). For information regarding provider requirements and enrollment in the CDC COVID-19 Vaccination Program, see https://www.cdc.gov/vaccines/covid-19/provider-enrollment.html.

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or https://TIPS.HHS.GOV.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. In response, FDA has issued an EUA for the unapproved product, Pfizer-BioNTech COVID-19 Vaccine, and for certain uses of FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) for active immunization to prevent COVID-19.

FDA issued this EUA, based on Pfizer-BioNTech's request and submitted data.

For the authorized uses, although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY (COVID-19 Vaccine, mRNA) may be effective for the prevention of COVID-19 in individuals as specified in the *Full EUA Prescribing Information*.

This EUA for the Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY (COVID-19 Vaccine, mRNA) will end when the Secretary of HHS determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

For additional information about Emergency Use Authorization visit FDA at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

The Countermeasures Injury Compensation Program

The Countermeasures Injury Compensation Program (CICP) is a federal program that has been created to help pay for related costs of medical care and other specific expenses to compensate people injured after use of certain medical countermeasures. Medical countermeasures are specific vaccines, medications, devices, or other items used to prevent, diagnose, or treat the public during a public health emergency or a security threat. For more information about CICP regarding the Pfizer-BioNTech COVID-19 Vaccine used to prevent COVID-19, visit www.hrsa.gov/cicp/, email cicp@hrsa.gov, or call: 1-855-266-2427.

BIONTECH

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1450-31.0

Revised: 22 December 2022

END SHORT VERSION FACT SHEET

Long Version (Full EUA Prescribing Information) Begins On Next Page

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[1] Certain kinds of immunocompromise refers to individuals who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

[2] When prepared according to their respective instructions for use, the FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the EUA-authorized Pfizer-BioNTech COVID-19 Vaccine for individuals 12 years of age and older can be used interchangeably without presenting any safety or effectiveness concerns.

[3] Notwithstanding the age limitations for use of the different formulations and presentations described above, individuals who will turn from 11 years to 12 years of age between doses in the primary regimen may receive, for any dose in the primary regimen, either: (1) the Pfizer-BioNTech COVID-19 Vaccine authorized for use in individuals 5 through 11 years of age (each 0.2 mL dose containing 10 mcg modRNA,

supplied in multiple dose vials with orange caps); or (2) COMIRNATY (COVID-19 Vaccine, mRNA) or the Pfizer-BioNTech COVID-19 Vaccine authorized for use in individuals 12 years of age and older (each 0.3 mL dose containing 30 mcg modRNA, supplied in multiple dose vials with gray caps and multiple dose vials with purple caps).

4 Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) must adhere to the same reporting requirements.

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION
PFIZER-BIONTECH COVID-19 VACCINE
FULL EMERGENCY USE AUTHORIZATION PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full emergency use authorization prescribing information are not listed.

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

1 AUTHORIZED USE

Pfizer-BioNTech COVID-19 Vaccine is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 6 months of age and older.

This EUA Prescribing Information pertains only to Pfizer-BioNTech COVID-19 Vaccine supplied in a multiple dose vial with a purple cap, which is authorized for use in individuals 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

For intramuscular injection only.

The storage, preparation, and administration information in this Prescribing Information apply to the Pfizer-BioNTech COVID-19 Vaccine for individuals 12 years of age and older, which is supplied in a multiple dose vial with a purple cap and **MUST BE DILUTED** before use.

Pfizer-BioNTech COVID-19 Vaccine, Multiple Dose Vial with Purple Cap

Age Range	Dilution Information	Doses Per Vial After Dilution	Dose Volume
12 years and older	Dilute with 1.8 mL sterile 0.9% Sodium Chloride Injection, USP prior to use	6	0.3 mL

2.1 Preparation for Administration

Dose Preparation

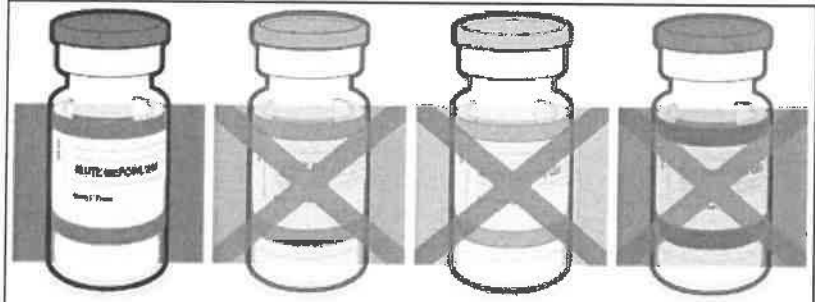
Each vial **MUST BE DILUTED** before administering the vaccine.

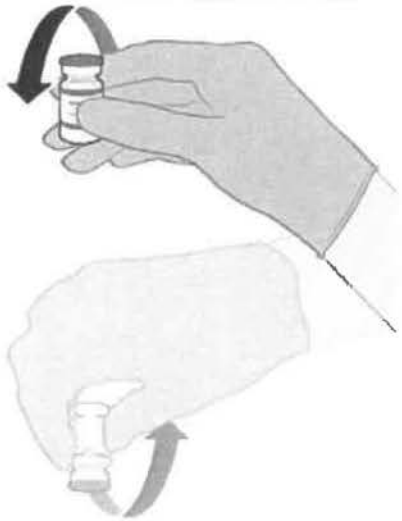
Prior to Dilution

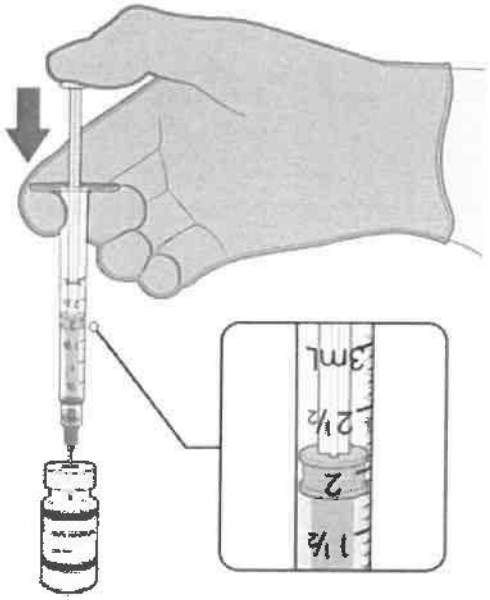
- The Pfizer-BioNTech COVID-19 Vaccine multiple dose vial with a purple cap contains a volume of 0.45 mL and is supplied as a frozen suspension that does not contain preservative.
- Each vial must be thawed before dilution.
- Vials may be thawed in the refrigerator [2°C to 8°C (35°F to 46°F)] or at room temperature [up to 25°C (77°F)] *[see How Supplied/Storage and Handling (19)]*.
- Refer to thawing instructions in the panels below.

Dilution

- Dilute the vial contents using 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP (not provided) to form the Pfizer-BioNTech COVID-19 Vaccine. Do not add more than 1.8 mL of diluent.
- ONLY use sterile 0.9% Sodium Chloride Injection, USP as the diluent. This diluent is not packaged with the vaccine and must be sourced separately. Do not use bacteriostatic 0.9% Sodium Chloride Injection or any other diluent.
- After dilution, 1 vial contains 6 doses of 0.3 mL.

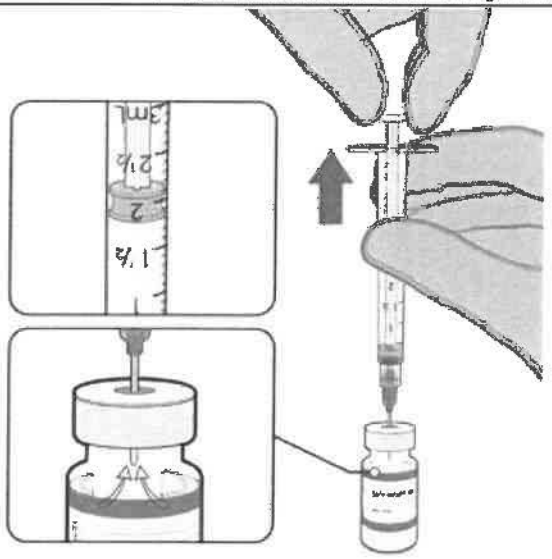
Dilution and Preparation Instructions	
Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – VIAL VERIFICATION	
 **✓ Purple plastic cap and purple label border.**	Verify that the vial of Pfizer-BioNTech COVID-19 Vaccine has a purple plastic cap. Some vials also may have a purple label border on the label.
Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – THAWING PRIOR TO DILUTION	

 **No more than 2 hours at room temperature (up to 25°C/77°F).**	• Thaw vial(s) of Pfizer-BioNTech COVID-19 Vaccine before use either by: o Allowing vial(s) to thaw in the refrigerator [2°C to 8°C (35°F to 46°F)]. A carton of vials may take up to 3 hours to thaw, and thawed vials can be stored in the refrigerator for up to 1 month. o Allowing vial(s) to sit at room temperature [up to 25°C (77°F)] for 30 minutes. • Using either thawing method, vials must reach room temperature before dilution and must be diluted within 2 hours.
 **Gently × 10**	• Before dilution invert vaccine vial gently 10 times. • Do not shake. • Inspect the liquid in the vial prior to dilution. The liquid is a white to off-white suspension and may contain white to off-white opaque amorphous particles. • Do not use if liquid is discolored or if other particles are observed.
Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – DILUTION	



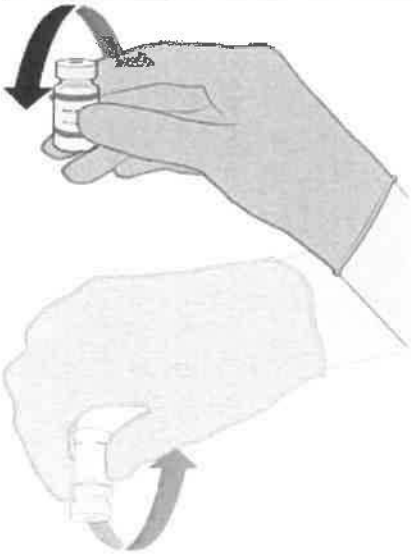
Add 1.8 mL of sterile 0.9% sodium chloride injection, USP.

- Obtain sterile 0.9% Sodium Chloride Injection, USP. Use only this as the diluent.
- Using aseptic technique, withdraw 1.8 mL of diluent into a transfer syringe (21-gauge or narrower needle).
- Cleanse the vaccine vial stopper with a single-use antiseptic swab.
- Add 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP into the vaccine vial.



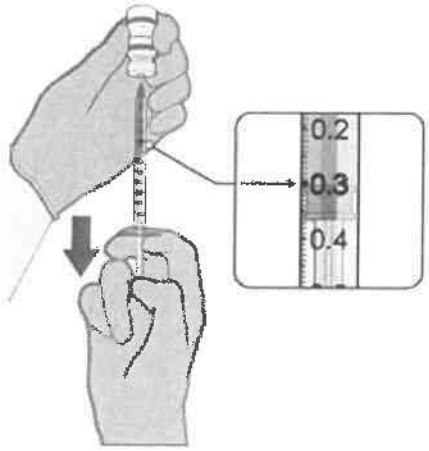
Pull back plunger to 1.8 mL to remove air from vial.

Equalize vial pressure before removing the needle from the vial by withdrawing 1.8 mL air into the empty diluent syringe.



Gently × 10

- Gently invert the vial containing the Pfizer-BioNTech COVID-19 Vaccine 10 times to mix.
- <u>Do not shake</u>.
- Inspect the vaccine in the vial.
- The vaccine will be an off-white suspension. Do not use if vaccine is discolored or contains particulate matter.

 **Record the date and time of dilution.** **Use within 6 hours after dilution.**	• Record the date and time of dilution on the Pfizer-BioNTech COVID-19 Vaccine vial label. • Store between 2°C to 25°C (35°F to 77°F). • Discard any unused vaccine 6 hours after dilution.
Pfizer-BioNTech COVID-19 Vaccine Vial with Purple Cap – WITHDRAWAL OF INDIVIDUAL 0.3 mL DOSES	
 **Withdraw 0.3 mL dose of vaccine.**	• Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab, and withdraw 0.3 mL of the Pfizer-BioNTech COVID-19 Vaccine preferentially using a low dead-volume syringe and/or needle. • Each dose must contain 0.3 mL of vaccine. • If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume. • Administer immediately.

2.2 Administration Information

Visually inspect each dose in the dosing syringe prior to administration. The vaccine will be an off-white suspension. During the visual inspection,

- verify the final dosing volume of 0.3 mL.
- confirm there are no particulates and that no discoloration is observed.
- do not administer if vaccine is discolored or contains particulate matter.

Administer the Pfizer-BioNTech COVID-19 Vaccine intramuscularly.

After dilution, vials of Pfizer-BioNTech COVID-19 Vaccine with purple caps contain 6 doses of 0.3 mL of vaccine. Low dead-volume syringes and/or needles can be used to extract 6 doses from a single vial. If standard syringes and needles are used, there may not be sufficient volume to extract 6 doses from a single vial. Irrespective of the type of syringe and needle:

- Each dose must contain 0.3 mL of vaccine.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.3 mL, discard the vial and any excess volume.
- Do not pool excess vaccine from multiple vials.

2.3 Vaccination Schedule

Primary Series[5]

The Pfizer-BioNTech COVID-19 Vaccine is administered intramuscularly as a primary series of 2 doses (0.3 mL each) 3 weeks apart in individuals 12 years of age and older.

A third primary series dose of the Pfizer-BioNTech COVID-19 Vaccine (0.3 mL) at least 28 days following the second dose is authorized for administration to individuals at least 12 years of age with certain kinds of immunocompromise.[6]

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[5] The FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the EUA-authorized Pfizer-BioNTech COVID-19 Vaccine for individuals 12 years of age and older when prepared according to their respective instructions for use, can be used interchangeably.

[6] Certain kinds of immunocompromise refers to individuals who have undergone solid organ transplantation, or who are diagnosed with conditions that are considered to have an equivalent level of immunocompromise.

3 DOSAGE FORMS AND STRENGTHS

Pfizer-BioNTech COVID-19 Vaccine is a suspension for injection.

After preparation, each dose of the Pfizer-BioNTech COVID-19 Vaccine supplied in vials with purple caps is 0.3 mL for individuals 12 years of age and older *[see Dosage and Administration (2.1)]*.

4 CONTRAINDICATIONS

Do not administer Pfizer-BioNTech COVID-19 Vaccine to individuals with known history of a severe allergic reaction (e.g., anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 Vaccine *[see Description (13)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Management of Acute Allergic Reactions

Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Pfizer-BioNTech COVID-19 Vaccine.

Monitor Pfizer-BioNTech COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention (CDC) guidelines (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html).

5.2 Myocarditis and Pericarditis

Postmarketing data with Pfizer-BioNTech COVID-19 Vaccine demonstrate increased risks of myocarditis and pericarditis, particularly within the period 0 through 7 days following the second dose of the primary series. The observed risk is higher among adolescent males and adult males under 40 years of age than among females and older males. The observed risk is highest in males 12 through 17 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae. The CDC has published considerations related to myocarditis and pericarditis after vaccination, including for vaccination of individuals with a history of myocarditis or pericarditis (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/myocarditis.html).

5.3 Syncope

Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting.

5.4 Altered Immunocompetence

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Pfizer-BioNTech COVID-19 Vaccine.

5.5 Limitation of Effectiveness

The Pfizer-BioNTech COVID-19 Vaccine may not protect all vaccine recipients.

6 OVERALL SAFETY SUMMARY

It is MANDATORY for vaccination providers to report to the Vaccine Adverse Event Reporting System (VAERS) all vaccine administration errors, all serious adverse events, cases of myocarditis, cases of pericarditis, cases of Multisystem Inflammatory Syndrome (MIS) in adults and children, and hospitalized or fatal cases of COVID-19

following vaccination with the Pfizer-BioNTech COVID-19 Vaccine.[7] To the extent feasible, provide a copy of the VAERS form to Pfizer Inc. Please see the REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS section for details on reporting to VAERS and Pfizer Inc.

[7] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) must adhere to the same reporting requirements.

Primary Series

In clinical studies of participants 16 years of age and older who received Pfizer-BioNTech COVID-19 Vaccine containing 30 mcg of a nucleoside-modified messenger RNA encoding the viral spike (S) glycoprotein of SARS-CoV-2 (30 mcg modRNA), adverse reactions following administration of the primary series included pain at the injection site (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%), injection site swelling (10.5%), injection site redness (9.5%), nausea (1.1%), malaise (0.5%), and lymphadenopathy (0.3%).

In a clinical study in adolescents 12 through 15 years of age who received Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA), adverse reactions following administration of the primary series included pain at the injection site (90.5%), fatigue (77.5%), headache (75.5%), chills (49.2%), muscle pain (42.2%), fever (24.3%), joint pain (20.2%), injection site swelling (9.2%), injection site redness (8.6%), lymphadenopathy (0.8%), and nausea (0.4%).

Post Authorization Experience

Severe allergic reactions, including anaphylaxis, have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine.

Myocarditis and pericarditis have been reported following administration of the Pfizer-BioNTech COVID-19 Vaccine.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Primary Series

The safety of the primary series Pfizer-BioNTech COVID-19 Vaccine was evaluated in participants 12 years of age and older in two clinical studies conducted in the United States, Europe, Turkey, South Africa, and South America.

Study BNT162-01 (Study 1) was a Phase 1/2, 2-part, dose-escalation trial that enrolled 60 participants, 18 through 55 years of age. Study C4591001 (Study 2) is a Phase 1/2/3, multicenter, multinational, randomized, saline placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection (Phase 1) and efficacy (Phase 2/3) study that has enrolled approximately 46,000 participants, 12 years of age or older. Of these, approximately 43,448 participants [21,720 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) encoding the viral spike (S) glycoprotein of SARS-CoV-2; 21,728 placebo] in Phase 2/3 are 16 years of age or older (including 138 and 145 adolescents 16 and 17 years of age in the vaccine and placebo groups, respectively) and 2,260 adolescents are 12 through 15 years of age (1,131 and 1,129 in the vaccine and placebo groups, respectively).

In Study 2, all participants 12 through 15 years of age, and 16 years of age and older in the reactogenicity subset, were monitored for solicited local and systemic reactions and use of antipyretic medication after each vaccination in an electronic diary. Participants are being monitored for unsolicited adverse events, including serious adverse events, throughout the study [from Dose 1 through 1 month (all unsolicited adverse events) or 6 months (serious adverse events) after the last vaccination]. Tables 1 through 6 present the frequency and severity of solicited local and systemic reactions, respectively, within 7 days following each dose of Pfizer-BioNTech COVID 19 Vaccine and placebo.

Participants 16 Years of Age and Older

At the time of the analysis of Study 2 for the EUA, 37,586 [18,801 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) and 18,785 placebo] participants 16 years of age or older had been followed for a median of 2 months after the second dose.

The safety evaluation in Study 2 is ongoing. The safety population includes participants 16 years of age and older enrolled by October 9, 2020, and includes safety data accrued through November 14, 2020.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among participants who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Overall, among the total participants who received either the Pfizer-BioNTech COVID-19 Vaccine or placebo, 50.6% were male and 49.4% were female, 83.1% were White, 9.1% were Black or African American, 28.0% were Hispanic/Latino, 4.3% were Asian, and 0.5% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions

Across both age groups, 18 through 55 years of age and 56 years of age and older, the mean duration of pain at the injection site after Dose 2 was 2.5 days (range 1 to 36 days), for redness 2.6 days (range 1 to 34 days), and for swelling 2.3 days (range 1 to 34 days) for participants in the Pfizer-BioNTech COVID-19 Vaccine group.

Solicited reactogenicity data in 16 and 17 year-old participants are limited.

Table 1:Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 18 Through 55 Years of Age* – Reactogenicity Subset of the Safety Population†

	Pfizer-BioNTech COVID-19 Vaccine‡ Dose 1 N§=2291 n¶ (%)	Placebo Dose 1 N§=2298 n¶ (%)	Pfizer-BioNTech COVID-19 Vaccine‡ Dose 2 N§=2098 n¶ (%)	Placebo Dose 2 N§=2103 n¶ (%)
Redness#				
Any (>2 cm)	104 (4.5)	26 (1.1)	123 (5.9)	14 (0.7)
Mild	70 (3.1)	16 (0.7)	73 (3.5)	8 (0.4)
Moderate	28 (1.2)	6 (0.3)	40 (1.9)	6 (0.3)
Severe	6 (0.3)	4 (0.2)	10 (0.5)	0 (0.0)
Swelling#				
Any (>2 cm)	132 (5.8)	11 (0.5)	132 (6.3)	5 (0.2)
Mild	88 (3.8)	3 (0.1)	80 (3.8)	3 (0.1)
Moderate	39 (1.7)	5 (0.2)	45 (2.1)	2 (0.1)
Severe	5 (0.2)	3 (0.1)	7 (0.3)	0 (0.0)
Pain at the injection siteÞ				
Any	1904 (83.1)	322 (14.0)	1632 (77.8)	245 (11.7)
Mild	1170 (51.1)	308 (13.4)	1039 (49.5)	225 (10.7)
Moderate	710 (31.0)	12 (0.5)	568 (27.1)	20 (1.0)
Severe	24 (1.0)	2 (0.1)	25 (1.2)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.

* Eight participants were between 16 and 17 years of age.

† Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

‡ Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

§ N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

¶ n = Number of participants with the specified reaction.

Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

Þ Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 2: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 18 Through 55 Years of Age* – Reactogenicity Subset of the Safety Population†

	Pfizer-BioNTech COVID-19 Vaccine‡ Dose 1 N§=2291 n¶ (%)	Placebo Dose 1 N§=2298 n¶ (%)	Pfizer-BioNTech COVID-19 Vaccine‡ Dose 2 N§=2098 n¶ (%)	Placebo Dose 2 N§=2103 n¶ (%)

	Pfizer-BioNTech COVID-19 Vaccine‡ Dose 1 N§=2291 n¶ (%)	Placebo Dose 1 N§=2298 n¶ (%)	Pfizer-BioNTech COVID-19 Vaccine‡ Dose 2 N§=2098 n¶ (%)	Placebo Dose 2 N§=2103 n¶ (%)
Fever				
≥38.0°C	85 (3.7)	20 (0.9)	331 (15.8)	10 (0.5)
≥38.0°C to 38.4°C	64 (2.8)	10 (0.4)	194 (9.2)	5 (0.2)
>38.4°C to 38.9°C	15 (0.7)	5 (0.2)	110 (5.2)	3 (0.1)
>38.9°C to 40.0°C	6 (0.3)	3 (0.1)	26 (1.2)	2 (0.1)
>40.0°C	0 (0.0)	2 (0.1)	1 (0.0)	0 (0.0)
Fatigue#				
Any	1085 (47.4)	767 (33.4)	1247 (59.4)	479 (22.8)
Mild	597 (26.1)	467 (20.3)	442 (21.1)	248 (11.8)
Moderate	455 (19.9)	289 (12.6)	708 (33.7)	217 (10.3)
Severe	33 (1.4)	11 (0.5)	97 (4.6)	14 (0.7)
Headache#				
Any	959 (41.9)	775 (33.7)	1085 (51.7)	506 (24.1)
Mild	628 (27.4)	505 (22.0)	538 (25.6)	321 (15.3)
Moderate	308 (13.4)	251 (10.9)	480 (22.9)	170 (8.1)
Severe	23 (1.0)	19 (0.8)	67 (3.2)	15 (0.7)
Chills#				
Any	321 (14.0)	146 (6.4)	737 (35.1)	79 (3.8)
Mild	230 (10.0)	111 (4.8)	359 (17.1)	65 (3.1)
Moderate	82 (3.6)	33 (1.4)	333 (15.9)	14 (0.7)
Severe	9 (0.4)	2 (0.1)	45 (2.1)	0 (0.0)
Vomiting Þ				
Any	28 (1.2)	28 (1.2)	40 (1.9)	25 (1.2)
Mild	24 (1.0)	22 (1.0)	28 (1.3)	16 (0.8)
Moderate	4 (0.2)	5 (0.2)	8 (0.4)	9 (0.4)
Severe	0 (0.0)	1 (0.0)	4 (0.2)	0 (0.0)
Diarrhea ß				
Any	255 (11.1)	270 (11.7)	219 (10.4)	177 (8.4)
Mild	206 (9.0)	217 (9.4)	179 (8.5)	144 (6.8)
Moderate	46 (2.0)	52 (2.3)	36 (1.7)	32 (1.5)
Severe	3 (0.1)	1 (0.0)	4 (0.2)	1 (0.0)
New or worsened muscle pain#				
Any	487 (21.3)	249 (10.8)	783 (37.3)	173 (8.2)
Mild	256 (11.2)	175 (7.6)	326 (15.5)	111 (5.3)
Moderate	218 (9.5)	72 (3.1)	410 (19.5)	59 (2.8)
Severe	13 (0.6)	2 (0.1)	47 (2.2)	3 (0.1)
New or worsened joint pain#				
Any	251 (11.0)	138 (6.0)	459 (21.9)	109 (5.2)
Mild	147 (6.4)	95 (4.1)	205 (9.8)	54 (2.6)
Moderate	99 (4.3)	43 (1.9)	234 (11.2)	51 (2.4)
Severe	5 (0.2)	0 (0.0)	20 (1.0)	4 (0.2)
Use of antipyretic or pain medication à	638 (27.8)	332 (14.4)	945 (45.0)	266 (12.6)

	Pfizer-BioNTech COVID-19 Vaccine‡ Dose 1 N§=2291 n¶ (%)	Placebo Dose 1 N§=2298 n¶ (%)	Pfizer-BioNTech COVID-19 Vaccine‡ Dose 2 N§=2098 n¶ (%)	Placebo Dose 2 N§=2103 n¶ (%)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

* Eight participants were between 16 and 17 years of age.

† Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

‡ Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

§ N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.

¶ n = Number of participants with the specified reaction.

Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

Þ Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

ß Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

à Severity was not collected for use of antipyretic or pain medication.

Table 3: Study 2 – Frequency and Percentages of Participants with Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N‡=1802 n§ (%)	Placebo Dose 1 N‡=1792 n§ (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N‡=1660 n§ (%)	Placebo Dose 2 N‡=1646 n§ (%)
Redness¶				
Any (>2 cm)	85 (4.7)	19 (1.1)	120 (7.2)	12 (0.7)
Mild	55 (3.1)	12 (0.7)	59 (3.6)	8 (0.5)
Moderate	27 (1.5)	5 (0.3)	53 (3.2)	3 (0.2)
Severe	3 (0.2)	2 (0.1)	8 (0.5)	1 (0.1)
Swelling¶				
Any (>2 cm)	118 (6.5)	21 (1.2)	124 (7.5)	11 (0.7)
Mild	71 (3.9)	10 (0.6)	68 (4.1)	5 (0.3)
Moderate	45 (2.5)	11 (0.6)	53 (3.2)	5 (0.3)
Severe	2 (0.1)	0 (0.0)	3 (0.2)	1 (0.1)
Pain at the injection site#				
Any (>2 cm)	1282 (71.1)	166 (9.3)	1098 (66.1)	127 (7.7)
Mild	1008 (55.9)	160 (8.9)	792 (47.7)	125 (7.6)
Moderate	270 (15.0)	6 (0.3)	298 (18.0)	2 (0.1)
Severe	4 (0.2)	0 (0.0)	8 (0.5)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

§ n = Number of participants with the specified reaction.

¶ Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 4: Study 2 – Frequency and Percentages of Participants with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Participants 56 Years of Age and Older – Reactogenicity Subset of the Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N‡=1802 n§ (%)	Placebo Dose 1 N‡=1792 n§ (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N‡=1660 n§ (%)	Placebo Dose 2 N‡=1646 n§ (%)
Fever				
≥38.0°C	26 (1.4)	7 (0.4)	181 (10.9)	4 (0.2)
≥38.0°C to 38.4°C	23 (1.3)	2 (0.1)	131 (7.9)	2 (0.1)
>38.4°C to 38.9°C	1 (0.1)	3 (0.2)	45 (2.7)	1 (0.1)
>38.9°C to 40.0°C	1 (0.1)	2 (0.1)	5 (0.3)	1 (0.1)
>40.0°C	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue¶				
Any	615 (34.1)	405 (22.6)	839 (50.5)	277 (16.8)
Mild	373 (20.7)	252 (14.1)	351 (21.1)	161 (9.8)
Moderate	240 (13.3)	150 (8.4)	442 (26.6)	114 (6.9)
Severe	2 (0.1)	3 (0.2)	46 (2.8)	2 (0.1)
Headache¶				
Any	454 (25.2)	325 (18.1)	647 (39.0)	229 (13.9)
Mild	348 (19.3)	242 (13.5)	422 (25.4)	165 (10.0)
Moderate	104 (5.8)	80 (4.5)	216 (13.0)	60 (3.6)
Severe	2 (0.1)	3 (0.2)	9 (0.5)	4 (0.2)
Chills¶				
Any	113 (6.3)	57 (3.2)	377 (22.7)	46 (2.8)
Mild	87 (4.8)	40 (2.2)	199 (12.0)	35 (2.1)
Moderate	26 (1.4)	16 (0.9)	161 (9.7)	11 (0.7)
Severe	0 (0.0)	1 (0.1)	17 (1.0)	0 (0.0)
Vomiting#				
Any	9 (0.5)	9 (0.5)	11 (0.7)	5 (0.3)
Mild	8 (0.4)	9 (0.5)	9 (0.5)	5 (0.3)
Moderate	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)
Diarrhea♭				
Any	147 (8.2)	118 (6.6)	137 (8.3)	99 (6.0)
Mild	118 (6.5)	100 (5.6)	114 (6.9)	73 (4.4)
Moderate	26 (1.4)	17 (0.9)	21 (1.3)	22 (1.3)
Severe	3 (0.2)	1 (0.1)	2 (0.1)	4 (0.2)
New or worsened muscle pain¶				
Any	251 (13.9)	149 (8.3)	477 (28.7)	87 (5.3)
Mild	168 (9.3)	100 (5.6)	202 (12.2)	57 (3.5)
Moderate	82 (4.6)	46 (2.6)	259 (15.6)	29 (1.8)
Severe	1 (0.1)	3 (0.2)	16 (1.0)	1 (0.1)
New or worsened joint pain¶				

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.

§ n = Number of participants with the specified reaction.

¶ Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

♭ Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N‡=1802 n§ (%)	Placebo Dose 1 N‡=1792 n§ (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N‡=1660 n§ (%)	Placebo Dose 2 N‡=1646 n§ (%)
Any	155 (8.6)	109 (6.1)	313 (18.9)	61 (3.7)
Mild	101 (5.6)	68 (3.8)	161 (9.7)	35 (2.1)
Moderate	52 (2.9)	40 (2.2)	145 (8.7)	25 (1.5)
Severe	2 (0.1)	1 (0.1)	7 (0.4)	1 (0.1)
Use of antipyretic or pain medication	358 (19.9)	213 (11.9)	625 (37.7)	161 (9.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.

§ n = Number of participants with the specified reaction.

¶ Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

Þ Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, in 99 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously who received a third vaccine dose, the adverse event profile was similar to that after the second dose and no grade 3 or grade 4 events were reported in recipients who were followed for 1 month following post Dose 3.

Unsolicited Adverse Events

Serious Adverse Events

In Study 2, among participants 16 through 55 years of age who had received at least 1 dose of vaccine or placebo (Pfizer-BioNTech COVID-19 Vaccine = 10,841; placebo = 10,851), serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 0.4% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.3% of placebo recipients. In a similar analysis, in participants 56 years of age and older (Pfizer-BioNTech COVID-19 Vaccine = 7,960, placebo = 7,934), serious adverse events were reported by 0.8% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.6% of placebo recipients who received at least 1 dose of Pfizer-BioNTech COVID-19 Vaccine or placebo, respectively. In these analyses, 91.6% of study participants had at least 30 days of follow-up after Dose 2.

Appendicitis was reported as a serious adverse event for 12 participants, and numerically higher in the vaccine group, 8 vaccine participants and 4 placebo participants. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of serious adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Non-Serious Adverse Events

In Study 2 in which 10,841 participants 16 through 55 years of age received Pfizer-BioNTech COVID-19 Vaccine and 10,851 participants received placebo, non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported in 29.3% of participants who received Pfizer-BioNTech COVID-19 Vaccine and 13.2% of participants in the placebo group, for participants who received at least 1 dose. Overall in a similar analysis in which 7960 participants 56 years of age and older received Pfizer-BioNTech COVID-19 Vaccine, non-serious adverse events within 30 days were reported in 23.8% of participants who received Pfizer-BioNTech COVID-19 Vaccine and 11.7% of participants in the placebo group, for participants who received at least 1 dose. In these analyses, 91.6% of study participants had at least 30 days of follow-up after Dose 2.

The higher frequency of reported unsolicited non-serious adverse events among Pfizer-BioNTech COVID-19 Vaccine recipients compared to placebo recipients was primarily attributed to local and systemic adverse events reported during the first 7 days following vaccination that are consistent with adverse reactions solicited among participants in the reactogenicity

subset and presented in Tables 3 and 4. From Dose 1 through 30 days after Dose 2, reports of lymphadenopathy were imbalanced with notably more cases in the Pfizer-BioNTech COVID-19 Vaccine group (64) vs. the placebo group (6), which is plausibly related to vaccination. Throughout the safety follow-up period to date, Bell's palsy (facial paralysis) was reported by 4 participants in the Pfizer-BioNTech COVID-19 Vaccine group. Onset of facial paralysis was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of Bell's palsy were reported in the placebo group. Currently available information is insufficient to determine a causal relationship with the vaccine. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including other neurologic or neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Adolescents 12 Through 15 Years of Age

In an analysis of Study 2, based on data up to the cutoff date of March 13, 2021, 2,260 adolescents (1,131 Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA); 1,129 placebo) were 12 through 15 years of age. Of these, 1,308 (660 Pfizer-BioNTech COVID-19 Vaccine and 648 placebo) adolescents have been followed for at least 2 months after the second dose. The safety evaluation in Study 2 is ongoing.

Demographic characteristics in Study 2 were generally similar with regard to age, gender, race, and ethnicity among adolescents who received Pfizer-BioNTech COVID-19 Vaccine and those who received placebo. Overall, among the adolescents who received the Pfizer-BioNTech COVID-19 Vaccine, 50.1% were male and 49.9% were female, 85.9% were White, 4.6% were Black or African American, 11.7% were Hispanic/Latino, 6.4% were Asian, and 0.4% were American Indian/Alaska Native.

Solicited Local and Systemic Adverse Reactions

The mean duration of pain at the injection site after Dose 1 was 2.4 days (range 1 to 10 days), for redness 2.4 days (range 1 to 16 days), and for swelling 1.9 days (range 1 to 5 days) for adolescents in the Pfizer-BioNTech COVID-19 Vaccine group.

Table 5: Study 2 – Frequency and Percentages of Adolescents With Solicited Local Reactions, by Maximum Severity, Within 7 Days After Each Dose – Adolescents 12 Through 15 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N‡=1127 n§ (%)	Placebo Dose 1 N‡=1127 n§ (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N‡=1097 n§ (%)	Placebo Dose 2 N‡=1078 n§ (%)
Redness¶				
Any (>2 cm)	65 (5.8)	12 (1.1)	55 (5.0)	10 (0.9)
Mild	44 (3.9)	11 (1.0)	29 (2.6)	8 (0.7)
Moderate	20 (1.8)	1 (0.1)	26 (2.4)	2 (0.2)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Swelling¶				
Any (>2 cm)	78 (6.9)	11 (1.0)	54 (4.9)	6 (0.6)
Mild	55 (4.9)	9 (0.8)	36 (3.3)	4 (0.4)
Moderate	23 (2.0)	2 (0.2)	18 (1.6)	2 (0.2)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pain at the injection site#				
Any	971 (86.2)	263 (23.3)	866 (78.9)	193 (17.9)
Mild	467 (41.4)	227 (20.1)	466 (42.5)	164 (15.2)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

§ n = Number of participants with the specified reaction.

¶ Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N‡=1127 n§ (%)	Placebo Dose 1 N‡=1127 n§ (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N‡=1097 n§ (%)	Placebo Dose 2 N‡=1078 n§ (%)
Moderate	493 (43.7)	36 (3.2)	393 (35.8)	29 (2.7)
Severe	11 (1.0)	0 (0.0)	7 (0.6)	0 (0.0)

Note: Reactions were collected in the electronic diary (e-diary) from Day 1 to Day 7 after vaccination.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ N = Number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

§ n = Number of participants with the specified reaction.

¶ Mild: >2.0 to ≤5.0 cm; Moderate: >5.0 to ≤10.0 cm; Severe: >10.0 cm.

Mild: does not interfere with activity; Moderate: interferes with activity; Severe: prevents daily activity.

Table 6: Study 2 – Frequency and Percentages of Adolescents with Solicited Systemic Reactions, by Maximum Severity, Within 7 Days After Each Dose – Adolescents 12 Through 15 Years of Age – Safety Population*

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N‡=1127 n§ (%)	Placebo Dose 1 N‡=1127 n§ (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N‡=1097 n§ (%)	Placebo Dose 2 N‡=1078 n§ (%)
Fever				
≥38.0°C	114 (10.1)	12 (1.1)	215 (19.6)	7 (0.6)
≥38.0°C to 38.4°C	74 (6.6)	8 (0.7)	107 (9.8)	5 (0.5)
>38.4°C to 38.9°C	29 (2.6)	2 (0.2)	83 (7.6)	1 (0.1)
>38.9°C to 40.0°C	10 (0.9)	2 (0.2)	25 (2.3)	1 (0.1)
>40.0°C	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue¶				
Any	677 (60.1)	457 (40.6)	726 (66.2)	264 (24.5)
Mild	278 (24.7)	250 (22.2)	232 (21.1)	133 (12.3)
Moderate	384 (34.1)	199 (17.7)	468 (42.7)	127 (11.8)
Severe	15 (1.3)	8 (0.7)	26 (2.4)	4 (0.4)
Headache¶				
Any	623 (55.3)	396 (35.1)	708 (64.5)	263 (24.4)
Mild	361 (32.0)	256 (22.7)	302 (27.5)	169 (15.7)
Moderate	251 (22.3)	131 (11.6)	384 (35.0)	93 (8.6)
Severe	11 (1.0)	9 (0.8)	22 (2.0)	1 (0.1)
Chills¶				
Any	311 (27.6)	109 (9.7)	455 (41.5)	73 (6.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.

§ n = Number of participants with the specified reaction.

¶ Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

Þ Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

ß Severity was not collected for use of antipyretic or pain medication.

	Pfizer-BioNTech COVID-19 Vaccine† Dose 1 N‡=1127 n§ (%)	Placebo Dose 1 N‡=1127 n§ (%)	Pfizer-BioNTech COVID-19 Vaccine† Dose 2 N‡=1097 n§ (%)	Placebo Dose 2 N‡=1078 n§ (%)
Mild	195 (17.3)	82 (7.3)	221 (20.1)	52 (4.8)
Moderate	111 (9.8)	25 (2.2)	214 (19.5)	21 (1.9)
Severe	5 (0.4)	2 (0.2)	20 (1.8)	0 (0.0)
Vomiting#				
Any	31 (2.8)	10 (0.9)	29 (2.6)	12 (1.1)
Mild	30 (2.7)	8 (0.7)	25 (2.3)	11 (1.0)
Moderate	0 (0.0)	2 (0.2)	4 (0.4)	1 (0.1)
Severe	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhea Þ				
Any	90 (8.0)	82 (7.3)	65 (5.9)	43 (4.0)
Mild	77 (6.8)	72 (6.4)	59 (5.4)	38 (3.5)
Moderate	13 (1.2)	10 (0.9)	6 (0.5)	5 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
New or worsened muscle pain¶				
Any	272 (24.1)	148 (13.1)	355 (32.4)	90 (8.3)
Mild	125 (11.1)	88 (7.8)	152 (13.9)	51 (4.7)
Moderate	145 (12.9)	60 (5.3)	197 (18.0)	37 (3.4)
Severe	2 (0.2)	0 (0.0)	6 (0.5)	2 (0.2)
New or worsened joint pain¶				
Any	109 (9.7)	77 (6.8)	173 (15.8)	51 (4.7)
Mild	66 (5.9)	50 (4.4)	91 (8.3)	30 (2.8)
Moderate	42 (3.7)	27 (2.4)	78 (7.1)	21 (1.9)
Severe	1 (0.1)	0 (0.0)	4 (0.4)	0 (0.0)
Use of antipyretic or pain medication ß	413 (36.6)	111 (9.8)	557 (50.8)	95 (8.8)

Note: Events and use of antipyretic or pain medication were collected in the electronic diary (e-diary) from Day 1 to Day 7 after each dose.

* Randomized participants in the safety analysis population who received at least 1 dose of the study intervention.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ N = Number of participants reporting at least 1 yes or no response for the specified event after the specified dose.

§ n = Number of participants with the specified reaction.

¶ Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily activity.

Mild: 1 to 2 times in 24 hours; Moderate: >2 times in 24 hours; Severe: requires intravenous hydration.

Þ Mild: 2 to 3 loose stools in 24 hours; Moderate: 4 to 5 loose stools in 24 hours; Severe: 6 or more loose stools in 24 hours.

ß Severity was not collected for use of antipyretic or pain medication.

Unsolicited Adverse Events

In the following analyses of Study 2 in adolescents 12 through 15 years of age (1,131 of whom received Pfizer-BioNTech COVID-19 Vaccine and 1,129 of whom received placebo), 98.3% of study participants had at least 30 days of follow-up after Dose 2.

Serious Adverse Events

Serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 0.4% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 0.1% of placebo recipients. There were no notable patterns or numerical imbalances between treatment groups for specific categories of serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

Non-Serious Adverse Events

Non-serious adverse events from Dose 1 through up to 30 days after Dose 2 in ongoing follow-up were reported by 5.8% of Pfizer-BioNTech COVID-19 Vaccine recipients and by 5.8% of placebo recipients. From Dose 1 through 30 days after Dose 2, reports of lymphadenopathy plausibly related to the study intervention were imbalanced, with notably more cases in the Pfizer-BioNTech COVID-19 Vaccine group (7) vs. the placebo group (1). There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events that would suggest a causal relationship to Pfizer-BioNTech COVID-19 Vaccine.

6.2 Post Authorization Experience

The following adverse reactions have been identified during post authorization use of Pfizer-BioNTech COVID-19 Vaccine. Because these reactions are reported voluntarily, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccine exposure.

Cardiac Disorders: myocarditis, pericarditis

Gastrointestinal Disorders: diarrhea, vomiting

Immune System Disorders: severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions (e.g., rash, pruritus, urticaria, angioedema)

Musculoskeletal and Connective Tissue Disorders: pain in extremity (arm)

Nervous System Disorders: syncope, dizziness

8 REQUIREMENTS AND INSTRUCTIONS FOR REPORTING ADVERSE EVENTS AND VACCINE ADMINISTRATION ERRORS[8]

See Overall Safety Summary (Section 6) for additional information.

The vaccination provider enrolled in the federal COVID-19 Vaccination Program is responsible for MANDATORY reporting of the listed events following Pfizer-BioNTech COVID-19 Vaccine to the Vaccine Adverse Event Reporting System (VAERS):

- Vaccine administration errors whether or not associated with an adverse event
- Serious adverse events* (irrespective of attribution to vaccination)
- Cases of myocarditis
- Cases of pericarditis
- Cases of Multisystem Inflammatory Syndrome (MIS) in children and adults
- Cases of COVID-19 that result in hospitalization or death

*Serious adverse events are defined as:

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect
- An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent 1 of the outcomes listed above

Instructions for Reporting to VAERS

The vaccination provider enrolled in the federal COVID-19 Vaccination Program should complete and submit a VAERS form to FDA using 1 of the following methods:

- Complete and submit the report online: https://vaers.hhs.gov/reportevent.html, or
- If you are unable to submit this form electronically, you may fax it to VAERS at 1-877-721-0366. If you need additional help submitting a report you may call the VAERS toll-free information line at 1-800-822-7967 or send an email to info@vaers.org.

IMPORTANT: When reporting adverse events or vaccine administration errors to VAERS, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as

possible. Information to include:

- Patient demographics (e.g., patient name, date of birth)
- Pertinent medical history
- Pertinent details regarding admission and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of the Pfizer-BioNTech COVID-19 Vaccine
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the VAERS report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

1. In Box 17, provide information on Pfizer-BioNTech COVID-19 Vaccine and any other vaccines administered on the same day; and in Box 22, provide information on any other vaccines received within 1 month prior.
2. In Box 18, description of the event:

    a. Write "Pfizer-BioNTech COVID-19 Vaccine EUA" as the first line.
    b. Provide a detailed report of vaccine administration error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved vaccine. Please see information to include listed above.

3. Contact information:

    a. In Box 13, provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
    b. In Box 14, provide the name and contact information of the best doctor/healthcare professional to contact about the adverse event.
    c. In Box 15, provide the address of the facility where vaccine was given (NOT the healthcare provider's office address).

Other Reporting Instructions

Vaccination providers may report to VAERS other adverse events that are not required to be reported using the contact information above.

To the extent feasible, report adverse events to Pfizer Inc. using the contact information below or by providing a copy of the VAERS form to Pfizer Inc.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

[8] Vaccination providers administering COMIRNATY (COVID-19 Vaccine, mRNA) must adhere to the same reporting requirements.

10 DRUG INTERACTIONS

There are no data to assess the concomitant administration of the Pfizer-BioNTech COVID-19 Vaccine with other vaccines.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%,

respectively. Available data on Pfizer-BioNTech COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.

In a reproductive and developmental toxicity study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified messenger ribonucleic acid (modRNA) (30 mcg) and other ingredients included in a single human dose of Pfizer-BioNTech COVID-19 Vaccine was administered to female rats by the intramuscular route on 4 occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

11.2 Lactation

Risk Summary

Data are not available to assess the effects of Pfizer-BioNTech COVID-19 Vaccine on the breastfed infant or on milk production/excretion.

11.3 Pediatric Use

Pfizer-BioNTech COVID-19 Vaccine is authorized for use in individuals 6 months through 17 years of age. This authorization is based on safety and effectiveness data in this age group and adults.

Pfizer-BioNTech COVID-19 Vaccine is not authorized for use in individuals younger than 6 months of age.

11.4 Geriatric Use

Clinical studies of Pfizer-BioNTech COVID-19 Vaccine include participants 65 years of age and older who received the primary series and their data contributes to the overall assessment of safety and efficacy *[see Overall Safety Summary (6.1) and Clinical Trial Results and Supporting Data for EUA (18.1)]*. Of the total number of Pfizer-BioNTech COVID-19 Vaccine recipients in Study 2 (N=20,033), 21.4% (n=4,294) were 65 years of age and older and 4.3% (n=860) were 75 years of age and older.

11.5 Use in Immunocompromised

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, safety and effectiveness of a third dose of the Pfizer-BioNTech COVID-19 vaccine have been evaluated in persons that received solid organ transplants. The administration of a third dose of vaccine appears to be only moderately effective in increasing potentially protective antibody titers. Patients should still be counselled to maintain physical precautions to help prevent COVID-19. In addition, close contacts of immunocompromised persons should be vaccinated as appropriate for their health status.

13 DESCRIPTION

The Pfizer-BioNTech COVID-19 Vaccine is supplied as a frozen suspension in multiple dose vials with purple caps; each vial must be diluted with 1.8 mL of sterile 0.9% Sodium Chloride Injection, USP prior to use to form the vaccine. Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with purple caps contains 30 mcg of a nucleoside-modified messenger RNA (modRNA) encoding the viral spike (S) glycoprotein of the SARS-CoV-2 Wuhan-Hu-1 strain.

Each 0.3 mL dose of the Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with purple caps also includes the following ingredients: lipids (0.43 mg ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 0.05 mg 2[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 0.09 mg 1,2-distearoyl-sn-glycero-3-phosphocholine, and 0.2 mg cholesterol), 0.01 mg potassium chloride, 0.01 mg monobasic potassium phosphate, 0.36 mg sodium chloride, 0.07 mg dibasic sodium phosphate dihydrate, and 6 mg sucrose. The diluent (sterile 0.9% Sodium Chloride Injection, USP) contributes an additional 2.16 mg sodium chloride per dose.

The Pfizer-BioNTech COVID-19 Vaccine does not contain preservative. The vial stoppers are not made with natural rubber latex.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

The modRNA in the Pfizer-BioNTech COVID-19 Vaccine is formulated in lipid particles, which enable delivery of the RNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen,

which protects against COVID-19.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Efficacy of Primary Series in Participants 16 Years of Age and Older

Study 2 is a multicenter, multinational, Phase 1/2/3, randomized, placebo-controlled, observer-blind, dose-finding, vaccine candidate-selection, and efficacy study in participants 12 years of age and older. Randomization was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV).

In the Phase 2/3 portion of Study 2, based on data accrued through November 14, 2020, approximately 44,000 participants 12 years of age and older were randomized equally and received 2 doses of Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA) or placebo separated by 21 days. Participants are planned to be followed for up to 24 months, for assessments of safety and efficacy against COVID-19.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the Pfizer-BioNTech COVID-19 Vaccine group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. Table 7 presents the specific demographic characteristics in the studied population.

Table 7: Demographics (population for the primary efficacy endpoint)*

	Pfizer-BioNTech COVID-19 Vaccine† (N=18,242) n (%)	**Placebo (N=18,379) n (%)**
Sex		
Male	9318 (51.1)	9225 (50.2)
Female	8924 (48.9)	9154 (49.8)
Age (years)		
Mean (SD)	50.6 (15.70)	50.4 (15.81)
Median	52.0	52.0
Min, max	(12, 89)	(12, 91)
Age group		
≥12 through 15 years‡	46 (0.3)	42 (0.2)
≥16 through 17 years	66 (0.4)	68 (0.4)
≥16 through 64 years	14,216 (77.9)	14,299 (77.8)
≥65 through 74 years	3176 (17.4)	3226 (17.6)
≥75 years	804 (4.4)	812 (4.4)
Race		
White	15,110 (82.8)	15,301 (83.3)
Black or African American	1617 (8.9)	1617 (8.8)
American Indian or Alaska Native	118 (0.6)	106 (0.6)
Asian	815 (4.5)	810 (4.4)
Native Hawaiian or other Pacific Islander	48 (0.3)	29 (0.2)
Other§	534 (2.9)	516 (2.8)
Ethnicity		
Hispanic or Latino	4886 (26.8)	4857 (26.4)
Not Hispanic or Latino	13,253 (72.7)	13,412 (73.0)

Not reported	103 (0.6)	110 (0.6)
Comorbidities¶		
Yes	8432 (46.2)	8450 (46.0)
No	9810 (53.8)	9929 (54.0)

* All eligible randomized participants who receive all vaccination(s) as randomized within the predefined window, have no other important protocol deviations as determined by the clinician, and have no evidence of SARS-CoV-2 infection prior to 7 days after Dose 2.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ 100 participants 12 through 15 years of age with limited follow-up in the randomized population received at least 1 dose (49 in the vaccine group and 51 in the placebo group). Some of these participants were included in the efficacy evaluation depending on the population analyzed. They contributed to exposure information but with no confirmed COVID-19 cases, and did not affect efficacy conclusions.

§ Includes multiracial and not reported.

¶ Number of participants who have 1 or more comorbidities that increase the risk of severe COVID-19 disease
- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (e.g., heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and pulmonary hypertension)
- Obesity (body mass index ≥30 kg/m^2)
- Diabetes (Type 1, Type 2 or gestational)
- Liver disease

Human Immunodeficiency Virus (HIV) infection (not included in the efficacy evaluation)

The population in the primary efficacy analysis included all participants 12 years of age and older who had been enrolled from July 27, 2020, and followed for the development of COVID-19 through November 14, 2020. Participants 18 through 55 years of age and 56 years of age and older began enrollment from July 27, 2020, 16 through 17 years of age began enrollment from September 16, 2020, and 12 through 15 years of age began enrollment from October 15, 2020.

The vaccine efficacy information is presented in Table 8.

Table 8: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Age Subgroup – Participants Without Evidence of Infection and Participants With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	**Pfizer-BioNTech COVID-19 Vaccine† N‡=18,198 Cases n1§ Surveillance Time¶ (n2#)**	**Placebo N‡=18,325 Cases n1§ Surveillance Time¶ (n2#)**	**Vaccine Efficacy % (95% CI)**
All subjects[Þ]	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.3, 97.6)[ß]
16 through 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)[à]
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)[à]
First COVID-19 occurrence from 7 days after Dose 2 in participants with or without evidence of prior SARS-CoV-2 infection			
Subgroup	**Pfizer-BioNTech COVID-19 Vaccine† N‡=19,965 Cases n1§ Surveillance Time¶ (n2#)**	**Placebo N‡=20,172 Cases n1§ Surveillance Time¶ (n2#)**	**Vaccine Efficacy % (95% CI)**

All subjects[Þ]	9 2.332 (18,559)	169 2.345 (18,708)	94.6 (89.9, 97.3)[ß]
16 through 64 years	8 1.802 (14,501)	150 1.814 (14,627)	94.6 (89.1, 97.7)[à]
65 years and older	1 0.530 (4044)	19 0.532 (4067)	94.7 (66.8, 99.9)[à]

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ N = Number of participants in the specified group.

§ n1 = Number of participants meeting the endpoint definition.

¶ Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

n2 = Number of participants at risk for the endpoint.

Þ No confirmed cases were identified in adolescents 12 through 15 years of age.

ß Credible interval for vaccine efficacy (VE) was calculated using a beta-binomial model with a beta (0.700102, 1) prior for $\theta=r(1-VE)/(1+r(1-VE))$, where r is the ratio of surveillance time in the active vaccine group over that in the placebo group.

à Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time.

18.2 Efficacy of Primary Series in Adolescents 12 Through 15 Years of Age

A descriptive efficacy analysis of Study 2 has been performed in approximately 2,200 adolescents 12 through 15 years of age evaluating confirmed COVID-19 cases accrued up to a data cutoff date of March 13, 2021.

The efficacy information in adolescents 12 through 15 years of age is presented in Table 9.

Table 9: Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2: Without Evidence of Infection and With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period, Adolescents 12 Through 15 Years of Age Evaluable Efficacy (7 Days) Population

First COVID-19 occurrence from 7 days after Dose 2 in adolescents 12 through 15 years of age without evidence of prior SARS-CoV-2 infection*			
	Pfizer-BioNTech COVID-19 Vaccine† N‡=1005 Cases n1§ Surveillance Time¶ (n2#)	**Placebo N‡=978 Cases n1§ Surveillance Time¶ (n2#)**	**Vaccine Efficacy % (95% CI)Þ**
Adolescents 12 through 15 years of age	0 0.154 (1001)	16 0.147 (972)	100.0 (75.3, 100.0)
First COVID-19 occurrence from 7 days after Dose 2 in adolescents 12 through 15 years of age with or without evidence of prior SARS-CoV-2 infection			
	Pfizer-BioNTech COVID-19 Vaccine† N‡=1119 Cases	**Placebo N‡=1110 Cases n1§ Surveillance Time¶ (n2#)**	**Vaccine Efficacy % (95% CI)Þ**

	n1[§] Surveillance Time[¶] (n2[#])		
Adolescents 12 through 15 years of age	0 0.170 (1109)	18 0.163 (1094)	100.0 (78.1, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 (symptoms included: fever; new or increased cough; new or increased shortness of breath; chills; new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea; vomiting).

* Participants who had no evidence of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

† Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

‡ N = Number of participants in the specified group.

§ n1 = Number of participants meeting the endpoint definition.

¶ Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

n2 = Number of participants at risk for the endpoint.

Þ Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time.

18.3 Immunogenicity of Primary Series in Adolescents 12 Through 15 Years of Age

In Study 2, an analysis of SARS-CoV-2 50% neutralizing titers (NT50) 1 month after Dose 2 in a randomly selected subset of participants demonstrated non-inferior immune responses (within 1.5-fold) comparing adolescents 12 through 15 years of age to participants 16 through 25 years of age who had no serological or virological evidence of past SARS-CoV-2 infection up to 1 month after Dose 2 (Table 10).

Table 10: Summary of Geometric Mean Ratio for 50% Neutralizing Titer – Comparison of Adolescents 12 Through 15 Years of Age to Participants 16 Through 25 Years of Age (Immunogenicity Subset) –Participants Without Evidence of Infection up to 1 Month After Dose 2 – Dose 2 Evaluable Immunogenicity Population

		Pfizer-BioNTech COVID-19 Vaccine*			
		12 Through 15 Years n†=190	16 Through 25 Years n†=170	12 Through 15 Years/16 Through 25 Years	
Assay	Time Point‡	GMT§ (95% CI§)	GMT§ (95% CI§)	GMR¶ (95% CI¶)	Met Noninferiority Objective# (Y/N)
SARS-CoV-2 neutralization assay - NT50 (titer)Þ	1 month after Dose 2	1239.5 (1095.5, 1402.5)	705.1 (621.4, 800.2)	1.76 (1.47, 2.10)	Y

		Pfizer-BioNTech COVID-19 Vaccine*			
		12 Through 15 Years n†=190	16 Through 25 Years n†=170	12 Through 15 Years/16 Through 25 Years	
Assay	Time Point‡	GMT§ (95% CI§)	GMT§ (95% CI§)	GMR¶ (95% CI¶)	Met Noninferiority Objective# (Y/N)

Abbreviations: CI = confidence interval; GMR = geometric mean ratio; GMT = geometric mean titer; LLOQ = lower limit of quantitation; NAAT = nucleic-acid amplification test; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Participants who had no serological or virological evidence (up to 1 month after receipt of the last dose) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit up to 1 month after Dose 2 were included in the analysis.

* Pfizer-BioNTech COVID-19 Vaccine (30 mcg modRNA).

† n = Number of participants with valid and determinate assay results for the specified assay at the given dose/sampling time point.

‡ Protocol-specified timing for blood sample collection.

§ GMTs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

¶ GMRs and 2-sided 95% CIs were calculated by exponentiating the mean difference of the logarithms of the titers (12 through 15 years of age minus 16 through 25 years of age) and the corresponding CI (based on the Student t distribution).

Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is greater than 0.67.

Þ SARS-CoV-2 NT50 were determined using the SARS-CoV-2 mNeonGreen Virus Microneutralization Assay. The assay uses a fluorescent reporter virus derived from the USA_WA1/2020 strain and virus neutralization is read on Vero cell monolayers. The sample NT50 is defined as the reciprocal serum dilution at which 50% of the virus is neutralized.

18.4 Immunogenicity of a Third Primary Series Dose in Individuals with Certain Kinds of Immunocompromise

From an independent report *(Kamar N, Abravanel F, Marion O, et al. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med)*, a single arm study has been conducted in 101 individuals who had undergone various solid organ transplant procedures (heart, kidney, liver, lung, pancreas) 97±8 months previously. A third dose of the Pfizer-BioNTech COVID-19 vaccine was administered to 99 of these individuals approximately 2 months after they had received a second dose. Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at 4 weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive 4 weeks later. The prevalence of anti-SARS-CoV-2 antibodies was 68% (67 of 99 patients) 4 weeks after the third dose.

19 HOW SUPPLIED/STORAGE AND HANDLING

The information in this section applies to the Pfizer-BioNTech COVID-19 Vaccine that is supplied in multiple dose vials with a purple cap. These multiple dose vials are supplied in a carton containing 25 multiple dose vials (NDC 59267-1000-3) or 195 multiple dose vials (NDC 59267-1000-2). After dilution, 1 vial contains 6 doses of 0.3 mL. Vial labels and cartons may state that after dilution, a vial contains 5 doses of 0.3 mL. The information in this Full EUA Prescribing Information regarding the number of doses per vial after dilution supersedes the number of doses stated on vial labels and cartons.

During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Do not refreeze thawed vials.

Frozen Vials Prior to Use

Cartons of Pfizer-BioNTech COVID-19 Vaccine multiple dose vials with purple caps arrive in thermal containers with dry ice. Once received, remove the vial cartons immediately from the thermal container and preferably store in an ultra-low temperature freezer between -90°C to -60°C (-130°F to -76°F) until the expiry date printed on the label. This information in the package insert supersedes the storage conditions printed on the vial cartons.

Cartons and vials of Pfizer-BioNTech COVID-19 Vaccine supplied in multiple dose vials with purple caps with an expiry date of December 2021 through December 2022 printed on the label may remain in use beyond the printed date until the updated

expiry date shown below; as long as approved storage conditions have been maintained.

Printed Expiry Date		Updated Expiry Date
12/2021	→	31-Dec-2022
01/2022	→	31-Jan-2023
02/2022	→	28-Feb-2023
03/2022	→	31-Mar-2023
06/2022	→	31-Mar-2023
07/2022	→	30-Apr-2023
08/2022	→	31-May-2023
09/2022	→	30-Jun-2023
10/2022	→	31-Jul-2023
11/2022	→	31-Aug-2023
12/2022	→	30-Sep-2023

If not stored between -90°C to -60°C (-130°F to -76°F), vials may be stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored at -25°C to -15°C (-13°F to 5°F) for up to 2 weeks may be returned one time to the recommended storage condition of -90°C to -60°C (-130°F to -76°F). Total cumulative time the vials are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.

If an ultra-low temperature freezer is not available, the thermal container in which the Pfizer-BioNTech COVID-19 Vaccine arrives may be used as temporary storage when consistently re-filled to the top of the container with dry ice. Refer to the re-icing guidelines packed in the original thermal container for instructions regarding the use of the thermal container for temporary storage. The thermal container maintains a temperature range of -90°C to -60°C (-130°F to -76°F). Storage of the vials between -96°C to -60°C (-141°F to -76°F) is not considered an excursion from the recommended storage condition.

Transportation of Frozen Vials

If local redistribution is needed and full cartons containing vials cannot be transported at -90°C to -60°C (-130°F to -76°F), vials may be transported at -25°C to -15°C (-13°F to 5°F). Any hours used for transport at -25°C to -15°C (-13°F to 5°F) count against the 2-week limit for storage at -25°C to -15°C (-13°F to 5°F). Frozen vials transported at -25°C to -15°C (-13°F to 5°F) may be returned one time to the recommended storage condition of -90°C to -60°C (-130°F to -76°F).

Thawed Vials Before Dilution

Thawed Under Refrigeration

Thaw and then store undiluted vials in the refrigerator [2°C to 8°C (35°F to 46°F)] for up to 1 month. A carton of 25 vials or 195 vials may take up to 2 or 3 hours, respectively, to thaw in the refrigerator, whereas a fewer number of vials will thaw in less time.

Thawed at Room Temperature

For immediate use, thaw undiluted vials at room temperature [up to 25°C (77°F)] for 30 minutes. Thawed vials can be handled in room light conditions.

Vials must reach room temperature before dilution.

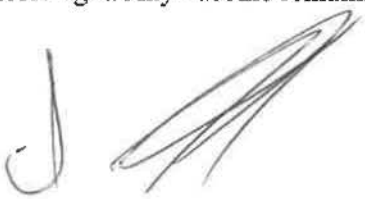
Undiluted vials may be stored at room temperature for no more than 2 hours.

Transportation of Thawed Vials

Available data support transportation of one or more thawed vials at 2°C to 8°C (35°F to 46°F) for up to 48 hours.

Vials After Dilution

After dilution, store vials between 2°C to 25°C (35°F to 77°F) and use within 6 hours from the time of dilution. During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light. Any vaccine remaining in vials must be discarded after 6 hours. Do not refreeze.



20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Vaccine Information Fact Sheet for Recipients and Caregivers.

The vaccination provider must include vaccination information in the state/local jurisdiction's Immunization Information System (IIS) or other designated system. Advise recipient or caregiver that more information about IISs can be found at: https://www.cdc.gov/vaccines/programs/iis/about.html.

21 CONTACT INFORMATION

For general questions, visit the website or call the telephone number provided below.

Website	Telephone number
www.cvdvaccine.com	1-877-829-2619 (1-877-VAX-CO19)

This Full EUA Prescribing Information may have been updated. For the most recent Full EUA Prescribing Information, please see www.cvdvaccine.com.

BIONTECH

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Pfizer

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LAB-1457-30.0

Revised: 22 December 2022

VACCINE INFORMATION FACT SHEET FOR RECIPIENTS AND CAREGIVERS ABOUT COMIRNATY (COVID-19 VACCINE, mRNA), THE PFIZER-BIONTECH COVID-19 VACCINE, AND THE PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT (ORIGINAL AND OMICRON BA.4/BA.5) TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19) FOR USE IN INDIVIDUALS 12 YEARS OF AGE AND OLDER

FOR 12 YEARS OF AGE AND OLDER

You are being offered either COMIRNATY (COVID-19 Vaccine, mRNA), the Pfizer-BioNTech COVID-19 Vaccine, or the Pfizer-BioNTech COVID-19 Vaccine, Bivalent (Original and Omicron BA.4/BA.5), hereafter referred to as the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2.

This Vaccine Information Fact Sheet for Recipients and Caregivers comprises the Fact Sheet for the authorized Pfizer-BioNTech COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, and also includes information about the U.S. Food and Drug Administration (FDA)-licensed vaccine, COMIRNATY (COVID-19 Vaccine, mRNA) for use in individuals 12 years of age and older[9].

The FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the Pfizer-BioNTech COVID-19 Vaccine authorized under Emergency Use Authorization (EUA) for individuals 12 years of age and older, when prepared according to their respective instructions for use, can be used interchangeably.[10]

COMIRNATY (COVID-19 Vaccine, mRNA) is an FDA-approved COVID-19 vaccine made by Pfizer for BioNTech. It is approved as a 2-dose series for prevention of COVID-19 in individuals 12 years of age and older. It is also authorized under EUA to provide:

- **a third primary series dose to individuals 12 years of age and older with certain kinds of immunocompromise.**

The Pfizer-BioNTech COVID-19 Vaccine has received EUA from FDA to provide:

- **a 2-dose primary series to individuals 12 years of age and older; and**
- **a third primary series dose to individuals 12 years of age and older with certain kinds of immunocompromise.**

The Pfizer-BioNTech COVID-19 Vaccine, Bivalent has received EUA from FDA to provide either:

- **a single booster dose to individuals 12 years of age and older at least 2 months after completion of primary vaccination with any authorized or approved COVID-19 vaccine; or**
- **a single booster dose to individuals 12 years of age and older at least 2 months after receipt of the most recent booster dose with any authorized or approved monovalent[11] COVID-19 vaccine.**

This Vaccine Information Fact Sheet contains information to help you understand the risks and benefits of COMIRNATY (COVID-19 Vaccine, mRNA), the Pfizer-BioNTech COVID-19 Vaccine, and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, which you may receive because there is currently a pandemic of COVID-19. Talk to your vaccination provider if you have questions.

This Fact Sheet may have been updated. For the most recent Fact Sheet, please see www.cvdvaccine.com.

WHAT YOU NEED TO KNOW BEFORE YOU GET ANY OF THESE VACCINES

WHAT IS COVID-19?

COVID-19 disease is caused by a coronavirus called SARS-CoV-2. You can get COVID-19 through contact with another person who has the virus. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 have had a wide range of symptoms reported, ranging from mild symptoms to severe illness leading to death. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

HOW ARE COMIRNATY (COVID-19 VACCINE, mRNA), THE PFIZER-BIONTECH COVID-19 VACCINE, AND THE PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT RELATED?

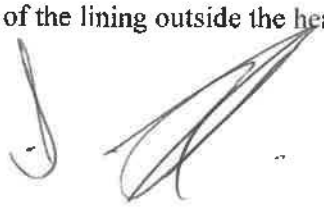
COMIRNATY (COVID-19 Vaccine, mRNA) and the Pfizer-BioNTech COVID-19 Vaccine, when prepared according to their respective instructions for use, can be used interchangeably. The Pfizer-BioNTech COVID-19 Vaccine, Bivalent is made in the same way as COMIRNATY and Pfizer-BioNTech COVID-19 Vaccine but it also contains an Omicron component to help prevent COVID-19 caused by the Omicron variant of SARS-CoV-2.

For more information on EUA, see the "**What is an Emergency Use Authorization (EUA)?**" section at the end of this Fact Sheet.

WHAT SHOULD YOU MENTION TO YOUR VACCINATION PROVIDER BEFORE YOU GET ANY OF THESE VACCINES?

Tell the vaccination provider about all of your medical conditions, including if you:

- have any allergies
- have had myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining outside the heart)
- have a fever
- have a bleeding disorder or are on a blood thinner



- are immunocompromised or are on a medicine that affects your immune system
- are pregnant or plan to become pregnant
- are breastfeeding
- have received another COVID-19 vaccine
- have ever fainted in association with an injection

HOW ARE THESE VACCINES GIVEN?

The Pfizer-BioNTech COVID-19 Vaccine, the Pfizer-BioNTech COVID-19 Vaccine, Bivalent, or COMIRNATY (COVID-19 Vaccine, mRNA) will be given to you as an injection into the muscle.

Primary Series: The Pfizer-BioNTech COVID-19 Vaccine and COMIRNATY (COVID-19 Vaccine, mRNA) are given for the primary series. The vaccine is administered as a 2-dose series, 3 weeks apart. A third primary series dose may be administered at least 4 weeks after the second dose to individuals with certain kinds of immunocompromise.

Booster Dose: Pfizer-BioNTech COVID-19 Vaccine, Bivalent is administered as a single booster dose at least 2 months after:

- completion of primary vaccination with any authorized or approved COVID-19 vaccine; or
- receipt of the most recent booster dose with any authorized or approved monovalent COVID-19 vaccine

The vaccine may not protect everyone.

WHO SHOULD NOT GET COMIRNATY (COVID-19 VACCINE, mRNA), THE PFIZER-BIONTECH COVID-19 VACCINE, OR THE PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT?

You should not get any of these vaccines if you:

- had a severe allergic reaction after a previous dose of COMIRNATY (COVID-19 Vaccine, mRNA) or the Pfizer-BioNTech COVID-19 Vaccine
- had a severe allergic reaction to any ingredient in these vaccines.

WHAT ARE THE INGREDIENTS IN THESE VACCINES?

COMIRNATY (COVID-19 Vaccine, mRNA), Pfizer-BioNTech COVID-19 Vaccine, and Pfizer-BioNTech COVID-19 Vaccine, Bivalent include the following ingredients:

- mRNA and lipids (((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), 2 [(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, 1,2-Distearoyl-sn-glycero-3-phosphocholine, and cholesterol).

Pfizer-BioNTech COVID-19 Vaccine for individuals 12 years of age and older contains 1 of the following sets of additional ingredients; ask the vaccination provider which version is being administered:

- potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, and sucrose

OR

- tromethamine, tromethamine hydrochloride, and sucrose

Pfizer-BioNTech COVID-19 Vaccine, Bivalent for individuals 12 years of age and older contains the following additional ingredients:

- tromethamine, tromethamine hydrochloride, and sucrose

COMIRNATY (COVID-19 Vaccine, mRNA) contains 1 of the following sets of additional ingredients; ask the vaccination provider which version is being administered:

- potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, and sucrose

OR

- tromethamine, tromethamine hydrochloride, and sucrose

HAVE THESE VACCINES BEEN USED BEFORE?

In clinical trials, approximately 23,000 individuals 12 years of age and older have received at least 1 dose of Pfizer-BioNTech COVID-19 Vaccine. Millions of individuals have received the Pfizer-BioNTech COVID-19 Vaccine under EUA since December 11, 2020.

In a clinical trial, approximately 300 individuals greater than 55 years of age received one dose of a bivalent vaccine that differs from the Pfizer-BioNTech COVID-19 Vaccine, Bivalent in that it contains a different Omicron component.

WHAT ARE THE BENEFITS OF THESE VACCINES?

COMIRNATY (COVID-19 Vaccine, mRNA) and the Pfizer-BioNTech COVID-19 Vaccine have been shown to prevent COVID-19. FDA has authorized Pfizer-BioNTech COVID-19 Vaccine, Bivalent to provide better protection against COVID-19 caused by the Omicron variant of SARS-CoV-2.

The duration of protection against COVID-19 is currently unknown.

WHAT ARE THE RISKS OF THESE VACCINES?

There is a remote chance that these vaccines could cause a severe allergic reaction. A severe allergic reaction would usually occur within a few minutes to 1 hour after getting a dose. For this reason, your vaccination provider may ask you to stay at the place where you received your vaccine for monitoring after vaccination. Signs of a severe allergic reaction can include:

- Difficulty breathing
- Swelling of your face and throat
- A fast heartbeat
- A bad rash all over your body
- Dizziness and weakness

Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have occurred in some people who have received COMIRNATY (COVID-19 Vaccine, mRNA) or Pfizer-BioNTech COVID-19 Vaccine, more commonly in adolescent males and adult males under 40 years of age than among females and older males. In most of these people, symptoms began within a few days following receipt of the second dose of vaccine. The chance of having this occur is very low. You should seek medical attention right away if you have any of the following symptoms after receiving the vaccine:

- Chest pain
- Shortness of breath
- Feelings of having a fast-beating, fluttering, or pounding heart

Side effects that have been reported with these vaccines include:

- Severe allergic reactions
- Non-severe allergic reactions such as rash, itching, hives, or swelling of the face
- Myocarditis (inflammation of the heart muscle)
- Pericarditis (inflammation of the lining outside the heart)
- Injection site pain
- Tiredness
- Headache
- Muscle pain
- Chills
- Joint pain
- Fever
- Injection site swelling
- Injection site redness
- Nausea
- Feeling unwell
- Swollen lymph nodes (lymphadenopathy)
- Decreased appetite
- Diarrhea

- Vomiting
- Arm pain
- Fainting in association with injection of the vaccine
- Dizziness

These may not be all the possible side effects of these vaccines. Serious and unexpected side effects may occur. The possible side effects of these vaccines are still being studied.

WHAT SHOULD I DO ABOUT SIDE EFFECTS?

If you experience a severe allergic reaction, call 9-1-1, or go to the nearest hospital.

Call the vaccination provider or your healthcare provider if you have any side effects that bother you or do not go away.

Report vaccine side effects to FDA/CDC Vaccine Adverse Event Reporting System (VAERS). The VAERS toll-free number is 1-800-822-7967 or report online to https://vaers.hhs.gov/reportevent.html. Please include either "COMIRNATY (COVID-19 Vaccine, mRNA)", "Pfizer-BioNTech COVID-19 Vaccine EUA", or "Pfizer-BioNTech COVID-19 Vaccine, Bivalent EUA" as appropriate, in the first line of box #18 of the report form.

In addition, you can report side effects to Pfizer Inc. at the contact information provided below.

Website	Fax number	Telephone number
www.pfizersafetyreporting.com	1-866-635-8337	1-800-438-1985

You may also be given an option to enroll in v-safe. V-safe is a voluntary smartphone-based tool that uses text messaging and web surveys to check in with people who have been vaccinated to identify potential side effects after COVID-19 vaccination. V-safe asks questions that help CDC monitor the safety of COVID-19 vaccines. V-safe also provides second-dose reminders if needed and live telephone follow-up by CDC if participants report a significant health impact following COVID-19 vaccination. For more information on how to sign up, visit: www.cdc.gov/vsafe.

WHAT IF I DECIDE NOT TO GET COMIRNATY (COVID-19 VACCINE, mRNA), THE PFIZER-BIONTECH COVID-19 VACCINE, OR THE PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT?

Under the EUA, it is your choice to receive or not receive any of these vaccines. Should you decide not to receive any of these vaccines, it will not change your standard medical care.

ARE OTHER CHOICES AVAILABLE FOR PREVENTING COVID-19 BESIDES COMIRNATY (COVID-19 VACCINE, mRNA), THE PFIZER-BIONTECH COVID-19 VACCINE, OR THE PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT?

For primary vaccination, another choice for preventing COVID-19 is SPIKEVAX (COVID-19 Vaccine, mRNA), an FDA-approved COVID-19 vaccine. Other vaccines to prevent COVID-19 may be available under EUA, including bivalent vaccines that contain an Omicron component of SARS-CoV-2.

CAN I RECEIVE COMIRNATY (COVID-19 VACCINE, mRNA), PFIZER-BIONTECH COVID-19 VACCINE, OR THE PFIZER-BIONTECH COVID-19 VACCINE, BIVALENT AT THE SAME TIME AS OTHER VACCINES?

Data have not yet been submitted to FDA on administration of COMIRNATY (COVID-19 Vaccine, mRNA), the Pfizer-BioNTech COVID-19 Vaccine, or the Pfizer-BioNTech COVID-19 Vaccine, Bivalent at the same time with other vaccines. If you are considering receiving COMIRNATY (COVID-19 Vaccine, mRNA), the Pfizer-BioNTech COVID-19 Vaccine, or the Pfizer-BioNTech COVID-19 Vaccine, Bivalent with other vaccines, discuss your options with your healthcare provider.

WHAT IF I AM IMMUNOCOMPROMISED?

If you are immunocompromised, you may receive a third primary series dose of Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY (COVID-19 Vaccine, mRNA). Individuals 12 years of age and older may receive a booster dose with Pfizer-BioNTech COVID-19 Vaccine, Bivalent. Vaccinations may not provide full immunity to COVID-19 in people who are immunocompromised, and you should continue to maintain physical precautions to help prevent COVID-19. Your close contacts should be vaccinated as appropriate.

WHAT IF I AM PREGNANT OR BREASTFEEDING?

If you are pregnant or breastfeeding, discuss your options with your healthcare provider.

WILL THESE VACCINES GIVE ME COVID-19?

No. These vaccines do not contain SARS-CoV-2 and cannot give you COVID-19.

KEEP YOUR VACCINATION CARD

When you get your first COVID-19 vaccine, you will get a vaccination card. Remember to bring your card when you return.

ADDITIONAL INFORMATION

If you have questions, visit the website or call the telephone number provided below.

To access the most recent Fact Sheets, please scan the QR code provided below.

Global website	Telephone number
www.cvdvaccine.com	1-877-829-2619 (1-877-VAX-CO19)

HOW CAN I LEARN MORE?

- Ask the vaccination provider.
- Visit CDC at https://www.cdc.gov/coronavirus/2019-ncov/index.html.
- Visit FDA at https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.
- Contact your local or state public health department.

WHERE WILL MY VACCINATION INFORMATION BE RECORDED?

The vaccination provider may include your vaccination information in your state/local jurisdiction's Immunization Information System (IIS) or other designated system. For more information about IISs visit: https://www.cdc.gov/vaccines/programs/iis/about.html.

CAN I BE CHARGED AN ADMINISTRATION FEE FOR RECEIPT OF THESE COVID-19 VACCINES?

No. At this time, the provider cannot charge you for a vaccine dose and you cannot be charged an out-of-pocket vaccine administration fee or any other fee if only receiving a COVID-19 vaccination. However, vaccination providers may seek appropriate reimbursement from a program or plan that covers COVID-19 vaccine administration fees for the vaccine recipient (private insurance, Medicare, Medicaid, Health Resources & Services Administration [HRSA] COVID-19 Uninsured Program for non-insured recipients).

WHERE CAN I REPORT CASES OF SUSPECTED FRAUD?

Individuals becoming aware of any potential violations of the CDC COVID-19 Vaccination Program requirements are encouraged to report them to the Office of the Inspector General, U.S. Department of Health and Human Services, at 1-800-HHS-TIPS or https://TIPS.HHS.GOV.

WHAT IS THE COUNTERMEASURES INJURY COMPENSATION PROGRAM?

The Countermeasures Injury Compensation Program (CICP) is a federal program that may help pay for costs of medical care and other specific expenses of certain people who have been seriously injured by certain medicines or vaccines, including these vaccines. Generally, a claim must be submitted to the CICP within one (1) year from the date of receiving the vaccine. To learn more about this program, visit http://www.hrsa.gov/cicp/ or call 1-855-266-2427.

WHAT IS AN EMERGENCY USE AUTHORIZATION (EUA)?

An EUA is a mechanism to facilitate the availability and use of medical products, including vaccines, during public health emergencies, such as the current COVID-19 pandemic. An EUA is supported by a Secretary of Health and Human Services (HHS) declaration that circumstances exist to justify the emergency use of drugs and biological products during the COVID-19 pandemic. A product authorized for emergency use has not undergone the same type of review by FDA as an FDA-approved product.

FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, and available alternatives. In addition, the FDA decision is based on the totality of the scientific evidence available showing that the product may be effective to prevent COVID-19 during the COVID-19 pandemic and that the known and potential benefits of the product outweigh the known and potential risks of the product. All of these criteria must be met to allow for the product to be used during the COVID-19 pandemic.

An EUA is in effect for the duration of the COVID-19 EUA declaration justifying emergency use of this product, unless terminated or revoked (after which the product may no longer be used).

BIONTECH

Manufactured for
BioNTech Manufacturing GmbH
An der Goldgrube 12
55131 Mainz, Germany

Pfizer

Manufactured by
Pfizer Inc., New York, NY 10017

LAB-1451-24.0

Revised: 8 December 2022

Scan to capture that this Fact Sheet was provided to vaccine recipient for the electronic medical records/immunization information systems.

GDTI: 0886983000332

[9] You may receive this Vaccine Information Fact Sheet even if your child is 11 years old. Children who will turn from 11 years to 12 years of age between doses in the primary regimen may receive, for any dose in the primary regimen, either: (1) the Pfizer-BioNTech COVID-19 Vaccine authorized for use in individuals 5 through 11 years of age; or (2) COMIRNATY (COVID-19 Vaccine, mRNA) or the Pfizer-BioNTech COVID-19 Vaccine authorized for use in individuals 12 years of age and older.

[10] When prepared according to their respective instructions for use, the FDA-approved COMIRNATY (COVID-19 Vaccine, mRNA) and the EUA-authorized Pfizer-BioNTech COVID-19 Vaccine for individuals 12 years of age and older can be used interchangeably without presenting any safety or effectiveness concerns.

[11] Monovalent refers to any authorized or approved COVID-19 vaccine that contains or encodes the spike protein of only the Original SARS-CoV-2.

"HE26"

5.3.6 CUMULATIVE ANALYSIS OF POST-AUTHORIZATION ADVERSE EVENT REPORTS OF PF-07302048 (BNT162B2) RECEIVED THROUGH 28-FEB-2021

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Report Prepared by:

Worldwide Safety

Pfizer

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LIST OF ABBREVIATIONS

Acronym	Term
AE	adverse event
AESI	adverse event of special interest
BC	Brighton Collaboration
CDC	Centers for Disease Control and Prevention
COVID-19	coronavirus disease 2019
DLP	data lock point
EUA	emergency use authorisation
HLGT	(MedDRA) High Group Level Term
HLT	(MedDRA) High Level Term
MAH	marketing authorisation holder
MedDRA	medical dictionary for regulatory activities
MHRA	Medicines and Healthcare products Regulatory Agency
PCR	Polymerase Chain Reaction
PT	(MedDRA) Preferred Term
PVP	pharmacovigilance plan
RT-PCR	Reverse Transcription-Polymerase Chain Reaction
RSI	reference safety information
TME	targeted medically event
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SMQ	standardised MedDRA query
SOC	(MedDRA) System Organ Class
UK	United Kingdom
US	United States
VAED	vaccine-associated enhanced disease
VAERD	vaccine-associated enhanced respiratory disease
VAERS	vaccine adverse event reporting system

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1. INTRODUCTION

Reference is made to the Request for Comments and Advice submitted 04 February 2021 regarding Pfizer/BioNTech's proposal for the clinical and post-authorization safety data package for the Biologics License Application (BLA) for our investigational COVID-19 Vaccine (BNT162b2). Further reference is made to the Agency's 09 March 2021 response to this request, and specifically, the following request from the Agency.

"Monthly safety reports primarily focus on events that occurred during the reporting interval and include information not relevant to a BLA submission such as line lists of adverse events by country. We are most interested in a cumulative analysis of post-authorization safety data to support your future BLA submission. Please submit an integrated analysis of your cumulative post-authorization safety data, including U.S. and foreign post-authorization experience, in your upcoming BLA submission. Please include a cumulative analysis of the Important Identified Risks, Important Potential Risks, and areas of Important Missing Information identified in your Pharmacovigilance Plan, as well as adverse events of special interest and vaccine administration errors (whether or not associated with an adverse event). Please also include distribution data and an analysis of the most common adverse events. In addition, please submit your updated Pharmacovigilance Plan with your BLA submission."

This document provides an integrated analysis of the cumulative post-authorization safety data, including U.S. and foreign post-authorization adverse event reports received through 28 February 2021.

2. METHODOLOGY

Pfizer is responsible for the management post-authorization safety data on behalf of the MAH BioNTech according to the Pharmacovigilance Agreement in place. Data from BioNTech are included in the report when applicable.

Pfizer's safety database contains cases of AEs reported spontaneously to Pfizer, cases reported by the health authorities, cases published in the medical literature, cases from Pfizer-sponsored marketing programs, non-interventional studies, and cases of serious AEs reported from clinical studies regardless of causality assessment.

The limitations of post-marketing adverse drug event reporting should be considered when interpreting these data:

- Reports are submitted voluntarily, and the magnitude of underreporting is unknown. Some of the factors that may influence whether an event is reported include: length of time since marketing, market share of the drug, publicity about a drug or an AE, seriousness of the reaction, regulatory actions, awareness by health professionals and consumers of adverse drug event reporting, and litigation.

- Because many external factors influence whether or not an AE is reported, the spontaneous reporting system yields reporting proportions not incidence rates. As a result, it is generally not appropriate to make between-drug comparisons using these

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proportions; the spontaneous reporting system should be used for signal detection rather than hypothesis testing.

- In some reports, clinical information (such as medical history, validation of diagnosis, time from drug use to onset of illness, dose, and use of concomitant drugs) is missing or incomplete, and follow-up information may not be available.

- An accumulation of adverse event reports (AERs) does not necessarily indicate that a particular AE was caused by the drug; rather, the event may be due to an underlying disease or some other factor(s) such as past medical history or concomitant medication.

- Among adverse event reports received into the Pfizer safety database during the cumulative period, only those having a complete workflow cycle in the safety database (meaning they progressed to Distribution or Closed workflow status) are included in the monthly SMSR. This approach prevents the inclusion of cases that are not fully processed hence not accurately reflecting final information. Due to the large numbers of spontaneous adverse event reports received for the product, the MAH has prioritised the processing of serious cases, in order to meet expedited regulatory reporting timelines and ensure these reports are available for signal detection and evaluation activity. The increased volume of reports has not impacted case processing for serious reports, and compliance metrics continue to be monitored weekly with prompt action taken as needed to maintain compliance with expedited reporting obligations. Non-serious cases are entered into the safety database no later than 4 calendar days from receipt. Entrance into the database includes the coding of all adverse events; this allow for a manual review of events being received but may not include immediate case processing to completion. Non-serious cases are processed as soon as possible and no later than 90 days from receipt. Pfizer has also taken a multiple actions to help alleviate the large increase of adverse event reports. This includes significant technology enhancements, and process and workflow solutions, as well as increasing the number of data entry and case processing colleagues. To date, Pfizer has onboarded approximately (b) (4) additional full-time employees (FTEs). More are joining each month with an expected total of more than (b) (4) additional resources by the end of June 2021.

3. RESULTS

3.1. Safety Database

3.1.1. General Overview

It is estimated that approximately (b) (4) doses of BNT162b2 were shipped worldwide from the receipt of the first temporary authorisation for emergency supply on 01 December 2020 through 28 February 2021.

Cumulatively, through 28 February 2021, there was a total of 42,086 case reports (25,379 medically confirmed and 16,707 non-medically confirmed) containing 158,893 events. Most cases (34,762) were received from United States (13,739), United Kingdom (13,404) Italy (2,578), Germany (1913), France (1506), Portugal (866) and Spain (756); the remaining 7,324 were distributed among 56 other countries.

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Table 1 below presents the main characteristics of the overall cases.

Table 1. General Overview: Selected Characteristics of All Cases Received During the Reporting Interval

Characteristics		Relevant cases (N=42086)
Gender:	Female	29914
	Male	9182
	No Data	2990
Age range (years): 0.01 -107 years Mean = 50.9 years n = 34952	≤ 17 18-30 31-50 51-64 65-74 ≥ 75 Unknown	175[a] 4953 13886 7884 3098 5214 6876
Case outcome:	Recovered/Recovering	19582
	Recovered with sequelae	520
	Not recovered at the time of report	11361
	Fatal	1223
	Unknown	9400

a. in 46 cases reported age was <16-year-old and in 34 cases <12-year-old.

As shown in Figure 1, the System Organ Classes (SOCs) that contained the greatest number (≥2%) of events, in the overall dataset, were General disorders and administration site conditions (51,335 AEs), Nervous system disorders (25,957), Musculoskeletal and connective tissue disorders (17,283), Gastrointestinal disorders (14,096), Skin and subcutaneous tissue disorders (8,476), Respiratory, thoracic and mediastinal disorders (8,848), Infections and infestations (4,610), Injury, poisoning and procedural complications (5,590), and Investigations (3,693).

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Figure 1. Total Number of BNT162b2 AEs by System Organ Classes and Event Seriousness

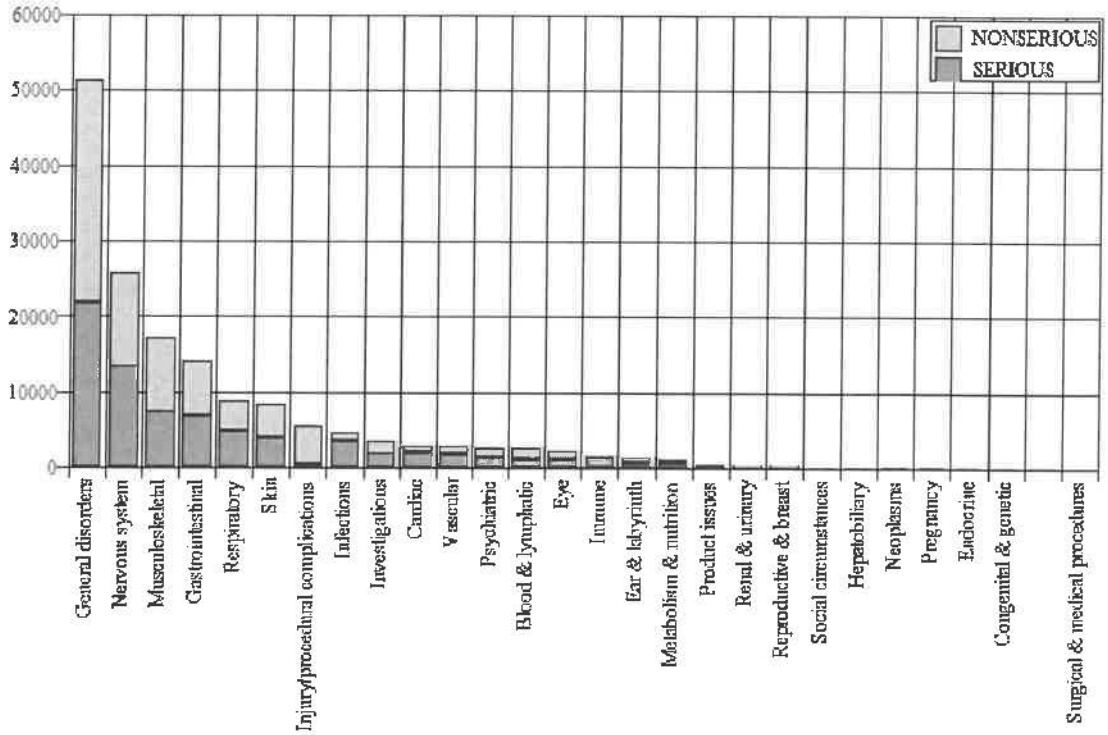

Table 2 shows the most commonly (≥2%) reported MedDRA (v. 23.1) PTs in the overall dataset (through 28 February 2021),

Table 2. Events Reported in ≥2% Cases

MedDRA SOC	MedDRA PT	Cumulatively Through 28 February 2021 AEs (AERP%) N = 42086
Blood and lymphatic system disorders		
	Lymphadenopathy	1972 (4.7%)
Cardiac disorders		
	Tachycardia	1098 (2.6%)
Gastrointestinal disorders		
	Nausea	5182 (12.3%)
	Diarrhoea	1880 (4.5%)
	Vomiting	1698 (4.0%)
General disorders and administration site conditions		
	Pyrexia	7666 (18.2%)
	Fatigue	7338 (17.4%)
	Chills	5514 (13.1%)
	Vaccination site pain	5181 (12.3%)

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Table 2. Events Reported in ≥2% Cases

		Cumulatively Through 28 February 2021
MedDRA SOC	**MedDRA PT**	**AEs (AERP%) N = 42086**
	Pain	3691 (8.8%)
	Malaise	2897 (6.9%)
	Asthenia	2285 (5.4%)
	Drug ineffective	2201 (5.2%)
	Vaccination site erythema	930 (2.2%)
	Vaccination site swelling	913 (2.2%)
	Influenza like illness	835 (2%)
Infections and infestations		
	COVID-19	1927 (4.6%)
Injury, poisoning and procedural complications		
	Off label use	880 (2.1%)
	Product use issue	828 (2.0%)
Musculoskeletal and connective tissue disorders		
	Myalgia	4915 (11.7%)
	Pain in extremity	3959 (9.4%)
	Arthralgia	3525 (8.4%)
Nervous system disorders		
	Headache	10131 (24.1%)
	Dizziness	3720 (8.8%)
	Paraesthesia	1500 (3.6%)
	Hypoaesthesia	999 (2.4%)
Respiratory, thoracic and mediastinal disorders		
	Dyspnoea	2057 (4.9%)
	Cough	1146 (2.7%)
	Oropharyngeal pain	948 (2.3%)
Skin and subcutaneous tissue disorders		
	Pruritus	1447 (3.4%)
	Rash	1404 (3.3%)
	Erythema	1044 (2.5%)
	Hyperhidrosis	900 (2.1%)
	Urticaria	862 (2.1%)
Total number of events		**93473**

3.1.2. Summary of Safety Concerns in the US Pharmacovigilance Plan

Table 3. Safety concerns

Important identified risks	Anaphylaxis
Important potential risks	Vaccine-Associated Enhanced Disease (VAED), Including Vaccine-associated Enhanced Respiratory Disease (VAERD)
Missing information	Use in Pregnancy and lactation Use in Paediatric Individuals <12 Years of Age Vaccine Effectiveness

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Table 4. Important Identified Risk

<table>
<tr><th>Topic</th><th>Description</th></tr>
<tr><td>Important Identified Risk</td><td>Post Authorization Cases Evaluation (cumulative to 28 Feb 2021)
Total Number of Cases in the Reporting Period (N=42086)</td></tr>
<tr><td>Anaphylaxis</td><td>Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, 1833 potentially relevant cases were retrieved from the Anaphylactic reaction SMQ (Narrow and Broad) search strategy, applying the MedDRA algorithm. These cases were individually reviewed and assessed according to Brighton Collaboration (BC) definition and level of diagnostic certainty as shown in the Table below:

<table>
<tr><td>Brighton Collaboration Level</td><td>Number of cases</td></tr>
<tr><td>BC 1</td><td>290</td></tr>
<tr><td>BC 2</td><td>311</td></tr>
<tr><td>BC 3</td><td>10</td></tr>
<tr><td>BC 4</td><td>391</td></tr>
<tr><td>BC 5</td><td>831</td></tr>
<tr><td>Total</td><td>1833</td></tr>
</table>
Level 1 indicates a case with the highest level of diagnostic certainty of anaphylaxis, whereas the diagnostic certainty is lowest for Level 3. Level 4 is defined as "reported event of anaphylaxis with insufficient evidence to meet the case definition" and Level 5 as not a case of anaphylaxis.

There were 1002 cases (54.0% of the potentially relevant cases retrieved), 2958 potentially relevant events, from the Anaphylactic reaction SMQ (Broad and Narrow) search strategy, meeting BC Level 1 to 4:

Country of incidence: UK (261), US (184), Mexico (99), Italy (82), Germany (67), Spain (38), France (36), Portugal (22), Denmark (20), Finland, Greece (19 each), Sweden (17), Czech Republic , Netherlands (16 each), Belgium, Ireland (13 each), Poland (12), Austria (11); the remaining 57 cases originated from 15 different countries.
Relevant event seriousness: Serious (2341), Non-Serious (617);
Gender: Females (876), Males (106), Unknown (20);
Age (n=961) ranged from 16 to 98 years (mean = 54.8 years, median – 42.5 years);
Relevant even outcome[a]: fatal (9)[b], resolved/resolving (1922), not resolved (229), resolved with sequelae (48), unknown (754);
Most frequently reported relevant PTs (≥2%), from the Anaphylactic reaction SMQ (Broad and Narrow) search strategy: Anaphylactic reaction (435), Dyspnoea (356), Rash (190), Pruritus (175), Erythema (159), Urticaria (133), Cough (115), Respiratory distress, Throat tightness (97 each), Swollen tongue (93), Anaphylactic shock (80), Hypotension (72), Chest discomfort (71), Swelling face (70), Pharyngeal swelling (68), and Lip swelling (64).

Conclusion: Evaluation of BC cases Level 1 - 4 did not reveal any significant new safety information. Anaphylaxis is appropriately described in the product labeling as are non-anaphylactic hypersensitivity events. Surveillance will continue.</td></tr>
</table>

a Different clinical outcome may be reported for an event that occurred more than once to the same individual.
b There were 4 individuals in the anaphylaxis evaluation who died on the same day they were vaccinated. Although these patients experienced adverse events (9) that are potential symptoms of anaphylaxis, they all had serious underlying medical conditions, and one individual appeared to also have COVID-19 pneumonia, that likely contributed to their deaths

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Table 5. Important Potential Risk

Topic	Description
Important Potential Risk	**Post Authorization Cases Evaluation (cumulative to 28 Feb 2021) Total Number of Cases in the Reporting Period (N=42086)**
Vaccine-Associated Enhanced Disease (VAED), including Vaccine-Associated Enhanced Respiratory Disease (VAERD)	No post-authorized AE reports have been identified as cases of VAED/VAERD, therefore, there is no observed data at this time. An expected rate of VAED is difficult to establish so a meaningful observed/expected analysis cannot be conducted at this point based on available data. The feasibility of conducting such an analysis will be re-evaluated on an ongoing basis as data on the virus grows and the vaccine safety data continues to accrue. The search criteria utilised to identify potential cases of VAED for this report includes PTs indicating a lack of effect of the vaccine and PTs potentially indicative of severe or atypical COVID-19[a]. Since the first temporary authorization for emergency supply under Regulation 174 in the UK (01 December 2020) and through 28 February 2021, 138 cases [0.33% of the total PM dataset], reporting 317 potentially relevant events were retrieved: Country of incidence: UK (71), US (25), Germany (14), France, Italy, Mexico, Spain, (4 each), Denmark (3); the remaining 9 cases originated from 9 different countries; Cases Seriousness: 138; Seriousness criteria for the total 138 cases: Medically significant (71, of which 8 also serious for disability), Hospitalization required (non-fatal/non-life threatening) (16, of which 1 also serious for disability), Life threatening (13, of which 7 were also serious for hospitalization), Death (38). Gender: Females (73), Males (57), Unknown (8); Age (n=132) ranged from 21 to 100 years (mean = 57.2 years, median = 59.5); Case outcome: fatal (38), resolved/resolving (26), not resolved (65), resolved with sequelae (1), unknown (8); Of the 317 relevant events, the most frequently reported PTs (≥2%) were: Drug ineffective (135), Dyspnoea (53), Diarrhoea (30), COVID-19 pneumonia (23), Vomiting (20), Respiratory failure (8), and Seizure (7). Conclusion: VAED may present as severe or unusual clinical manifestations of COVID-19. Overall, there were 37 subjects with suspected COVID-19 and 101 subjects with confirmed COVID-19 following one or both doses of the vaccine; 75 of the 101 cases were severe, resulting in hospitalisation, disability, life-threatening consequences or death. None of the 75 cases could be definitively considered as VAED/VAERD. In this review of subjects with COVID-19 following vaccination, based on the current evidence, VAED/VAERD remains a theoretical risk for the vaccine. Surveillance will continue.

a. Search criteria: Standard Decreased Therapeutic Response Search AND PTs Dyspnoea; Tachypnoea; Hypoxia; COVID 19 pneumonia; Respiratory Failure; Acute Respiratory Distress Syndrome; Cardiac Failure; Cardiogenic shock; Acute myocardial infarction; Arrhythmia; Myocarditis; Vomiting; Diarrhoea; Abdominal pain; Jaundice; Acute hepatic failure; Deep vein thrombosis; Pulmonary embolism; Peripheral Ischaemia; Vasculitis; Shock; Acute kidney injury; Renal failure; Altered state of consciousness; Seizure; Encephalopathy; Meningitis; Cerebrovascular accident; Thrombocytopenia; Disseminated intravascular coagulation; Chillblains; Erythema multiforme; Multiple organ dysfunction syndrome; Multisystem inflammatory syndrome in children.

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Table 6. Description of Missing Information

Topic	Description
Missing Information	**Post Authorization Cases Evaluation (cumulative to 28 Feb 2021) Total Number of Cases in the Reporting Period (N=42086)**
Use in Pregnancy and lactation	• Number of cases: 413[a] (0.98% of the total PM dataset); 84 serious and 329 non-serious; • Country of incidence: US (205), UK (64), Canada (31), Germany (30), Poland (13), Israel (11); Italy (9), Portugal (8), Mexico (6), Estonia, Hungary and Ireland, (5 each), Romania (4), Spain (3), Czech Republic and France (2 each), the remaining 10 cases were distributed among 10 other countries. Pregnancy cases: 274 cases including: • 270 mother cases and 4 foetus/baby cases representing 270 unique pregnancies (the 4 foetus/baby cases were linked to 3 mother cases; 1 mother case involved twins). • Pregnancy outcomes for the 270 pregnancies were reported as spontaneous abortion (23), outcome pending (5), premature birth with neonatal death, spontaneous abortion with intrauterine death (2 each), spontaneous abortion with neonatal death, and normal outcome (1 each). No outcome was provided for 238 pregnancies (note that 2 different outcomes were reported for each twin, and both were counted). 270 - 238 = 32 Incidence of abortion/foetal death = 31/32 = 97%. • 146 non-serious mother cases reported exposure to vaccine in utero without the occurrence of any clinical adverse event. The exposure PTs coded to the PTs Maternal exposure during pregnancy (111), Exposure during pregnancy (29) and Maternal exposure timing unspecified (6). Trimester of exposure was reported in 21 of these cases: 1st trimester (15 cases), 2nd trimester (7), and 3rd trimester (2). • 124 mother cases, 49 non-serious and 75 serious, reported clinical events, which occurred in the vaccinated mothers. Pregnancy related events reported in these cases coded to the PTs Abortion spontaneous (25), Uterine contraction during pregnancy, Premature rupture of membranes, Abortion, Abortion missed, and Foetal death (1 each). Other clinical events which occurred in more than 5 cases coded to the PTs Headache (33), Vaccination site pain (24), Pain in extremity and Fatigue (22 each), Myalgia and Pyrexia (16 each), Chills (13) Nausea (12), Pain (11), Arthralgia (9), Lymphadenopathy and Drug ineffective (7 each), Chest pain, Dizziness and Asthenia (6 each), Malaise and COVID-19 (5 each). Trimester of exposure was reported in 22 of these cases: 1st trimester (19 cases), 2nd trimester (1 case), 3rd trimester (2 cases). • 4 serious foetus/baby cases reported the PTs Exposure during pregnancy, Foetal growth restriction, Maternal exposure during pregnancy, Premature baby (2 each), and Death neonatal (1). Trimester of exposure was reported for 2 cases (twins) as occurring during the 1st trimester. Breast feeding baby cases: 133, of which: • 116 cases reported exposure to vaccine during breastfeeding (PT Exposure via breast milk) without the occurrence of any clinical adverse events; • 17 cases, 3 serious and 14 non-serious, reported the following clinical events that occurred in the infant/child exposed to vaccine via breastfeeding: Pyrexia (5), Rash (4), Infant irritability (3), Infantile vomiting, Diarrhoea, Insomnia, and Illness (2 each), Poor feeding infant, Lethargy, Abdominal discomfort, Vomiting, Allergy to vaccine, Increased appetite, Anxiety, Crying, Poor quality sleep, Eructation, Agitation, Pain and Urticaria (1 each). Breast feeding mother cases (6): • 1 serious case reported 3 clinical events that occurred in a mother during breast feeding (PT Maternal exposure during breast feeding); these events coded to the PTs Chills, Malaise, and Pyrexia • 1 non-serious case reported with very limited information and without associated AEs.

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Table 6. Description of Missing Information

Topic	Description
Missing Information	**Post Authorization Cases Evaluation (cumulative to 28 Feb 2021) Total Number of Cases in the Reporting Period (N=42086)**
	• In 4 cases (3 non-serious; 1 serious) Suppressed lactation occurred in a breast feeding women with the following co-reported events: Pyrexia (2), Paresis, Headache, Chills, Vomiting, Pain in extremity, Arthralgia, Breast pain, Scar pain, Nausea, Migraine, Myalgia, Fatigue and Breast milk discolouration (1 each). Conclusion. There were no safety signals that emerged from the review of these cases of use in pregnancy and while breast feeding.
Use in Paediatric Individuals <12 Years of Age	Paediatric individuals <12 years of age • Number of cases: 34[d] (0.1% of the total PM dataset), indicative of administration in paediatric subjects <12 years of age; • Country of incidence: UK (29), US (3), Germany and Andorra (1 each); • Cases Seriousness: Serious (24), Non-Serious (10); • Gender: Females (25), Males (7), Unknown (2); • Age (n=34) ranged from 2 months to 9 years, mean = 3.7 years, median = 4.0; • Case outcome: resolved/resolving (16), not resolved (13), and unknown (5). • Of the 132 reported events, those reported more than once were as follows: Product administered to patient of inappropriate age (27, see Medication Error), Off label use (11), Pyrexia (6), Product use issue (5), Fatigue, Headache and Nausea (4 each), Vaccination site pain (3), Abdominal pain upper, COVID-19, Facial paralysis, Lymphadenopathy, Malaise, Pruritus and Swelling (2 each). Conclusion: No new significant safety information was identified based on a review of these cases compared with the non-paediatric population.
Vaccine Effectiveness	Company conventions for coding cases indicative of lack of efficacy: The coding conventions for lack of efficacy in the context of administration of the COVID-19 vaccine were revised on 15 February 2021, as shown below: • PT "Vaccination failure" is coded when ALL of the following criteria are met: o The subject has received the series of two doses per the dosing regimen in local labeling. o At least 7 days have elapsed since the second dose of vaccine has been administered. o The subject experiences SARS-CoV-2 infection (confirmed laboratory tests). • PT "Drug ineffective" is coded when either of the following applies: o The infection is not confirmed as SARS-CoV-2 through laboratory tests (irrespective of the vaccination schedule). This includes scenarios where LOE is stated or implied, e.g., "the vaccine did not work", "I got COVID-19". o It is unknown: ▪ Whether the subject has received the series of two doses per the dosing regimen in local labeling; ▪ How many days have passed since the first dose (including unspecified number of days like" a few days", "some days", etc.); ▪ If 7 days have passed since the second dose; o The subject experiences a vaccine preventable illness 14 days after receiving the first dose up to and through 6 days after receipt of the second dose. Note: after the immune system as had sufficient time (14 days) to respond to the vaccine, a report of COVID-19 is considered a potential lack of efficacy even if the vaccination course is not complete. Summary of the coding conventions for onset of vaccine preventable disease versus the vaccination date:

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Table 6. Description of Missing Information

Topic	Description
Missing Information	**Post Authorization Cases Evaluation (cumulative to 28 Feb 2021)** **Total Number of Cases in the Reporting Period (N=42086)**

1st dose (day 1-13)	From day 14 post 1st dose to day 6 post 2nd dose	Day 7 post 2nd dose
Code only the events describing the SARS-CoV-2 infection	Code "Drug ineffective"	Code "Vaccination failure"
Scenario Not considered LOE	Scenario considered LOE as "Drug ineffective"	Scenario considered LOE as "Vaccination failure"

Lack of efficacy cases

- Number of cases: 1665[b] (3.9 % of the total PM dataset) of which 1100 were medically confirmed and 565 non medically confirmed;
- Number of lack of efficacy events: 1665 [PT: Drug ineffective (1646) and Vaccination failure (19)[c]].
- Country of incidence: US (665), UK (405), Germany (181), France (85), Italy (58), Romania (47), Belgium (33), Israel (30), Poland (28), Spain (21), Austria (18), Portugal (17), Greece (15), Mexico (13), Denmark (8), Canada (7), Hungary, Sweden and United Arab Emirates (5 each), Czech Republic (4), Switzerland (3); the remaining 12 cases originated from 9 different countries.
- COVID-19 infection was suspected in 155 cases, confirmed in 228 cases, in 1 case it was reported that the first dose was not effective (no other information).
- COVID-19 infection (suspected or confirmed) outcome was reported as resolved/resolving (165), not resolved (205) or unknown (1230) at the time of the reporting; there were 65 cases where a fatal outcome was reported.

Drug ineffective cases (1649)

- Drug ineffective event seriousness: serious (1625), non-serious (21)[c];
- Lack of efficacy term was reported:
  - after the 1st dose in 788 cases
  - after the 2nd dose in 139 cases
  - in 722 cases it was unknown after which dose the lack of efficacy occurred.
- Latency of lack of efficacy term reported after the first dose was known for 176 cases:
  - Within 9 days: 2 subjects;
  - Within 14 and 21 days: 154 subjects;
  - Within 22 and 50 days: 20 subjects;
- Latency of lack of efficacy term reported after the second dose was known for 69 cases:
  - Within 0 and 7 days: 42 subjects;
  - Within 8 and 21 days: 22 subjects;
  - Within 23 and 36 days: 5 subjects.
- Latency of lack of efficacy term reported in cases where the number of doses administered was not provided, was known in 409 cases:
  - Within 0 and 7 days after vaccination: 281 subjects.
  - Within 8 and 14 days after vaccination: 89 subjects.
  - Within 15 and 44 days after vaccination: 39 subjects.

According to the RSI, individuals may not be fully protected until 7 days after their second dose of vaccine, therefore for the above 1649 cases where lack of efficacy was reported after the 1st dose or the

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Table 6. Description of Missing Information

Topic	Description
Missing Information	**Post Authorization Cases Evaluation (cumulative to 28 Feb 2021) Total Number of Cases in the Reporting Period (N=42086)**
	2nd dose, the reported events may represent signs and symptoms of intercurrent or undiagnosed COVID-19 infection or infection in an individual who was not fully vaccinated, rather than vaccine ineffectiveness. *Vaccination failure cases (16)* • Vaccination failure seriousness: all serious; • Lack of efficacy term was reported in all cases after the 2nd dose: • Latency of lack of efficacy was known for 14 cases: o Within 7 and 13 days: 8 subjects; o Within 15 and 29 days: 6 subjects. COVID-19 (10) and Asymptomatic COVID-19 (6) were the reported vaccine preventable infections that occurred in these 16 cases. Conclusion: No new safety signals of vaccine lack of efficacy have emerged based on a review of these cases.

a. From a total of 417 cases, 4 cases were excluded from the analysis. In 3 cases, the MAH was informed that a 33-year-old and two unspecified age pregnant female patients were scheduled to receive bnt162b2 (PT reported Off label use and Product use issue in 2 cases; Circumstance or information capable of leading to medication error in one case). One case reported the PT Morning sickness; however, pregnancy was not confirmed in this case.
b. 558 additional cases retrieved in this dataset were excluded from the analysis; upon review, 546 cases cannot be considered true lack of efficacy cases because the PT Drug ineffective was coded but the subjects developed SARS-CoV-2 infection during the early days from the first dose (days 1 – 13); the vaccine has not had sufficient time to stimulate the immune system and, consequently, the development of a vaccine preventable disease during this time is not considered a potential lack of effect of the vaccine; in 5 cases the PT Drug ineffective was removed after data lock point (DLP) because the subjects did not develop COVID-19 infection; in 1 case, reporting Treatment failure and Transient ischaemic attack, the Lack of efficacy PT did not refer to BNT162b2 vaccine; 5 cases have been invalidated in the safety database after DLP; 1 case has been deleted from the discussion because the PTs reported Pathogen resistance and Product preparation issue were not indicative of a lack of efficacy, to be eliminated.
c. Upon review, 31 additional cases were excluded from the analysis as the data reported (e.g. clinical details, height, weight, etc.) were not consistent with paediatric subjects
d. Upon review, 28 additional cases were excluded from the analysis as the data reported (e.g. clinical details, height, weight, etc.) were not consistent with paediatric subjects.
e. Different clinical outcomes may be reported for an event that occurred more than once to the same individual
f. In 2 cases the PT Vaccination failure was replaced with Drug ineffective after DLP. Another case was not included in the discussion of the Vaccination failure cases because correct scheduling (21 days apart between the first and second dose) cannot be confirmed.

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3.1.3. Review of Adverse Events of Special Interest (AESIs)

Please refer to Appendix 1 for the list of the company's AESIs for BNT162b2.

The company's AESI list takes into consideration the lists of AESIs from the following expert groups and regulatory authorities: Brighton Collaboration (SPEAC), ACCESS protocol, US CDC (preliminary list of AESI for VAERS surveillance), MHRA (unpublished guideline).

The AESI terms are incorporated into a TME list and include events of interest due to their association with severe COVID-19 and events of interest for vaccines in general.

The AESI list is comprised of MedDRA PTs, HLTs, HLGTs or MedDRA SMQs and can be changed as appropriate based on the evolving safety profile of the vaccine.

Table 7 provides a summary review of cumulative cases within AESI categories in the Pfizer safety database. This is distinct from safety signal evaluations which are conducted and included, as appropriate, in the Summary Monthly Safety Reports submitted regularly to the FDA and other Health Authorities.

Table 7. AESIs Evaluation for BNT162b2

AESIs[a] **Category**	**Post-Marketing Cases Evaluation[b]** **Total Number of Cases (N=42086)**
Anaphylactic Reactions *Search criteria: Anaphylactic reaction SMQ (Narrow and Broad, with the algorithm applied), selecting relevant cases according to BC criteria*	Please refer to the Risk 'Anaphylaxis' included above in Table 4.
Cardiovascular AESIs *Search criteria: PTs Acute myocardial infarction; Arrhythmia; Cardiac failure; Cardiac failure acute; Cardiogenic shock; Coronary artery disease; Myocardial infarction; Postural orthostatic tachycardia syndrome; Stress cardiomyopathy; Tachycardia*	• Number of cases: 1403 (3.3% of the total PM dataset), of which 241 are medically confirmed and 1162 are non-medically confirmed; • Country of incidence: UK (268), US (233), Mexico (196), Italy (141), France (128), Germany (102), Spain (46), Greece (45), Portugal (37), Sweden (20), Ireland (17), Poland (16), Israel (13), Austria, Romania and Finland (12 each), Netherlands (11), Belgium and Norway (10 each), Czech Republic (9), Hungary and Canada (8 each), Croatia and Denmark (7 each), Iceland (5); the remaining 30 cases were distributed among 13 other countries; • Subjects' gender: female (1076), male (291) and unknown (36); • Subjects' age group (n = 1346): Adult[c] (1078), Elderly[d] (266) Child[e] and Adolescent[f] (1 each); • Number of relevant events: 1441, of which 946 serious, 495 non-serious; in the cases reporting relevant serious events; • Reported relevant PTs: Tachycardia (1098), Arrhythmia (102), Myocardial infarction (89), Cardiac failure (80), Acute myocardial infarction (41), Cardiac failure acute (11), Cardiogenic shock and Postural orthostatic tachycardia syndrome (7 each) and Coronary artery disease (6); • Relevant event onset latency (n = 1209): Range from <24 hours to 21 days, median <24 hours;

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Table 7. AESIs Evaluation for BNT162b2

AESIs[a] Category	Post-Marketing Cases Evaluation[b] Total Number of Cases (N=42086)
	• Relevant event outcome[g]: fatal (136), resolved/resolving (767), resolved with sequelae (21), not resolved (140) and unknown (380); Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue
COVID-19 AESIs *Search criteria: Covid-19 SMQ (Narrow and Broad) OR PTs Ageusia; Anosmia*	• Number of cases: 3067 (7.3% of the total PM dataset), of which 1013 are medically confirmed and 2054 are non-medically confirmed; • Country of incidence: US (1272), UK (609), Germany (360), France (161), Italy (94), Spain (69), Romania (62), Portugal (51), Poland (50), Mexico (43), Belgium (42), Israel (41), Sweden (30), Austria (27), Greece (24), Denmark (18), Czech Republic and Hungary (17 each), Canada (12), Ireland (11), Slovakia (9), Latvia and United Arab Emirates (6 each); the remaining 36 cases were distributed among 16 other different countries; • Subjects' gender: female (1650), male (844) and unknown (573); • Subjects' age group (n= 1880): Adult (1315), Elderly (560), Infant[a] and Adolescent (2 each), Child (1); • Number of relevant events: 3359, of which 2585 serious, 774 non-serious; • Most frequently reported relevant PTs (>1 occurrence): COVID-19 (1927), SARS-CoV-2 test positive (415), Suspected COVID-19 (270), Ageusia (228), Anosmia (194), SARS-CoV-2 antibody test negative (83), Exposure to SARS-CoV-2 (62), SARS-CoV-2 antibody test positive (53), COVID-19 pneumonia (51), Asymptomatic COVID-19 (31), Coronavirus infection (13), Occupational exposure to SARS-CoV-2 (11), SARS-CoV-2 test false positive (7), Coronavirus test positive (6), SARS-CoV-2 test negative (3) SARS-CoV-2 antibody test (2); • Relevant event onset latency (n = 2070): Range from <24 hours to 374 days, median 5 days; • Relevant event outcome: fatal (136), not resolved (547), resolved/resolving (558), resolved with sequelae (9) and unknown (2110). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue
Dermatological AESIs *Search criteria: PT Chilblains; Erythema multiforme*	• Number of cases: 20 cases (0.05% of the total PM dataset), of which 15 are medically confirmed and 5 are non-medically confirmed; • Country of incidence: UK (8), France and Poland (2 each), and the remaining 8 cases were distributed among 8 other different countries; • Subjects' gender: female (17) male and unknown (1 each); • Subjects' age group (n=19): Adult (18), Elderly (1); • Number of relevant events: 20 events, 16 serious, 4 non-serious

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Table 7. AESIs Evaluation for BNT162b2

AESIs[a] Category	Post-Marketing Cases Evaluation[b] Total Number of Cases (N=42086)
	• Reported relevant PTs: Erythema multiforme (13) and Chillblains (7) • Relevant event onset latency (n = 18): Range from <24 hours to 17 days, median 3 days; • Relevant event outcome: resolved/resolving (7), not resolved (8) and unknown (6). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue.
Haematological AESIs *Search criteria: Leukopenias NEC (HLT) (Primary Path) OR Neutropenias (HLT) (Primary Path) OR PTs Immune thrombocytopenia, Thrombocytopenia OR SMQ Haemorrhage terms (excl laboratory terms*	• Number of cases: 932 (2.2 % of the total PM dataset), of which 524 medically confirmed and 408 non-medically confirmed; • Country of incidence: UK (343), US (308), France (50), Germany (43), Italy (37), Spain (27), Mexico and Poland (13 each), Sweden (10), Israel (9), Netherlands (8), Denmark, Finland, Portugal and Ireland (7 each), Austria and Norway (6 each), Croatia (4), Greece, Belgium, Hungary and Switzerland (3 each), Cyprus, Latvia and Serbia (2 each); the remaining 9 cases originated from 9 different countries; • Subjects' gender (n=898): female (676) and male (222); • Subjects' age group (n=837): Adult (543), Elderly (293), Infant (1); • Number of relevant events: 1080, of which 681 serious, 399 non-serious; • Most frequently reported relevant PTs (≥15 occurrences) include: Epistaxis (127), Contusion (112), Vaccination site bruising (96), Vaccination site haemorrhage (51), Petechiae (50), Haemorrhage (42), Haematochezia (34), Thrombocytopenia (33), Vaccination site haematoma (32), Conjunctival haemorrhage and Vaginal haemorrhage (29 each), Haematoma, Haemoptysis and Menorrhagia (27 each), Haematemesis (25), Eye haemorrhage (23), Rectal haemorrhage (22), Immune thrombocytopenia (20), Blood urine present (19), Haematuria, Neutropenia and Purpura (16 each) Diarrhoea haemorrhagic (15); • Relevant event onset latency (n = 787): Range from <24 hours to 33 days, median = 1 day; • Relevant event outcome: fatal (34), resolved/resolving (393), resolved with sequelae (17), not resolved (267) and unknown (371). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue
Hepatic AESIs *Search criteria: Liver related investigations, signs and symptoms (SMQ) (Narrow and Broad) OR PT Liver injury*	• Number of cases: 70 cases (0.2% of the total PM dataset), of which 54 medically confirmed and 16 non-medically confirmed; • Country of incidence: UK (19), US (14), France (7), Italy (5), Germany (4), Belgium, Mexico and Spain (3 each), Austria, and Iceland (2 each); the remaining 8 cases originated from 8 different countries; • Subjects' gender: female (43), male (26) and unknown (1); • Subjects' age group (n=64): Adult (37), Elderly (27);

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Table 7. AESIs Evaluation for BNT162b2

AESIs[c] Category	Post-Marketing Cases Evaluation[b] Total Number of Cases (N=42086)
	• Number of relevant events: 94, of which 53 serious, 41 non-serious; • Most frequently reported relevant PTs (≥3 occurrences) include: Alanine aminotransferase increased (16), Transaminases increased and Hepatic pain (9 each), Liver function test increased (8), Aspartate aminotransferase increased and Liver function test abnormal (7 each), Gamma-glutamyltransferase increased and Hepatic enzyme increased (6 each), Blood alkaline phosphatase increased and Liver injury (5 each), Ascites, Blood bilirubin increased and Hypertransaminasaemia (3 each); • Relevant event onset latency (n = 57): Range from <24 hours to 20 days, median 3 days; • Relevant event outcome: fatal (5), resolved/resolving (27), resolved with sequelae (1), not resolved (14) and unknown (47). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue
Facial Paralysis *Search criteria: PTs Facial paralysis, Facial paresis*	• Number of cases: 449[j] (1.07% of the total PM dataset), 314 medically confirmed and 135 non-medically confirmed; • Country of incidence: US (124), UK (119), Italy (40), France (27), Israel (20), Spain (18), Germany (13), Sweden (11), Ireland (9), Cyprus (8), Austria (7), Finland and Portugal (6 each), Hungary and Romania (5 each), Croatia and Mexico (4 each), Canada (3),Czech Republic, Malta, Netherlands, Norway, Poland and Puerto Rico (2 each); the remaining 8 cases originated from 8 different countries; • Subjects' gender: female (295), male (133), unknown (21); • Subjects' age group (n=411): Adult (313), Elderly (96), Infant[l] and Child (1 each); • Number of relevant events[k]: 453, of which 399 serious, 54 non-serious; • Reported relevant PTs: Facial paralysis (401), Facial paresis (64); • Relevant event onset latency (n = 404): Range from <24 hours to 46 days, median 2 days; • Relevant event outcome: resolved/resolving (184), resolved with sequelae (3), not resolved (183) and unknown (97); Overall Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue. Causality assessment will be further evaluated following availability of additional unblinded data from the clinical study C4591001, which will be unblinded for final analysis approximately mid-April 2021. Additionally, non-interventional post-authorisation safety studies, C4591011 and C4591012 are expected to capture data on a sufficiently large vaccinated population to detect an increased risk of Bell's palsy in vaccinated individuals. The timeline for conducting these analyses will be established based on the size of the vaccinated population captured in the study data sources by the first interim reports (due 30 June

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Table 7. AESIs Evaluation for BNT162b2

AESIs[a] Category	Post-Marketing Cases Evaluation[b] Total Number of Cases (N=42086)
	2021). Study C4591021, pending protocol endorsement by EMA, is also intended to inform this risk.
Immune-Mediated/Autoimmune AESIs *Search criteria: Immune-mediated/autoimmune disorders (SMQ) (Broad and Narrow) OR Autoimmune disorders HLGT (Primary Path) OR PTs Cytokine release syndrome; Cytokine storm; Hypersensitivity*	• Number of cases: 1050 (2.5 % of the total PM dataset), of which 760 medically confirmed and 290 non-medically confirmed; • Country of incidence (>10 cases): UK (267), US (257), Italy (70), France and Germany (69 each), Mexico (36), Sweden (35), Spain (32), Greece (31), Israel (21), Denmark (18), Portugal (17), Austria and Czech Republic (16 each), Canada (12), Finland (10). The remaining 74 cases were from 24 different countries. • Subjects' gender (n=682): female (526), male (156). • Subjects' age group (n=944): Adult (746), Elderly (196), Adolescent (2). • Number of relevant events: 1077, of which 780 serious, 297 non-serious. • Most frequently reported relevant PTs (>10 occurrences): Hypersensitivity (596), Neuropathy peripheral (49), Pericarditis (32), Myocarditis (25), Dermatitis (24), Diabetes mellitus and Encephalitis (16 each), Psoriasis (14), Dermatitis Bullous (13), Autoimmune disorder and Raynaud's phenomenon (11 each); • Relevant event onset latency (n = 807): Range from <24 hours to 30 days, median <24 hours. • Relevant event outcome[c]: resolved/resolving (517), not resolved (215), fatal (12), resolved with sequelae (22) and unknown (312). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue
Musculoskeletal AESIs *Search criteria: PTs Arthralgia; Arthritis; Arthritis bacterial[b]; Chronic fatigue syndrome; Polyarthritis; Polyneuropathy; Post viral fatigue syndrome; Rheumatoid arthritis*	• Number of cases: 3600 (8.5% of the total PM dataset), of which 2045 medically confirmed and 1555 non-medically confirmed; • Country of incidence: UK (1406), US (1004), Italy (285), Mexico (236), Germany (72), Portugal (70), France (48), Greece and Poland (46), Latvia (33), Czech Republic (32), Israel and Spain (26), Sweden (25), Romania (24), Denmark (23), Finland and Ireland (19 each), Austria and Belgium (18 each), Canada (16), Netherlands (14), Bulgaria (12), Croatia and Serbia (9 each), Cyprus and Hungary (8 each), Norway (7), Estonia and Puerto Rico (6 each), Iceland and Lithuania (4 each); the remaining 21 cases originated from 11 different countries; • Subjects' gender (n=3471): female (2760), male (711); • Subjects' age group (n=3372): Adult (2850), Elderly (515), Child (4), Adolescent (2), Infant (1); • Number of relevant events: 3640, of which 1614 serious, 2026 non-serious; • Reported relevant PTs: Arthralgia (3525), Arthritis (70), Rheumatoid arthritis (26), Polyarthritis (5), Polyneuropathy, Post viral fatigue syndrome, Chronic fatigue syndrome (4 each), Arthritis bacterial (1); • Relevant event onset latency (n = 2968): Range from <24 hours to 32 days, median 1 day;

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Table 7. AESIs Evaluation for BNT162b2

AESIs[a] Category	Post-Marketing Cases Evaluation[b] Total Number of Cases (N=42086)
	• Relevant event outcome: resolved/resolving (1801), not resolved (959), resolved with sequelae (49), and unknown (853). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue.
Neurological AESIs (including demyelination) *Search criteria: Convulsions (SMQ) (Broad and Narrow) OR Demyelination (SMQ) (Broad and Narrow) OR PTs Ataxia; Cataplexy; Encephalopathy; Fibromyalgia; Intracranial pressure increased; Meningitis; Meningitis aseptic; Narcolepsy*	• Number of cases: 501 (1.2% of the total PM dataset), of which 365 medically confirmed and 136 non-medically confirmed. • Country of incidence (≥9 cases): UK (157), US (68), Germany (49), Mexico (35), Italy (31), France (25), Spain (18), Poland (17), Netherlands and Israel (15 each), Sweden (9). The remaining 71 cases were from 22 different countries. • Subjects' gender (n=478): female (328), male (150). • Subjects' age group (n=478): Adult (329), Elderly (149); • Number of relevant events: 542, of which 515 serious, 27 non-serious. • Most frequently reported relevant PTs (>2 occurrences) included: Seizure (204), Epilepsy (83), Generalised tonic-clonic seizure (33), Guillain-Barre syndrome (24), Fibromyalgia and Trigeminal neuralgia (17 each), Febrile convulsion, (15), Status epilepticus (12), Aura and Myelitis transverse (11 each), Multiple sclerosis relapse and Optic neuritis (10 each), Petit mal epilepsy and Tonic convulsion (9 each), Ataxia (8), Encephalopathy and Tonic clonic movements (7 each), Foaming at mouth (5), Multiple sclerosis, Narcolepsy and Partial seizures (4 each), Bad sensation, Demyelination, Meningitis, Postictal state, Seizure like phenomena and Tongue biting (3 each); • Relevant event onset latency (n = 423): Range from <24 hours to 48 days, median 1 day; • Relevant events outcome: fatal (16), resolved/resolving (265), resolved with sequelae (13), not resolved (89) and unknown (161); Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue
Other AESIs *Search criteria: Herpes viral infections (HLT) (Primary Path) OR PTs Adverse event following immunisation; Inflammation; Manufacturing laboratory analytical testing issue; Manufacturing materials issue; Manufacturing production issue; MERS-CoV test; MERS-CoV test negative; MERS-CoV test positive; Middle East respiratory syndrome; Multiple organ dysfunction syndrome; Occupational exposure to communicable disease; Patient*	• Number of cases: 8152 (19.4% of the total PM dataset), of which 4977 were medically confirmed and 3175 non-medically confirmed; • Country of incidence (> 20 occurrences): UK (2715), US (2421), Italy (710), Mexico (223), Portugal (210), Germany (207), France (186), Spain (183), Sweden (133), Denmark (127), Poland (120), Greece (95), Israel (79), Czech Republic (76), Romania (57), Hungary (53), Finland (52), Norway (51), Latvia (49), Austria (47), Croatia (42), Belgium (41), Canada (39), Ireland (34), Serbia (28), Iceland (25), Netherlands (22). The remaining 127 cases were from 21 different countries; • Subjects' gender (n=7829): female (5969), male (1860); • Subjects' age group (n=7479): Adult (6330), Elderly (1125), Adolescent, Child (9 each), Infant (6);

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Table 7. AESIs Evaluation for BNT162b2

AESIs[a] Category	Post-Marketing Cases Evaluation[b] Total Number of Cases (N=42086)
isolation; Product availability issue; Product distribution issue; Product supply issue; Pyrexia; Quarantine; SARS-CoV-1 test; SARS-CoV-1 test negative; SARS-CoV-1 test positive	• Number of relevant events: 8241, of which 3674 serious, 4568 non-serious; • Most frequently reported relevant PTs (≥6 occurrences) included: Pyrexia (7666), Herpes zoster (259), Inflammation (132), Oral herpes (80), Multiple organ dysfunction syndrome (18), Herpes virus infection (17), Herpes simplex (13), Ophthalmic herpes zoster (10), Herpes ophthalmic and Herpes zoster reactivation (6 each); • Relevant event onset latency (n =6836): Range from <24 hours to 61 days, median 1 day; • Relevant events outcome: fatal (96), resolved/resolving (5008), resolved with sequelae (84), not resolved (1429) and unknown (1685). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue
Pregnancy Related AESIs *Search criteria: PTs Amniotic cavity infection; Caesarean section; Congenital anomaly; Death neonatal; Eclampsia; Foetal distress syndrome; Low birth weight baby; Maternal exposure during pregnancy; Placenta praevia; Pre-eclampsia; Premature labour; Stillbirth; Uterine rupture; Vasa praevia*	For relevant cases, please refer to Table 6, Description of Missing Information, *Use in Pregnancy and While Breast Feeding*
Renal AESIs *Search criteria: PTs Acute kidney injury; Renal failure.*	• Number of cases: 69 cases (0.17% of the total PM dataset), of which 57 medically confirmed, 12 non-medically confirmed; • Country of incidence: Germany (17), France and UK (13 each), US (6), Belgium, Italy and Spain (4 each), Sweden (2), Austria, Canada, Denmark, Finland, Luxembourg and Norway (1 each); • Subjects' gender: female (46), male (23); • Subjects' age group (n=68): Adult (7), Elderly (60), Infant (1); • Number of relevant events: 70, all serious; • Reported relevant PTs: Acute kidney injury (40) and Renal failure (30); • Relevant event onset latency (n = 42): Range from <24 hours to 15 days, median 4 days; • Relevant event outcome: fatal (23), resolved/resolving (10), not resolved (15) and unknown (22). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue.
Respiratory AESIs *Search criteria: Lower respiratory tract infections NEC (HLT)*	• Number of cases: 130 cases (0.3% of the total PM dataset), of which 107 medically confirmed;

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Table 7. AESIs Evaluation for BNT162b2

AESIs[a] Category	Post-Marketing Cases Evaluation[b] Total Number of Cases (N=42086)
(Primary Path) OR Respiratory failures (excl neonatal) (HLT) (Primary Path) OR Viral lower respiratory tract infections (HLT) (Primary Path) OR PTs: Acute respiratory distress syndrome; Endotracheal intubation; Hypoxia; Pulmonary haemorrhage; Respiratory disorder; Severe acute respiratory syndrome	• Countries of incidence: United Kingdom (20), France (18), United States (16), Germany (14), Spain (13), Belgium and Italy (9). Denmark (8), Norway (5), Czech Republic, Iceland (3 each); the remaining 12 cases originated from 8 different countries. • Subjects' gender (n=130): female (72), male (58). • Subjects's age group (n=126): Elderly (78), Adult (47), Adolescent (1). • Number of relevant events: 137, of which 126 serious, 11 non-serious; • Reported relevant PTs: Respiratory failure (44), Hypoxia (42), Respiratory disorder (36). Acute respiratory distress syndrome (10), Chronic respiratory syndrome (3), Severe acute respiratory syndrome (2). • Relevant event onset latency (n=102): range from < 24 hours to 18 days, median 1 day; • Relevant events outcome: fatal (41), Resolved/resolving (47), not recovered (18) and unknown (31). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue.
Thromboembolic Events *Search criteria: Embolism and thrombosis (HLGT) (Primary Path), excluding PTs reviewed as Stroke AESIs, OR PTs Deep vein thrombosis; Disseminated intravascular coagulation; Embolism; Embolism venous; Pulmonary embolism*	• Number of cases: 151 (0.3% of the total PM dataset), of which 111 medically confirmed and 40 non-medically confirmed; • Country of incidence: UK (34), US (31), France (20), Germany (15), Italy and Spain (6 each), Denmark and Sweden (5 each), Austria, Belgium and Israel (3 each), Canada, Cyprus, Netherlands and Portugal (2 each); the remaining 12 cases originated from 12 different countries; • Subjects' gender (n= 144): female (89), male (55); • Subjects' age group (n=136): Adult (66), Elderly (70); • Number of relevant events: 168, of which 165 serious, 3 non-serious; • Most frequently reported relevant PTs (>1 occurrence) included: Pulmonary embolism (60), Thrombosis (39), Deep vein thrombosis (35), Thrombophlebitis superficial (6), Venous thrombosis limb (4), Embolism, Microembolism, Thrombophlebitis and Venous thrombosis (3 each) Blue toe syndrome (2); • Relevant event onset latency (n = 124): Range from <24 hours to 28 days, median 4 days; • Relevant event outcome: fatal (18), resolved/resolving (54), resolved with sequelae (6), not resolved (49) and unknown (42). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue.
Stroke *Search criteria: HLT Central nervous system haemorrhages and cerebrovascular accidents*	• Number of cases: 275 (0.6% of the total PM dataset), of which 180 medically confirmed and 95 non-medically confirmed; • Country of incidence: UK (81), US (66), France (32), Germany (21), Norway (14), Netherlands and Spain (11 each), Sweden (9),

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Table 7. AESIs Evaluation for BNT162b2

AESIs[a] Category	Post-Marketing Cases Evaluation[b] Total Number of Cases (N=42086)
(Primary Path) OR HLT Cerebrovascular venous and sinus thrombosis (Primary Path)	Israel (6), Italy (5), Belgium (3), Denmark, Finland, Poland and Switzerland (2 each); the remaining 8 cases originated from 8 different countries; • Subjects' gender (n= 273): female (182), male (91); • Subjects' age group (n=265): Adult (59), Elderly (205), Child[m] (1); • Number of relevant events: 300, all serious; • Most frequently reported relevant PTs (>1 occurrence) included: o PTs indicative of Ischaemic stroke: Cerebrovascular accident (160), Ischaemic stroke (41), Cerebral infarction (15), Cerebral ischaemia, Cerebral thrombosis, Cerebral venous sinus thrombosis, Ischaemic cerebral infarction and Lacunal infarction (3 each) Basal ganglia stroke, Cerebellar infarction and Thrombotic stroke (2 each); o PTs indicative of Haemorrhagic stroke: Cerebral haemorrhage (26), Haemorrhagic stroke (11), Haemorrhage intracranical and Subarachnoid haemorrhage (5 each), Cerebral haematoma (4), Basal ganglia haemorrhage and Cerebellar haemorrhage (2 each); • Relevant event onset latency (n = 241): Range from <24 hours to 41 days, median 2 days; • Relevant event outcome: fatal and resolved/resolving (61 each), resolved with sequelae (10), not resolved (85) and unknown (83). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue.
Vasculitic Events *Search criteria: Vasculitides HLT*	• Number of cases: 32 cases (0.08% of the total PM dataset), of which 26 medically confirmed and 6 non-medically confirmed; • Country of incidence: UK (13), France (4), Portugal, US and Spain (3 each), Cyprus, Germany, Hungary, Italy and Slovakia and Costa rica (1 each); • Subjects' gender: female (26), male (6); • Subjects' age group (n=31): Adult (15), Elderly (16); • Number of relevant events: 34, of which 25 serious, 9 non-serious; • Reported relevant PTs: Vasculitis (14), Cutaneous vasculitis and Vasculitic rash (4 each), (3), Giant cell arteritis and Peripheral ischaemia (3 each), Behcet's syndrome and Hypersensitivity vasculitis (2 each) Palpable purpura, and Takayasu's arteritis (1 each); • Relevant event onset latency (n = 25): Range from <24 hours to 19 days, median 3 days; • Relevant event outcome: fatal (1), resolved/resolving (13), not resolved (12) and unknown (8). Conclusion: This cumulative case review does not raise new safety issues. Surveillance will continue

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Table 7. AESIs Evaluation for BNT162b2

AESIs[a]	Post-Marketing Cases Evaluation[b]
Category	Total Number of Cases (N=42086)

a. For the complete list of the AESIs, please refer to Appendix 5;
b. Please note that this corresponds to evidence from post-EUA/conditional marketing authorisation approval data sources;
c. Subjects with age ranged between 18 and 64 years;
d. Subjects with age equal to or above 65 years;
e. Subjects with age ranged between 2 and 11 years;
f. Subjects with age ranged between 12 and less than 18 years;
g. Multiple episodes of the same PT event were reported with a different clinical outcome within some cases hence the sum of the events outcome exceeds the total number of PT events;
h. Subjects with age ranged between 1 (28 days) and 23 months;
i. Twenty-four additional cases were excluded from the analysis as they were not cases of peripheral facial nerve palsy because they described other disorders (stroke, cerebral haemorrhage or transient ischaemic attack); 1 case was excluded from the analysis because it was invalid due to an unidentifiable reporter;
j. This UK case report received from the UK MHRA described a 1-year-old subject who received the vaccine, and had left postauricular ear pain that progressed to left-sided Bell's palsy 1 day following vaccination that had not resolved at the time of the report;
k. If a case included both PT Facial paresis and PT Facial paralysis, only the PT Facial paralysis was considered in the descriptions of the events as it is most clinically important;
l. Multiple episodes of the same PT event were reported with a different clinical outcome within some cases hence the sum of the events outcome exceeds the total number of PT events
m. This UK case report received from the UK MHRA described a 7-year-old female subject who received the vaccine and had stroke (unknown outcome); no follow-up is possible for clarification.
n. This PT not included in the AESIs/TME list was included in the review as relevant for ACCESS protocol criteria;

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3.1.4. Medication error

Cases potentially indicative of medication errors[1] that cumulatively occurred are summarized below.

- Number of relevant medication error cases: 2056[2] (4.9%) of which 1569 (3.7%) are medically confirmed.
- Number of relevant events: 2792
- Top 10 countries of incidence:
  - US (1201), France (171), UK (138), Germany (88), Czech Republic (87), Sweden (49), Israel (45), Italy (42), Canada (35), Romania (33), Finland (21), Portugal (20), Norway (14), Puerto Rico (13), Poland (12), Austria and Spain (10 each).

Medication error case outcomes:

- Fatal (7)[3],
- Recovered/recovering (354, of which 4 are serious),
- Recovered with sequelae (8, of which 3 serious)

[1] MedDRA (version 23.1) Higher Level Terms: Accidental exposures to product; Product administration errors and issues; Product confusion errors and issues; Product dispensing errors and issues; Product label issues; Product monitoring errors and issues; Product preparation errors and issues; Product selection errors and issues; Product storage errors and issues in the product use system; Product transcribing errors and communication issues, OR Preferred Terms: Accidental poisoning; Circumstance or information capable of leading to device use error; Circumstance or information capable of leading to medication error; Contraindicated device used; Deprescribing error; Device use error; Dose calculation error; Drug titration error; Expired device used; Exposure via direct contact; Exposure via eye contact; Exposure via mucosa; Exposure via skin contact; Failure of child resistant product closure; Inadequate aseptic technique in use of product; Incorrect disposal of product; Intercepted medication error; Intercepted product prescribing error; Medication error; Multiple use of single-use product; Product advertising issue; Product distribution issue; Product prescribing error; Product prescribing issue; Product substitution error; Product temperature excursion issue; Product use in unapproved therapeutic environment; Radiation underdose; Underdose; Unintentional medical device removal; Unintentional use for unapproved indication; Vaccination error; Wrong device used; Wrong dosage form; Wrong dosage formulation; Wrong dose; Wrong drug; Wrong patient; Wrong product procured; Wrong product stored; Wrong rate; Wrong route; Wrong schedule; Wrong strength; Wrong technique in device usage process; Wrong technique in product usage process.

[2] Thirty-five (35) cases were exclude from the analysis because describing medication errors occurring in an unspecified number of individuals or describing medication errors occurring with co suspects were determined to be non-contributory.

[3] All the medication errors reported in these cases were assessed as non-serious occurrences with an unknown outcome; based on the available information including the causes of death, the relationship between the medication error and the death is weak.

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- Not recovered (189, of which 84 are serious),
- Unknown (1498, of which 33 are serious).

1371 cases reported only MEs without any associated clinical adverse event. The PTs most frequently reported (≥12 occurrences) were: Poor quality product administered (539), Product temperature excursion issue (253), Inappropriate schedule of product administration (225), Product preparation error (206), Underdose (202), Circumstance or information capable of leading to medication error (120), Product preparation issue (119), Wrong technique in product usage process (76), Incorrect route of product administration (66), Accidental overdose (33), Product administered at inappropriate site (27), Incorrect dose administered and Accidental exposure to the product (25 each), Exposure via skin contact (22), Wrong product administered (17), Incomplete course of vaccination, and Product administration error (14 each) Product administered to patient of inappropriate age (12).

In 685 cases, there were co-reported AEs. The most frequently co- associated AEs (> 40 occurrences) were: Headache (187), Pyrexia (161), Fatigue (135), Chills (127), Pain (107), Vaccination site pain (100), Nausea (89), Myalgia (88), Pain in extremity (85) Arthralgia (68), Off label use (57), Dizziness (52), Lymphadenopathy (47), Asthenia (46) and Malaise (41). These cases are summarized in Table 8.

Table 8. ME PTs by seriousness with or without harm co-association (Through 28 February 2021)

	Serious		Non-Serious	
ME PTs	**With Harm**	**Without Harm**	**With Harm**	**Without Harm**
Accidental exposure to product	0	0	0	5
Accidental overdose	4	1	9	6
Booster dose missed	0	0	0	1
Circumstance or information capable of leading to medication error	0	0	5	11
Contraindicated product administered	1	0	0	2
Expired product administered	0	0	0	2
Exposure via skin contact	0	0	0	5
Inappropriate schedule of product administration	0	2	8	264
Incorrect dose administered	1	1	0	0

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Table 8. ME PTs by seriousness with or without harm co-association (Through 28 February 2021)

	Serious		Non-Serious	
ME PTs	**With Harm**	**Without Harm**	**With Harm**	**Without Harm**
Incorrect route of product administration	2	6	16	127
Lack of vaccination site rotation	1	0	0	0
Medication error	0	0	0	1
Poor quality product administered	1	0	0	34
Product administered at inappropriate site	2	1	13	29
Product administered to patient of inappropriate age	0	4	0	40
Product administration error	1	0	0	3
Product dose omission issue	0	1	0	3
Product preparation error	1	0	4	11
Product preparation issue	1	1	0	14

Overall, there were 68 cases with co-reported AEs reporting Harm and 599 cases with co-reported AEs without harm. Additionally, Intercepted medication errors was reported in 1 case (PTs Malaise, clinical outcome unknow) and Potential medication errors were reported in 17 cases.

4. DISCUSSION

Pfizer performs frequent and rigorous signal detection on BNT162b2 cases. The findings of these signal detection analyses are consistent with the known safety profile of the vaccine. This cumulative analysis to support the Biologics License Application for BNT162b2, is an integrated analysis of post-authorization safety data, from U.S. and foreign experience, focused on Important Identified Risks, Important Potential Risks, and areas of Important Missing Information identified in the Pharmacovigilance Plan, as well as adverse events of special interest and vaccine administration errors (whether or not associated with an adverse event). The data do not reveal any novel safety concerns or risks requiring label changes and support a favorable benefit risk profile of to the BNT162b2 vaccine.

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5. SUMMARY AND CONCLUSION

Review of the available data for this cumulative PM experience, confirms a favorable benefit: risk balance for BNT162b2.

Pfizer will continue routine pharmacovigilance activities on behalf of BioNTech according to the Pharmacovigilance Agreement in place, in order to assure patient safety and will inform the Agency if an evaluation of the safety data yields significant new information for BNT162b2.

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APPENDIX 1. LIST OF ADVERSE EVENTS OF SPECIAL INTEREST

1p36 deletion syndrome;2-Hydroxyglutaric aciduria;5'nucleotidase increased;Acoustic neuritis;Acquired C1 inhibitor deficiency;Acquired epidermolysis bullosa;Acquired epileptic aphasia;Acute cutaneous lupus erythematosus;Acute disseminated encephalomyelitis;Acute encephalitis with refractory, repetitive partial seizures;Acute febrile neutrophilic dermatosis;Acute flaccid myelitis;Acute haemorrhagic leukoencephalitis;Acute haemorrhagic oedema of infancy;Acute kidney injury;Acute macular outer retinopathy;Acute motor axonal neuropathy;Acute motor-sensory axonal neuropathy;Acute myocardial infarction;Acute respiratory distress syndrome;Acute respiratory failure;Addison's disease;Administration site thrombosis;Administration site vasculitis;Adrenal thrombosis;Adverse event following immunisation;Ageusia;Agranulocytosis;Air embolism;Alanine aminotransferase abnormal;Alanine aminotransferase increased;Alcoholic seizure;Allergic bronchopulmonary mycosis;Allergic oedema;Alloimmune hepatitis;Alopecia areata;Alpers disease;Alveolar proteinosis;Ammonia abnormal;Ammonia increased;Amniotic cavity infection;Amygdalohippocampectomy;Amyloid arthropathy;Amyloidosis;Amyloidosis senile;Anaphylactic reaction;Anaphylactic shock;Anaphylactic transfusion reaction;Anaphylactoid reaction;Anaphylactoid shock;Anaphylactoid syndrome of pregnancy;Angioedema;Angiopathic neuropathy;Ankylosing spondylitis;Anosmia;Antiacetylcholine receptor antibody positive;Anti-actin antibody positive;Anti-aquaporin-4 antibody positive;Anti-basal ganglia antibody positive;Anti-cyclic citrullinated peptide antibody positive;Anti-epithelial antibody positive;Anti-erythrocyte antibody positive;Anti-exosome complex antibody positive;Anti-GAD antibody negative;Anti-GAD antibody positive;Anti-ganglioside antibody positive;Antigliadin antibody positive;Anti-glomerular basement membrane antibody positive;Anti-glomerular basement membrane disease;Anti-glycyl-tRNA synthetase antibody positive;Anti-HLA antibody test positive;Anti-IA2 antibody positive;Anti-insulin antibody increased;Anti-insulin antibody positive;Anti-insulin receptor antibody increased;Anti-insulin receptor antibody positive;Anti-interferon antibody negative;Anti-interferon antibody positive;Anti-islet cell antibody positive;Antimitochondrial antibody positive;Anti-muscle specific kinase antibody positive;Anti-myelin-associated glycoprotein antibodies positive;Anti-myelin-associated glycoprotein associated polyneuropathy;Antimyocardial antibody positive;Anti-neuronal antibody positive;Antineutrophil cytoplasmic antibody increased;Antineutrophil cytoplasmic antibody positive;Anti-neutrophil cytoplasmic antibody positive vasculitis;Anti-NMDA antibody positive;Antinuclear antibody increased;Antinuclear antibody positive;Antiphospholipid antibodies positive;Antiphospholipid syndrome;Anti-platelet antibody positive;Anti-prothrombin antibody positive;Antiribosomal P antibody positive;Anti-RNA polymerase III antibody positive;Anti-saccharomyces cerevisiae antibody test positive;Anti-sperm antibody positive;Anti-SRP antibody positive;Antisynthetase syndrome;Anti-thyroid antibody positive;Anti-transglutaminase antibody increased;Anti-VGCC antibody positive;Anti-VGKC antibody positive;Anti-vimentin antibody positive;Antiviral prophylaxis;Antiviral treatment;Anti-zinc transporter 8 antibody positive;Aortic embolus;Aortic thrombosis;Aortitis;Aplasia pure red cell;Aplastic anaemia;Application site thrombosis;Application site vasculitis;Arrhythmia;Arterial bypass occlusion;Arterial bypass thrombosis;Arterial thrombosis;Arteriovenous fistula thrombosis;Arteriovenous graft site stenosis;Arteriovenous graft thrombosis;Arteritis;Arteritis

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coronary;Arthralgia;Arthritis;Arthritis enteropathic;Ascites;Aseptic cavernous sinus thrombosis;Aspartate aminotransferase abnormal;Aspartate aminotransferase increased;Aspartate-glutamate-transporter deficiency;AST to platelet ratio index increased;AST/ALT ratio abnormal;Asthma;Asymptomatic COVID-19;Ataxia;Atheroembolism;Atonic seizures;Atrial thrombosis;Atrophic thyroiditis;Atypical benign partial epilepsy;Atypical pneumonia;Aura;Autoantibody positive;Autoimmune anaemia;Autoimmune aplastic anaemia;Autoimmune arthritis;Autoimmune blistering disease;Autoimmune cholangitis;Autoimmune colitis;Autoimmune demyelinating disease;Autoimmune dermatitis;Autoimmune disorder;Autoimmune encephalopathy;Autoimmune endocrine disorder;Autoimmune enteropathy;Autoimmune eye disorder;Autoimmune haemolytic anaemia;Autoimmune heparin-induced thrombocytopenia;Autoimmune hepatitis;Autoimmune hyperlipidaemia;Autoimmune hypothyroidism;Autoimmune inner ear disease;Autoimmune lung disease;Autoimmune lymphoproliferative syndrome;Autoimmune myocarditis;Autoimmune myositis;Autoimmune nephritis;Autoimmune neuropathy;Autoimmune neutropenia;Autoimmune pancreatitis;Autoimmune pancytopenia;Autoimmune pericarditis;Autoimmune retinopathy;Autoimmune thyroid disorder;Autoimmune thyroiditis;Autoimmune uveitis;Autoinflammation with infantile enterocolitis;Autoinflammatory disease;Automatism epileptic;Autonomic nervous system imbalance;Autonomic seizure;Axial spondyloarthritis;Axillary vein thrombosis;Axonal and demyelinating polyneuropathy;Axonal neuropathy;Bacterascites;Baltic myoclonic epilepsy;Band sensation;Basedow's disease;Basilar artery thrombosis;Basophilopenia;B-cell aplasia;Behcet's syndrome;Benign ethnic neutropenia;Benign familial neonatal convulsions;Benign familial pemphigus;Benign rolandic epilepsy;Beta-2 glycoprotein antibody positive;Bickerstaff's encephalitis;Bile output abnormal;Bile output decreased;Biliary ascites;Bilirubin conjugated abnormal;Bilirubin conjugated increased;Bilirubin urine present;Biopsy liver abnormal;Biotinidase deficiency;Birdshot chorioretinopathy;Blood alkaline phosphatase abnormal;Blood alkaline phosphatase increased;Blood bilirubin abnormal;Blood bilirubin increased;Blood bilirubin unconjugated increased;Blood cholinesterase abnormal;Blood cholinesterase decreased;Blood pressure decreased;Blood pressure diastolic decreased;Blood pressure systolic decreased;Blue toe syndrome;Brachiocephalic vein thrombosis;Brain stem embolism;Brain stem thrombosis;Bromosulphthalein test abnormal;Bronchial oedema;Bronchitis;Bronchitis mycoplasmal;Bronchitis viral;Bronchopulmonary aspergillosis allergic;Bronchospasm;Budd-Chiari syndrome;Bulbar palsy;Butterfly rash;C1q nephropathy;Caesarean section;Calcium embolism;Capillaritis;Caplan's syndrome;Cardiac amyloidosis;Cardiac arrest;Cardiac failure;Cardiac failure acute;Cardiac sarcoidosis;Cardiac ventricular thrombosis;Cardiogenic shock;Cardiolipin antibody positive;Cardiopulmonary failure;Cardio-respiratory arrest;Cardio-respiratory distress;Cardiovascular insufficiency;Carotid arterial embolus;Carotid artery thrombosis;Cataplexy;Catheter site thrombosis;Catheter site vasculitis;Cavernous sinus thrombosis;CDKL5 deficiency disorder;CEC syndrome;Cement embolism;Central nervous system lupus;Central nervous system vasculitis;Cerebellar artery thrombosis;Cerebellar embolism;Cerebral amyloid angiopathy;Cerebral arteritis;Cerebral artery embolism;Cerebral artery thrombosis;Cerebral gas embolism;Cerebral microembolism;Cerebral septic infarct;Cerebral thrombosis;Cerebral venous sinus thrombosis;Cerebral venous thrombosis;Cerebrospinal thrombotic

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tamponade;Cerebrovascular accident;Change in seizure presentation;Chest discomfort;Child-Pugh-Turcotte score abnormal;Child-Pugh-Turcotte score increased;Chillblains;Choking;Choking sensation;Cholangitis sclerosing;Chronic autoimmune glomerulonephritis;Chronic cutaneous lupus erythematosus;Chronic fatigue syndrome;Chronic gastritis;Chronic inflammatory demyelinating polyradiculoneuropathy;Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids;Chronic recurrent multifocal osteomyelitis;Chronic respiratory failure;Chronic spontaneous urticaria;Circulatory collapse;Circumoral oedema;Circumoral swelling;Clinically isolated syndrome;Clonic convulsion;Coeliac disease;Cogan's syndrome;Cold agglutinins positive;Cold type haemolytic anaemia;Colitis;Colitis erosive;Colitis herpes;Colitis microscopic;Colitis ulcerative;Collagen disorder;Collagen-vascular disease;Complement factor abnormal;Complement factor C1 decreased;Complement factor C2 decreased;Complement factor C3 decreased;Complement factor C4 decreased;Complement factor decreased;Computerised tomogram liver abnormal;Concentric sclerosis;Congenital anomaly;Congenital bilateral perisylvian syndrome;Congenital herpes simplex infection;Congenital myasthenic syndrome;Congenital varicella infection;Congestive hepatopathy;Convulsion in childhood;Convulsions local;Convulsive threshold lowered;Coombs positive haemolytic anaemia;Coronary artery disease;Coronary artery embolism;Coronary artery thrombosis;Coronary bypass thrombosis;Coronavirus infection;Coronavirus test;Coronavirus test negative;Coronavirus test positive;Corpus callosotomy;Cough;Cough variant asthma;COVID-19;COVID-19 immunisation;COVID-19 pneumonia;COVID-19 prophylaxis;COVID-19 treatment;Cranial nerve disorder;Cranial nerve palsies multiple;Cranial nerve paralysis;CREST syndrome;Crohn's disease;Cryofibrinogenaemia;Cryoglobulinaemia;CSF oligoclonal band present;CSWS syndrome;Cutaneous amyloidosis;Cutaneous lupus erythematosus;Cutaneous sarcoidosis;Cutaneous vasculitis;Cyanosis;Cyclic neutropenia;Cystitis interstitial;Cytokine release syndrome;Cytokine storm;De novo purine synthesis inhibitors associated acute inflammatory syndrome;Death neonatal;Deep vein thrombosis;Deep vein thrombosis postoperative;Deficiency of bile secretion;Deja vu;Demyelinating polyneuropathy;Demyelination;Dermatitis;Dermatitis bullous;Dermatitis herpetiformis;Dermatomyositis;Device embolisation;Device related thrombosis;Diabetes mellitus;Diabetic ketoacidosis;Diabetic mastopathy;Dialysis amyloidosis;Dialysis membrane reaction;Diastolic hypotension;Diffuse vasculitis;Digital pitting scar;Disseminated intravascular coagulation;Disseminated intravascular coagulation in newborn;Disseminated neonatal herpes simplex;Disseminated varicella;Disseminated varicella zoster vaccine virus infection;Disseminated varicella zoster virus infection;DNA antibody positive;Double cortex syndrome;Double stranded DNA antibody positive;Dreamy state;Dressler's syndrome;Drop attacks;Drug withdrawal convulsions;Dyspnoea;Early infantile epileptic encephalopathy with burst-suppression;Eclampsia;Eczema herpeticum;Embolia cutis medicamentosa;Embolic cerebellar infarction;Embolic cerebral infarction;Embolic pneumonia;Embolic stroke;Embolism;Embolism arterial;Embolism venous;Encephalitis;Encephalitis allergic;Encephalitis autoimmune;Encephalitis brain stem;Encephalitis haemorrhagic;Encephalitis periaxialis diffusa;Encephalitis post immunisation;Encephalomyelitis;Encephalopathy;Endocrine disorder;Endocrine ophthalmopathy;Endotracheal intubation;Enteritis;Enteritis leukopenic;Enterobacter pneumonia;Enterocolitis;Enteropathic spondylitis;Eosinopenia;Eosinophilic

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fasciitis;Eosinophilic granulomatosis with polyangiitis;Eosinophilic oesophagitis;Epidermolysis;Epilepsy;Epilepsy surgery;Epilepsy with myoclonic-atonic seizures;Epileptic aura;Epileptic psychosis;Erythema;Erythema induratum;Erythema multiforme;Erythema nodosum;Evans syndrome;Exanthema subitum;Expanded disability status scale score decreased;Expanded disability status scale score increased;Exposure to communicable disease;Exposure to SARS-CoV-2;Eye oedema;Eye pruritus;Eye swelling;Eyelid oedema;Face oedema;Facial paralysis;Facial paresis;Faciobrachial dystonic seizure;Fat embolism;Febrile convulsion;Febrile infection-related epilepsy syndrome;Febrile neutropenia;Felty's syndrome;Femoral artery embolism;Fibrillary glomerulonephritis;Fibromyalgia;Flushing;Foaming at mouth;Focal cortical resection;Focal dyscognitive seizures;Foetal distress syndrome;Foetal placental thrombosis;Foetor hepaticus;Foreign body embolism;Frontal lobe epilepsy;Fulminant type 1 diabetes mellitus;Galactose elimination capacity test abnormal;Galactose elimination capacity test decreased;Gamma-glutamyltransferase abnormal;Gamma-glutamyltransferase increased;Gastritis herpes;Gastrointestinal amyloidosis;Gelastic seizure;Generalised onset non-motor seizure;Generalised tonic-clonic seizure;Genital herpes;Genital herpes simplex;Genital herpes zoster;Giant cell arteritis;Glomerulonephritis;Glomerulonephritis membranoproliferative;Glomerulonephritis membranous;Glomerulonephritis rapidly progressive;Glossopharyngeal nerve paralysis;Glucose transporter type 1 deficiency syndrome;Glutamate dehydrogenase increased;Glycocholic acid increased;GM2 gangliosidosis;Goodpasture's syndrome;Graft thrombosis;Granulocytopenia;Granulocytopenia neonatal;Granulomatosis with polyangiitis;Granulomatous dermatitis;Grey matter heterotopia;Guanase increased;Guillain-Barre syndrome;Haemolytic anaemia;Haemophagocytic lymphohistiocytosis;Haemorrhage;Haemorrhagic ascites;Haemorrhagic disorder;Haemorrhagic pneumonia;Haemorrhagic varicella syndrome;Haemorrhagic vasculitis;Hantavirus pulmonary infection;Hashimoto's encephalopathy;Hashitoxicosis;Hemimegalencephaly;Henoch-Schonlein purpura;Henoch-Schonlein purpura nephritis;Hepaplastin abnormal;Hepaplastin decreased;Heparin-induced thrombocytopenia;Hepatic amyloidosis;Hepatic artery embolism;Hepatic artery flow decreased;Hepatic artery thrombosis;Hepatic enzyme abnormal;Hepatic enzyme decreased;Hepatic enzyme increased;Hepatic fibrosis marker abnormal;Hepatic fibrosis marker increased;Hepatic function abnormal;Hepatic hydrothorax;Hepatic hypertrophy;Hepatic hypoperfusion;Hepatic lymphocytic infiltration;Hepatic mass;Hepatic pain;Hepatic sequestration;Hepatic vascular resistance increased;Hepatic vascular thrombosis;Hepatic vein embolism;Hepatic vein thrombosis;Hepatic venous pressure gradient abnormal;Hepatic venous pressure gradient increased;Hepatitis;Hepatobiliary scan abnormal;Hepatomegaly;Hepatosplenomegaly;Hereditary angioedema with C1 esterase inhibitor deficiency;Herpes dermatitis;Herpes gestationis;Herpes oesophagitis;Herpes ophthalmic;Herpes pharyngitis;Herpes sepsis;Herpes simplex;Herpes simplex cervicitis;Herpes simplex colitis;Herpes simplex encephalitis;Herpes simplex gastritis;Herpes simplex hepatitis;Herpes simplex meningitis;Herpes simplex meningoencephalitis;Herpes simplex meningomyelitis;Herpes simplex necrotising retinopathy;Herpes simplex oesophagitis;Herpes simplex otitis externa;Herpes simplex pharyngitis;Herpes simplex pneumonia;Herpes simplex reactivation;Herpes simplex sepsis;Herpes simplex viraemia;Herpes simplex virus conjunctivitis neonatal;Herpes simplex visceral;Herpes virus

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infection;Herpes zoster;Herpes zoster cutaneous disseminated;Herpes zoster infection neurological;Herpes zoster meningitis;Herpes zoster meningoencephalitis;Herpes zoster meningomyelitis;Herpes zoster meningoradiculitis;Herpes zoster necrotising retinopathy;Herpes zoster oticus;Herpes zoster pharyngitis;Herpes zoster reactivation;Herpetic radiculopathy;Histone antibody positive;Hoigne's syndrome;Human herpesvirus 6 encephalitis;Human herpesvirus 6 infection;Human herpesvirus 6 infection reactivation;Human herpesvirus 7 infection;Human herpesvirus 8 infection;Hyperammonaemia;Hyperbilirubinaemia;Hypercholia;Hypergammaglobulinaemia benign monoclonal;Hyperglycaemic seizure;Hypersensitivity;Hypersensitivity vasculitis;Hyperthyroidism;Hypertransaminasaemia;Hyperventilation;Hypoalbuminaemia;Hypocalcaemic seizure;Hypogammaglobulinaemia;Hypoglossal nerve paralysis;Hypoglossal nerve paresis;Hypoglycaemic seizure;Hyponatraemic seizure;Hypotension;Hypotensive crisis;Hypothenar hammer syndrome;Hypothyroidism;Hypoxia;Idiopathic CD4 lymphocytopenia;Idiopathic generalised epilepsy;Idiopathic interstitial pneumonia;Idiopathic neutropenia;Idiopathic pulmonary fibrosis;IgA nephropathy;IgM nephropathy;IIIrd nerve paralysis;IIIrd nerve paresis;Iliac artery embolism;Immune thrombocytopenia;Immune-mediated adverse reaction;Immune-mediated cholangitis;Immune-mediated cholestasis;Immune-mediated cytopenia;Immune-mediated encephalitis;Immune-mediated encephalopathy;Immune-mediated endocrinopathy;Immune-mediated enterocolitis;Immune-mediated gastritis;Immune-mediated hepatic disorder;Immune-mediated hepatitis;Immune-mediated hyperthyroidism;Immune-mediated hypothyroidism;Immune-mediated myocarditis;Immune-mediated myositis;Immune-mediated nephritis;Immune-mediated neuropathy;Immune-mediated pancreatitis;Immune-mediated pneumonitis;Immune-mediated renal disorder;Immune-mediated thyroiditis;Immune-mediated uveitis;Immunoglobulin G4 related disease;Immunoglobulins abnormal;Implant site thrombosis;Inclusion body myositis;Infantile genetic agranulocytosis;Infantile spasms;Infected vasculitis;Infective thrombosis;Inflammation;Inflammatory bowel disease;Infusion site thrombosis;Infusion site vasculitis;Injection site thrombosis;Injection site urticaria;Injection site vasculitis;Instillation site thrombosis;Insulin autoimmune syndrome;Interstitial granulomatous dermatitis;Interstitial lung disease;Intracardiac mass;Intracardiac thrombus;Intracranial pressure increased;Intrapericardial thrombosis;Intrinsic factor antibody abnormal;Intrinsic factor antibody positive;IPEX syndrome;Irregular breathing;IRVAN syndrome;IVth nerve paralysis;IVth nerve paresis;JC polyomavirus test positive;JC virus CSF test positive;Jeavons syndrome;Jugular vein embolism;Jugular vein thrombosis;Juvenile idiopathic arthritis;Juvenile myoclonic epilepsy;Juvenile polymyositis;Juvenile psoriatic arthritis;Juvenile spondyloarthritis;Kaposi sarcoma inflammatory cytokine syndrome;Kawasaki's disease;Kayser-Fleischer ring;Keratoderma blenorrhagica;Ketosis-prone diabetes mellitus;Kounis syndrome;Lafora's myoclonic epilepsy;Lambl's excrescences;Laryngeal dyspnoea;Laryngeal oedema;Laryngeal rheumatoid arthritis;Laryngospasm;Laryngotracheal oedema;Latent autoimmune diabetes in adults;LE cells present;Lemierre syndrome;Lennox-Gastaut syndrome;Leucine aminopeptidase increased;Leukoencephalomyelitis;Leukoencephalopathy;Leukopenia;Leukopenia neonatal;Lewis-Sumner syndrome;Lhermitte's sign;Lichen planopilaris;Lichen planus;Lichen sclerosus;Limbic encephalitis;Linear IgA disease;Lip oedema;Lip swelling;Liver function test abnormal;Liver function test decreased;Liver function test increased;Liver induration;Liver injury;Liver iron concentration abnormal;Liver iron concentration

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increased;Liver opacity;Liver palpable;Liver sarcoidosis;Liver scan abnormal;Liver tenderness;Low birth weight baby;Lower respiratory tract herpes infection;Lower respiratory tract infection;Lower respiratory tract infection viral;Lung abscess;Lupoid hepatic cirrhosis;Lupus cystitis;Lupus encephalitis;Lupus endocarditis;Lupus enteritis;Lupus hepatitis;Lupus myocarditis;Lupus myositis;Lupus nephritis;Lupus pancreatitis;Lupus pleurisy;Lupus pneumonitis;Lupus vasculitis;Lupus-like syndrome;Lymphocytic hypophysitis;Lymphocytopenia neonatal;Lymphopenia;MAGIC syndrome;Magnetic resonance imaging liver abnormal;Magnetic resonance proton density fat fraction measurement;Mahler sign;Manufacturing laboratory analytical testing issue;Manufacturing materials issue;Manufacturing production issue;Marburg's variant multiple sclerosis;Marchiafava-Bignami disease;Marine Lenhart syndrome;Mastocytic enterocolitis;Maternal exposure during pregnancy;Medical device site thrombosis;Medical device site vasculitis;MELAS syndrome;Meningitis;Meningitis aseptic;Meningitis herpes;Meningoencephalitis herpes simplex neonatal;Meningoencephalitis herpetic;Meningomyelitis herpes;MERS-CoV test;MERS-CoV test negative;MERS-CoV test positive;Mesangioproliferative glomerulonephritis;Mesenteric artery embolism;Mesenteric artery thrombosis;Mesenteric vein thrombosis;Metapneumovirus infection;Metastatic cutaneous Crohn's disease;Metastatic pulmonary embolism;Microangiopathy;Microembolism;Microscopic polyangiitis;Middle East respiratory syndrome;Migraine-triggered seizure;Miliary pneumonia;Miller Fisher syndrome;Mitochondrial aspartate aminotransferase increased;Mixed connective tissue disease;Model for end stage liver disease score abnormal;Model for end stage liver disease score increased;Molar ratio of total branched-chain amino acid to tyrosine;Molybdenum cofactor deficiency;Monocytopenia;Mononeuritis;Mononeuropathy multiplex;Morphoea;Morvan syndrome;Mouth swelling;Moyamoya disease;Multifocal motor neuropathy;Multiple organ dysfunction syndrome;Multiple sclerosis;Multiple sclerosis relapse;Multiple sclerosis relapse prophylaxis;Multiple subpial transection;Multisystem inflammatory syndrome in children;Muscular sarcoidosis;Myasthenia gravis;Myasthenia gravis crisis;Myasthenia gravis neonatal;Myasthenic syndrome;Myelitis;Myelitis transverse;Myocardial infarction;Myocarditis;Myocarditis post infection;Myoclonic epilepsy;Myoclonic epilepsy and ragged-red fibres;Myokymia;Myositis;Narcolepsy;Nasal herpes;Nasal obstruction;Necrotising herpetic retinopathy;Neonatal Crohn's disease;Neonatal epileptic seizure;Neonatal lupus erythematosus;Neonatal mucocutaneous herpes simplex;Neonatal pneumonia;Neonatal seizure;Nephritis;Nephrogenic systemic fibrosis;Neuralgic amyotrophy;Neuritis;Neuritis cranial;Neuromyelitis optica pseudo relapse;Neuromyelitis optica spectrum disorder;Neuromyotonia;Neuronal neuropathy;Neuropathy peripheral;Neuropathy, ataxia, retinitis pigmentosa syndrome;Neuropsychiatric lupus;Neurosarcoidosis;Neutropenia;Neutropenia neonatal;Neutropenic colitis;Neutropenic infection;Neutropenic sepsis;Nodular rash;Nodular vasculitis;Noninfectious myelitis;Noninfective encephalitis;Noninfective encephalomyelitis;Noninfective oophoritis;Obstetrical pulmonary embolism;Occupational exposure to communicable disease;Occupational exposure to SARS-CoV-2;Ocular hyperaemia;Ocular myasthenia;Ocular pemphigoid;Ocular sarcoidosis;Ocular vasculitis;Oculofacial paralysis;Oedema;Oedema blister;Oedema due to hepatic disease;Oedema mouth;Oesophageal achalasia;Ophthalmic artery thrombosis;Ophthalmic herpes simplex;Ophthalmic herpes zoster;Ophthalmic vein thrombosis;Optic neuritis;Optic

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neuropathy;Optic perineuritis;Oral herpes;Oral lichen planus;Oropharyngeal oedema;Oropharyngeal spasm;Oropharyngeal swelling;Osmotic demyelination syndrome;Ovarian vein thrombosis;Overlap syndrome;Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection;Paget-Schroetter syndrome;Palindromic rheumatism;Palisaded neutrophilic granulomatous dermatitis;Palmoplantar keratoderma;Palpable purpura;Pancreatitis;Panencephalitis;Papillophlebitis;Paracancerous pneumonia;Paradoxical embolism;Parainfluenzae viral laryngotracheobronchitis;Paraneoplastic dermatomyositis;Paraneoplastic pemphigus;Paraneoplastic thrombosis;Paresis cranial nerve;Parietal cell antibody positive;Paroxysmal nocturnal haemoglobinuria;Partial seizures;Partial seizures with secondary generalisation;Patient isolation;Pelvic venous thrombosis;Pemphigoid;Pemphigus;Penile vein thrombosis;Pericarditis;Pericarditis lupus;Perihepatic discomfort;Periorbital oedema;Periorbital swelling;Peripheral artery thrombosis;Peripheral embolism;Peripheral ischaemia;Peripheral vein thrombus extension;Periportal oedema;Peritoneal fluid protein abnormal;Peritoneal fluid protein decreased;Peritoneal fluid protein increased;Peritonitis lupus;Pernicious anaemia;Petit mal epilepsy;Pharyngeal oedema;Pharyngeal swelling;Pityriasis lichenoides et varioliformis acuta;Placenta praevia;Pleuroparenchymal fibroelastosis;Pneumobilia;Pneumonia;Pneumonia adenoviral;Pneumonia cytomegaloviral;Pneumonia herpes viral;Pneumonia influenzal;Pneumonia measles;Pneumonia mycoplasmal;Pneumonia necrotising;Pneumonia parainfluenzae viral;Pneumonia respiratory syncytial viral;Pneumonia viral;POEMS syndrome;Polyarteritis nodosa;Polyarthritis;Polychondritis;Polyglandular autoimmune syndrome type I;Polyglandular autoimmune syndrome type II;Polyglandular autoimmune syndrome type III;Polyglandular disorder;Polymicrogyria;Polymyalgia rheumatica;Polymyositis;Polyneuropathy;Polyneuropathy idiopathic progressive;Portal pyaemia;Portal vein embolism;Portal vein flow decreased;Portal vein pressure increased;Portal vein thrombosis;Portosplenomesenteric venous thrombosis;Post procedural hypotension;Post procedural pneumonia;Post procedural pulmonary embolism;Post stroke epilepsy;Post stroke seizure;Post thrombotic retinopathy;Post thrombotic syndrome;Post viral fatigue syndrome;Postictal headache;Postictal paralysis;Postictal psychosis;Postictal state;Postoperative respiratory distress;Postoperative respiratory failure;Postoperative thrombosis;Postpartum thrombosis;Postpartum venous thrombosis;Postpericardiotomy syndrome;Post-traumatic epilepsy;Postural orthostatic tachycardia syndrome;Precerebral artery thrombosis;Pre-eclampsia;Preictal state;Premature labour;Premature menopause;Primary amyloidosis;Primary biliary cholangitis;Primary progressive multiple sclerosis;Procedural shock;Proctitis herpes;Proctitis ulcerative;Product availability issue;Product distribution issue;Product supply issue;Progressive facial hemiatrophy;Progressive multifocal leukoencephalopathy;Progressive multiple sclerosis;Progressive relapsing multiple sclerosis;Prosthetic cardiac valve thrombosis;Pruritus;Pruritus allergic;Pseudovasculitis;Psoriasis;Psoriatic arthropathy;Pulmonary amyloidosis;Pulmonary artery thrombosis;Pulmonary embolism;Pulmonary fibrosis;Pulmonary haemorrhage;Pulmonary microemboli;Pulmonary oil microembolism;Pulmonary renal syndrome;Pulmonary sarcoidosis;Pulmonary sepsis;Pulmonary thrombosis;Pulmonary tumour thrombotic microangiopathy;Pulmonary vasculitis;Pulmonary veno-occlusive disease;Pulmonary venous thrombosis;Pyoderma gangrenosum;Pyostomatitis vegetans;Pyrexia;Quarantine;Radiation leukopenia;Radiculitis

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brachial;Radiologically isolated syndrome;Rash;Rash erythematous;Rash pruritic;Rasmussen encephalitis;Raynaud's phenomenon;Reactive capillary endothelial proliferation;Relapsing multiple sclerosis;Relapsing-remitting multiple sclerosis;Renal amyloidosis;Renal arteritis;Renal artery thrombosis;Renal embolism;Renal failure;Renal vascular thrombosis;Renal vasculitis;Renal vein embolism;Renal vein thrombosis;Respiratory arrest;Respiratory disorder;Respiratory distress;Respiratory failure;Respiratory paralysis;Respiratory syncytial virus bronchiolitis;Respiratory syncytial virus bronchitis;Retinal artery embolism;Retinal artery occlusion;Retinal artery thrombosis;Retinal vascular thrombosis;Retinal vasculitis;Retinal vein occlusion;Retinal vein thrombosis;Retinol binding protein decreased;Retinopathy;Retrograde portal vein flow;Retroperitoneal fibrosis;Reversible airways obstruction;Reynold's syndrome;Rheumatic brain disease;Rheumatic disorder;Rheumatoid arthritis;Rheumatoid factor increased;Rheumatoid factor positive;Rheumatoid factor quantitative increased;Rheumatoid lung;Rheumatoid neutrophilic dermatosis;Rheumatoid nodule;Rheumatoid nodule removal;Rheumatoid scleritis;Rheumatoid vasculitis;Saccadic eye movement;SAPHO syndrome;Sarcoidosis;SARS-CoV-1 test;SARS-CoV-1 test negative;SARS-CoV-1 test positive;SARS-CoV-2 antibody test;SARS-CoV-2 antibody test negative;SARS-CoV-2 antibody test positive;SARS-CoV-2 carrier;SARS-CoV-2 sepsis;SARS-CoV-2 test;SARS-CoV-2 test false negative;SARS-CoV-2 test false positive;SARS-CoV-2 test negative;SARS-CoV-2 test positive;SARS-CoV-2 viraemia;Satoyoshi syndrome;Schizencephaly;Scleritis;Sclerodactylia;Scleroderma;Scleroderma associated digital ulcer;Scleroderma renal crisis;Scleroderma-like reaction;Secondary amyloidosis;Secondary cerebellar degeneration;Secondary progressive multiple sclerosis;Segmented hyalinising vasculitis;Seizure;Seizure anoxic;Seizure cluster;Seizure like phenomena;Seizure prophylaxis;Sensation of foreign body;Septic embolus;Septic pulmonary embolism;Severe acute respiratory syndrome;Severe myoclonic epilepsy of infancy;Shock;Shock symptom;Shrinking lung syndrome;Shunt thrombosis;Silent thyroiditis;Simple partial seizures;Sjogren's syndrome;Skin swelling;SLE arthritis;Smooth muscle antibody positive;Sneezing;Spinal artery embolism;Spinal artery thrombosis;Splenic artery thrombosis;Splenic embolism;Splenic thrombosis;Splenic vein thrombosis;Spondylitis;Spondyloarthropathy;Spontaneous heparin-induced thrombocytopenia syndrome;Status epilepticus;Stevens-Johnson syndrome;Stiff leg syndrome;Stiff person syndrome;Stillbirth;Still's disease;Stoma site thrombosis;Stoma site vasculitis;Stress cardiomyopathy;Stridor;Subacute cutaneous lupus erythematosus;Subacute endocarditis;Subacute inflammatory demyelinating polyneuropathy;Subclavian artery embolism;Subclavian artery thrombosis;Subclavian vein thrombosis;Sudden unexplained death in epilepsy;Superior sagittal sinus thrombosis;Susac's syndrome;Suspected COVID-19;Swelling;Swelling face;Swelling of eyelid;Swollen tongue;Sympathetic ophthalmia;Systemic lupus erythematosus;Systemic lupus erythematosus disease activity index abnormal;Systemic lupus erythematosus disease activity index decreased;Systemic lupus erythematosus disease activity index increased;Systemic lupus erythematosus rash;Systemic scleroderma;Systemic sclerosis pulmonary;Tachycardia;Tachypnoea;Takayasu's arteritis;Temporal lobe epilepsy;Terminal ileitis;Testicular autoimmunity;Throat tightness;Thromboangiitis obliterans;Thrombocytopenia;Thrombocytopenic purpura;Thrombophlebitis;Thrombophlebitis migrans;Thrombophlebitis

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neonatal;Thrombophlebitis septic;Thrombophlebitis superficial;Thromboplastin antibody positive;Thrombosis;Thrombosis corpora cavernosa;Thrombosis in device;Thrombosis mesenteric vessel;Thrombotic cerebral infarction;Thrombotic microangiopathy;Thrombotic stroke;Thrombotic thrombocytopenic purpura;Thyroid disorder;Thyroid stimulating immunoglobulin increased;Thyroiditis;Tongue amyloidosis;Tongue biting;Tongue oedema;Tonic clonic movements;Tonic convulsion;Tonic posturing;Topectomy;Total bile acids increased;Toxic epidermal necrolysis;Toxic leukoencephalopathy;Toxic oil syndrome;Tracheal obstruction;Tracheal oedema;Tracheobronchitis;Tracheobronchitis mycoplasmal;Tracheobronchitis viral;Transaminases abnormal;Transaminases increased;Transfusion-related alloimmune neutropenia;Transient epileptic amnesia;Transverse sinus thrombosis;Trigeminal nerve paresis;Trigeminal neuralgia;Trigeminal palsy;Truncus coeliacus thrombosis;Tuberous sclerosis complex;Tubulointerstitial nephritis and uveitis syndrome;Tumefactive multiple sclerosis;Tumour embolism;Tumour thrombosis;Type 1 diabetes mellitus;Type I hypersensitivity;Type III immune complex mediated reaction;Uhthoff's phenomenon;Ulcerative keratitis;Ultrasound liver abnormal;Umbilical cord thrombosis;Uncinate fits;Undifferentiated connective tissue disease;Upper airway obstruction;Urine bilirubin increased;Urobilinogen urine decreased;Urobilinogen urine increased;Urticaria;Urticaria papular;Urticarial vasculitis;Uterine rupture;Uveitis;Vaccination site thrombosis;Vaccination site vasculitis;Vagus nerve paralysis;Varicella;Varicella keratitis;Varicella post vaccine;Varicella zoster gastritis;Varicella zoster oesophagitis;Varicella zoster pneumonia;Varicella zoster sepsis;Varicella zoster virus infection;Vasa praevia;Vascular graft thrombosis;Vascular pseudoaneurysm thrombosis;Vascular purpura;Vascular stent thrombosis;Vasculitic rash;Vasculitic ulcer;Vasculitis;Vasculitis gastrointestinal;Vasculitis necrotising;Vena cava embolism;Vena cava thrombosis;Venous intravasation;Venous recanalisation;Venous thrombosis;Venous thrombosis in pregnancy;Venous thrombosis limb;Venous thrombosis neonatal;Vertebral artery thrombosis;Vessel puncture site thrombosis;Visceral venous thrombosis;VIth nerve paralysis;VIth nerve paresis;Vitiligo;Vocal cord paralysis;Vocal cord paresis;Vogt-Koyanagi-Harada disease;Warm type haemolytic anaemia;Wheezing;White nipple sign;XIth nerve paralysis;X-ray hepatobiliary abnormal;Young's syndrome;Zika virus associated Guillain Barre syndrome.

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"HE27"

Exercise and diet reduce risk of diabetes, US study shows

Fred Charatan *Florida*

Patients vulnerable to type 2 diabetes can more than halve their risk of developing the disease by eating a low fat diet and taking half an hour of exercise a day, says new US research from the National Institutes of Health.

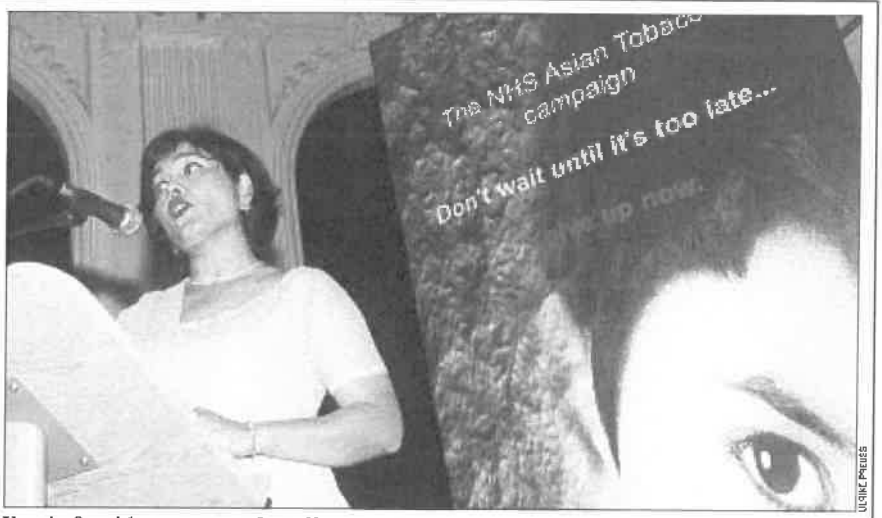
The study found that for patients at risk of type 2 diabetes diet and exercise were more effective than the drug metformin at preventing the disease. The findings come from the diabetes prevention programme, a clinical trial comparing diet and exercise with metformin treatment in preventing type 2 diabetes. It was conducted at 27 US medical centres and involved 3234 people with impaired glucose tolerance, a condition that often precedes diabetes.

On the advice of the diabetes prevention programme's external data monitoring board, the trial ended a year early because the data had clearly answered the main research questions. The research has not been published in a journal, but a full report of the study is available on the National Institutes of Health website (www.nih.gov).

Forty five per cent of the participants were from minority groups in whom type 2 diabetes is disproportionately prevalent, including African Americans, Hispanic Americans, Asian Americans, Pacific Islanders, and American Indians. The trial also recruited other high risk groups, including people aged 60 and above, women with a history of gestational diabetes, and people with a first degree relative with type 2 diabetes.

Participants were randomly assigned to one of three groups. One made intensive lifestyle changes, with the aim of reducing weight by 7% through a low fat diet and exercising for 150 minutes a week. A second was treated twice daily with 850 mg metformin, a drug to treat type 2 diabetes. A third was given a placebo drug.

The results showed that among people who make intensive lifestyle changes the risk of developing type 2 diabetes is reduced by 58% (compared with 31% among people who take metformin). Participants took on average 30 minutes of physical activity a day—usually walking or other moderately intensive exercise—and lost 5-7% of their body weight. Those treated with metformin reduced their risk of getting type 2 diabetes by 31%. □



Yasmin Querishe, a presenter from Channel East, a specialist South Asian television channel in Britain, helps to launch a £750 000 government drive to reduce the high level of smoking and tobacco chewing in Asian communities.
The campaign aims to make Asian people more aware of the impact tobacco can have on health risks already associated with South Asian groups, such as angina, stroke, heart attack and high blood pressure. It includes advertising in the Bangladeshi, Indian, and Pakistani press.
High rates of smoking are a particular problem among Bangladeshi men, 44% of whom smoke cigarettes compared with 27% of men in the general population. Research has also shown that chewing tobacco, popular among South Asian people, increases the risk of oral cancer as much as fivefold.
Helen Barratt *BMJ*

Bayer decides to withdraw cholesterol lowering drug

Fred Charatan *Florida*

Cerivastatin (Baycol in the United States, Lipobay in the United Kingdom), a cholesterol lowering drug made by Bayer Corporation and initially approved in the US in 1997, has been withdrawn by the manufacturer.

There have been 31 deaths in the US from severe rhabdomyolysis in patients taking the drug. Twelve patients were taking concomitant gemfibrozil, which lowers blood concentration of triglycerides.

Rhabdomyolysis, a serious and potentially fatal adverse effect of all statin (cholesterol lowering) drugs, is about 10 times more common with cerivastatin than with other statins, according to Dr John Jenkins, director of the office of drug evaluation at the US Food and Drug Administration (FDA).

Fatal rhabdomyolysis after cerivastatin treatment has been reported most frequently when the drug is given at high doses, when it is used in elderly patients, and particularly when it is prescribed with gemfibrozil.

In a letter to health professionals dated 8 August 2001, Bayer said that its data indicated "an increased reporting rate of rhabdomyolysis at the 0.8 mg dose of Baycol alone." The FDA agreed with and supported Bayer's decision to withdraw cerivastatin from the US market.

In a "Talk Paper" the FDA wrote: "Patients who are taking Baycol should consult with their physicians about switching to alternative medications to control their cholesterol levels. Patients taking Baycol who are experiencing muscle pain or are also taking gemfibrozil should discontinue Baycol immediately and consult their physician.

"There are five other statins available in the US that may be considered as alternatives to Baycol. They are: lovastatin (Mevacor), prevastatin (Pravachol), simvastatin (Zocor), fluvastatin (Lescol), and atorvastatin (Lipitor)."

The United Kingdom's Medicines Control Agency has issued similar advice that patients who are currently taking cerivastatin should change treatment when their next prescription is due. Doctors should recall for review any patients taking cerivastatin with gemfibrozil. Any patient being treated with cerivastatin who feels unwell, particularly with fever or muscle pain, should seek medical advice, the agency says.

Meanwhile the European Agency for the Evaluation of Medicinal Products has announced that it plans to review all other cholesterol lowering drugs, as a precautionary measure. □

"HE28"

ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months

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ABSTRACT

BACKGROUND

BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine encoding a prefusion-stabilized, membrane-anchored severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) full-length spike protein. BNT162b2 is highly efficacious against coronavirus disease 2019 (Covid-19) and is currently approved, conditionally approved, or authorized for emergency use worldwide. At the time of initial authorization, data beyond 2 months after vaccination were unavailable.

METHODS

In an ongoing, placebo-controlled, observer-blinded, multinational, pivotal efficacy trial, we randomly assigned 44,165 participants 16 years of age or older and 2264 participants 12 to 15 years of age to receive two 30-μg doses, at 21 days apart, of BNT162b2 or placebo. The trial end points were vaccine efficacy against laboratory-confirmed Covid-19 and safety, which were both evaluated through 6 months after vaccination.

RESULTS

BNT162b2 continued to be safe and have an acceptable adverse-event profile. Few participants had adverse events leading to withdrawal from the trial. Vaccine efficacy against Covid-19 was 91.3% (95% confidence interval [CI], 89.0 to 93.2) through 6 months of follow-up among the participants without evidence of previous SARS-CoV-2 infection who could be evaluated. There was a gradual decline in vaccine efficacy. Vaccine efficacy of 86 to 100% was seen across countries and in populations with diverse ages, sexes, race or ethnic groups, and risk factors for Covid-19 among participants without evidence of previous infection with SARS-CoV-2. Vaccine efficacy against severe disease was 96.7% (95% CI, 80.3 to 99.9). In South Africa, where the SARS-CoV-2 variant of concern B.1.351 (or beta) was predominant, a vaccine efficacy of 100% (95% CI, 53.5 to 100) was observed.

CONCLUSIONS

Through 6 months of follow-up and despite a gradual decline in vaccine efficacy, BNT162b2 had a favorable safety profile and was highly efficacious in preventing Covid-19. (Funded by BioNTech and Pfizer; ClinicalTrials.gov number, NCT04368728.)

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*A list of the investigators in the C4591001 Clinical Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

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THE CORONAVIRUS DISEASE 2019 (COVID-19) pandemic continues, with recent estimates of more than 187 million cases diagnosed and more than 4 million deaths.[1] Vaccines are currently available by means of full approval, conditional marketing approval, and emergency use authorization pathways.[2-5] BNT162b2 is a lipid nanoparticle–formulated,[6] nucleoside-modified RNA[7] encoding the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) full-length spike glycoprotein in a prefusion stabilized conformation.[8] To date, more than 1 billion doses of BNT162b2 have been distributed.

We previously reported safety and efficacy data obtained through a median of 2 months of postimmunization follow-up from a global phase 1–2–3 trial of BNT162b2 involving persons 16 years of age or older. Vaccine efficacy against Covid-19 was 95%. BNT162b2 had a favorable safety profile in diverse populations.[9] These data formed the basis for BNT162b2 emergency or conditional authorizations globally.[10] Safety, efficacy, and immunogenicity data from participants 12 to 15 years of age in this trial have been reported.[11] Here, we report safety and efficacy findings from a prespecified analysis of the phase 2–3 portion of the trial through approximately 6 months of follow-up. These additional data contributed to the full approval of BNT162b2 in the United States.

METHODS

OBJECTIVES, PARTICIPANTS, AND OVERSIGHT

This randomized, placebo-controlled, observer-blinded, phase 1–2–3 trial assessed the safety, efficacy, and immunogenicity of the BNT162b2 vaccine in adolescents and adults. The current report of the findings from the phase 2–3 portion of the trial focuses on safety assessments among participants 16 years of age or older and prespecified assessments of vaccine efficacy among participants 12 years of age or older through 6 months of follow-up after immunization. Because the enrollment of participants 12 to 15 years of age began on October 15, 2020, 6-month postimmunization data are currently unavailable for this age cohort. Shorter-duration safety, immunogenicity, and efficacy data for participants 12 to 15 years of age are reported separately[11]; however, data for this cohort are included in the analyses of vaccine efficacy in the overall population (all participants ≥12 years of age) reported here.

Participants who were healthy or had stable chronic medical conditions were eligible. An active immunocompromising condition or recent immunosuppressive therapy was an exclusion criterion. Participants with a history of Covid-19 were excluded, although evidence of current or previous SARS-CoV-2 infection on laboratory testing of trial-obtained samples was not an exclusion criterion. Trial-related responsibilities and ethical conduct are summarized in the Supplementary Appendix, available with the full text of this article at NEJM.org. The protocol contains additional details of the trial and is available at NEJM.org. The first draft of the manuscript was written by the fourth author. The authors had the opportunity to review the data included in this article and confirm the accuracy of the data presented through the specified data cutoff date. The authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol.

PROCEDURES

The participants were randomly assigned in a 1:1 ratio to receive two 30-μg intramuscular injections, 21 days apart, of BNT162b2 (0.3 ml volume per dose) or saline placebo. Randomization was performed with an interactive Web-based system. Starting in December 2020, after BNT162b2 became available under emergency or conditional use authorizations, participants 16 years of age or older who became eligible for Covid-19 vaccination according to national or local recommendations were given the option to learn their trial assignment. Those who had been randomly assigned to receive placebo were offered BNT162b2. After unblinding of the group assignments, participants were followed in an open-label trial period.

SAFETY

Safety end points included solicited, prespecified local reactions, systemic events, and antipyretic or pain medication use during the first 7 days after receipt of each vaccine or placebo dose, which were recorded in an electronic diary; unsolicited adverse events after receipt of the first dose through 1 month after the second dose; and serious adverse events after receipt of the first dose through 1 and 6 months after the second dose

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was received. Safety data are presented for the blinded follow-up and open-label periods.

EFFICACY

BNT162b2 efficacy against laboratory-confirmed Covid-19 with an onset of 7 days or more after the second dose was assessed and summarized descriptively in participants without serologic or virologic evidence of SARS-CoV-2 infection within 7 days after the second dose and in participants with or without evidence of previous infection. Efficacy against severe Covid-19 was also assessed. Lineages of SARS-CoV-2 detected in midturbinate specimens are reported here for Covid-19 cases that occurred 7 days or more after the second dose in South African participants without evidence of previous infection. Methods for determining SARS-CoV-2 lineages and case definitions for confirmed and severe cases of Covid-19 are summarized in the Supplementary Appendix.

STATISTICAL ANALYSIS

The analysis populations are summarized in Table S1 in the Supplementary Appendix. Safety analyses included participants 16 years of age or older without known human immunodeficiency virus (HIV) infection who provided informed consent and received at least one BNT162b2 or placebo dose. The results of the safety analyses, which are descriptive and not based on formal hypothesis testing, are presented as counts, percentages, and associated Clopper–Pearson 95% confidence intervals for adverse events, according to terms in the *Medical Dictionary for Regulatory Activities*, version 23.1, and reactogenicity events for each trial group. Safety data that were reported up to March 13, 2021, are summarized here. The 95% confidence intervals in this report were not adjusted for multiplicity.

The analysis of vaccine efficacy during the blinded period of the trial included all participants 12 years of age or older without known HIV infection who received at least one BNT162b2 or placebo dose. Vaccine efficacy was calculated as $100 \times (1-\text{IRR})$, where IRR (incidence rate ratio) is the ratio of the rate (number per 1000 person-years of follow-up) of confirmed cases of Covid-19 in the BNT162b2 group to the corresponding rate in the placebo group. Descriptive analyses of vaccine efficacy were performed and associated 95% confidence intervals were calculated with the use of the Clopper–Pearson method, with adjustment for surveillance time, which accounts for potential differential follow-up between the two trial groups. As described in the statistical analysis plan, available with the protocol, hypothesis-testing analyses were performed with the use of a Bayesian approach, and the descriptive analyses presented here were performed with a frequentist approach for clarity of communication. Because the percentage of participants who reported symptoms but were missing a valid polymerase-chain-reaction test result was small and slightly higher in the placebo group, data for these participants were not imputed in the analysis.

The previously reported primary efficacy objective was achieved on the basis of an analysis of 170 accrued cases of Covid-19 that could be evaluated (data cutoff date, November 14, 2020).[9] The current report provides updated efficacy analyses that were performed with data from cases that had accrued up to March 13, 2021.

RESULTS

PARTICIPANTS

Between July 27, 2020, and October 29, 2020, a total of 45,441 participants 16 years of age or older underwent screening, and 44,165 underwent randomization at 152 sites (130 sites in the United States, 1 site in Argentina, 2 sites in Brazil, 4 sites in South Africa, 6 sites in Germany, and 9 sites in Turkey) in the phase 2–3 portion of the trial. Of these participants, 44,060 received at least one dose of BNT162b2 (22,030 participants) or placebo (22,030), and 98% (21,759 in the BNT162b2 group and 21,650 in the placebo group) received the second dose (Fig. 1). During the blinded period of the trial, 51% of the participants in each group had 4 to less than 6 months of follow-up after the second dose; 8% of the participants in the BNT162b2 group and 6% of those in the placebo group had 6 months of follow-up or more after the second dose. During the combined blinded and open-label periods, 55% of the participants in the BNT162b2 group had 6 months of follow-up or more after the second dose. A total of 49% of the participants were female, 82% were White, 10% were Black, and 26% were Hispanic or Latinx; the median age was 51 years. A total of 34% of the participants had a body-mass index (the weight in kilograms divided by the square of the height in meters) of

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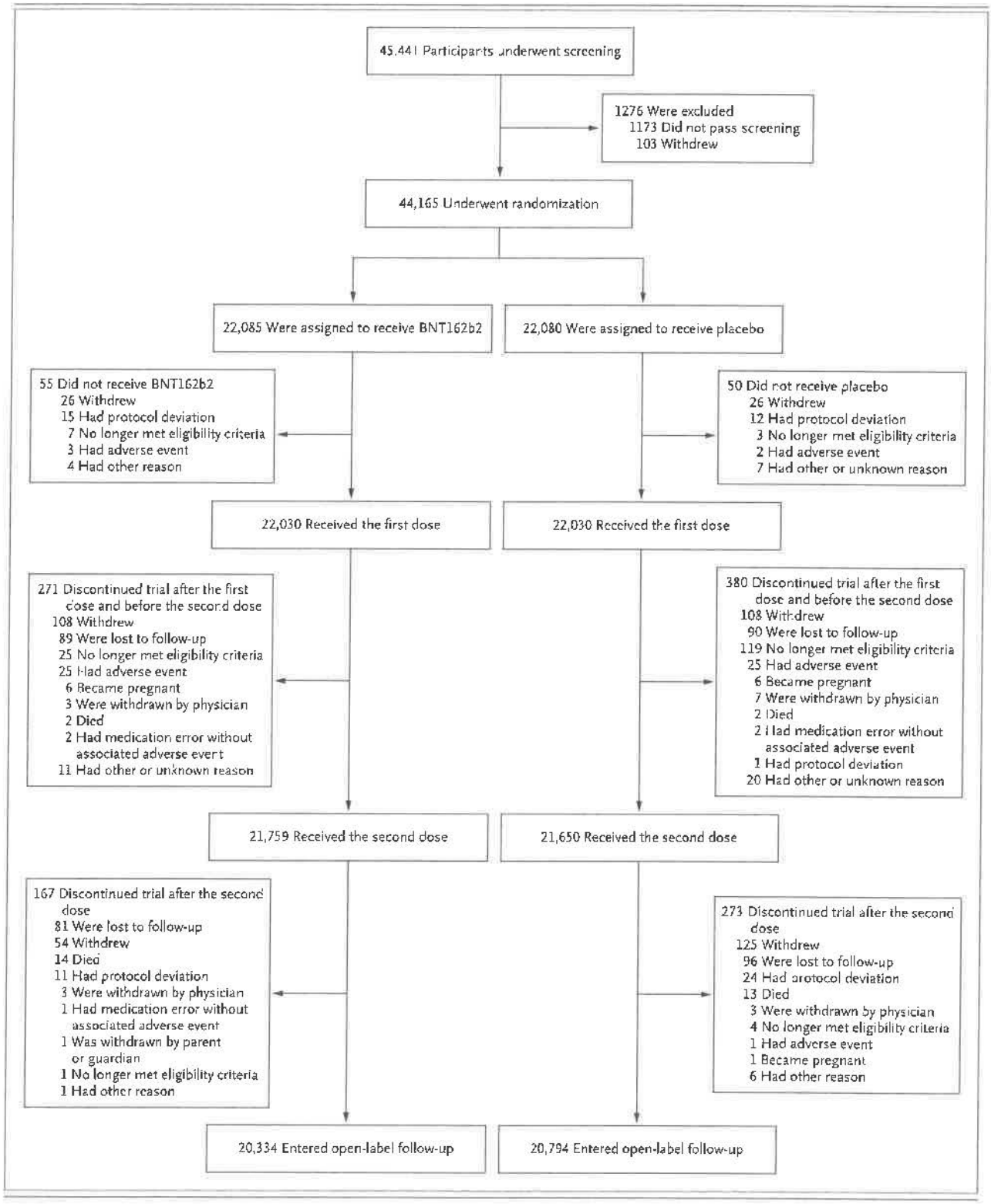

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Figure 1 (facing page). Screening, Randomization, and Follow-up.

The diagram represents all enrolled participants 16 years of age or older through the data cutoff date (March 13, 2021). The diagram includes two deaths that occurred after the second dose in human immunodeficiency virus (HIV)–infected participants (one in the BNT162b2 group and one in the placebo group; these deaths were not reported in the Results section of this article because the analysis of HIV-infected participants is being conducted separately). Information on the screening, randomization, and follow-up of the participants 12 to 15 years of age has been reported previously.[11]

30.0 or more, 21% had at least one underlying medical condition, and 3% had baseline evidence of a previous or current SARS-CoV-2 infection (Table 1 and Table S2).

Between October 15, 2020, and January 12, 2021, a total of 2306 participants 12 to 15 years of age underwent screening, and 2264 underwent randomization at 29 U.S. sites. Of these participants, 2260 received at least one dose of BNT162b2 (1131 participants) or placebo (1129), and 99% (1124 in the BNT162b2 group and 1117 in the placebo group) received the second dose.[11] Among participants who received at least one dose of BNT162b2 or placebo, 58% had at least 2 months of follow-up after the second dose, 49% were female, 86% were White, 5% were Black, and 12% were Hispanic or Latinx. Full details of the demographic characteristics of the participants have been reported previously.[11]

SAFETY

Reactogenicity

The subgroup that was evaluated for reactogenicity in the current report, in which reactions were reported in an electronic diary, included 9839 participants 16 years of age or older. In this subgroup, 8183 participants had been included in the previous analysis, and 1656 were enrolled after the data cutoff for that analysis.[9] The reactogenicity profile of BNT162b2 in this expanded subgroup did not differ substantially from that described previously.[9] This subgroup included 364 participants who had evidence of previous SARS-CoV-2 infection, 9426 who did not have evidence, and 49 who lacked the data needed to determine previous infection status.

More participants in the BNT162b2 group than in the placebo group reported local reactions, the most common of which was mild-to-moderate pain at the injection site (Fig. S1A). Local reactions were reported with similar frequency among the participants with or without evidence of previous SARS-CoV-2 infection, and the reactions were of similar severity. No local reactions of grade 4 (according to the guidelines of the Center for Biologics Evaluation and Research[12]) were reported.

More participants in the BNT162b2 group than in the placebo group reported systemic events, the most common of which was fatigue (Fig. S1B). Systemic events were mostly mild to moderate in severity, but there were occasional severe events. Systemic reactogenicity was similar among those with or without evidence of previous SARS-CoV-2 infection, although BNT162b2 recipients with evidence of previous infection reported systemic events more often after receipt of the first dose, and those without evidence reported systemic events more often after receipt of the second dose. For example, 12% of recipients with evidence of previous SARS-CoV-2 infection and 3% of those without evidence reported fever after receipt of the first dose; 8% of those with evidence of previous infection and 15% of those without evidence reported fever after the second dose. The highest temperature reported was a transient fever of higher than 40.0°C on day 2 after the second dose in a BNT162b2 recipient without evidence of previous infection.

Adverse Events

Analyses of adverse events during the blinded period included 43,847 participants 16 years of age or older (Table S3). Reactogenicity events among the participants who were not in the reactogenicity subgroup were reported as adverse events, which resulted in imbalances between the BNT162b2 group and the placebo group with respect to adverse events (30% vs. 14%), related adverse events (24% vs. 6%), and severe adverse events (1.2% vs. 0.7%). New adverse events attributable to BNT162b2 that were not previously

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Table 1. Demographic Characteristics of the Participants at Baseline.*

Characteristic	BNT162b2 (N=22,026)	Placebo (N=22,021)	Total (N=44,047)
Sex — no. (%)			
Male	11,322 (51.4)	11,098 (50.4)	22,420 (50.9)
Female	10,704 (48.6)	10,923 (49.6)	21,627 (49.1)
Race or ethnic group — no. (%)†			
White	18,056 (82.0)	18,064 (82.0)	36,120 (82.0)
Black or African American	2,098 (9.5)	2,118 (9.6)	4,216 (9.6)
Asian	952 (4.3)	942 (4.3)	1,894 (4.3)
American Indian or Alaska Native	221 (1.0)	217 (1.0)	438 (1.0)
Native Hawaiian or other Pacific Islander	58 (0.3)	32 (0.1)	90 (0.2)
Multiracial	550 (2.5)	533 (2.4)	1,083 (2.5)
Not reported	91 (0.4)	115 (0.5)	206 (0.5)
Ethnicity†			
Hispanic or Latinx	5,704 (25.9)	5,695 (25.9)	11,399 (25.9)
Not reported	111 (0.5)	114 (0.5)	225 (0.5)
Country — no. (%)			
Argentina	2,883 (13.1)	2,881 (13.1)	5,764 (13.1)
Brazil	1,452 (6.6)	1,448 (6.6)	2,900 (6.6)
Germany	249 (1.1)	250 (1.1)	499 (1.1)
South Africa	401 (1.8)	399 (1.8)	800 (1.8)
Turkey	249 (1.1)	249 (1.1)	498 (1.1)
United States	16,792 (76.2)	16,794 (76.3)	33,586 (76.3)
Age group at vaccination — no. (%)			
16–55 yr	13,069 (59.3)	13,095 (59.5)	26,164 (59.4)
>55 yr	8,957 (40.7)	8,926 (40.5)	17,883 (40.6)
Age at vaccination — yr			
Median	51.0	51.0	51.0
Range	16–89	16–91	16–91
SARS-CoV-2 status — no. (%)‡			
Positive	689 (3.1)	716 (3.3)	1,405 (3.2)
Negative	21,185 (96.2)	21,180 (96.2)	42,365 (96.2)
Missing data	152 (0.7)	125 (0.6)	277 (0.6)
Body-mass index — no. (%)§			
≥30.0: obese	7,543 (34.2)	7,629 (34.6)	15,172 (34.4)
Missing data	7 (<1)	6 (<1)	13 (<1)

* Data are summarized for participants 16 years of age or older in the safety population. The demographic characteristics of participants 12 to 15 years of age were reported previously.[11] Percentages may not total 100 because of rounding. SARS-CoV-2 denotes severe acute respiratory syndrome coronavirus 2.
† Race and ethnicity were reported by the participants. The categories shown are those that were used to collect the data.
‡ Positive status was defined as a positive N-binding antibody result or a positive nucleic acid amplification test (NAAT) result at visit 1 or medical history of coronavirus disease 2019 (Covid-19). Negative status was defined as a negative N-binding antibody result or a negative NAAT result at visit 1 and no medical history of Covid-19.
§ The body-mass index is the weight in kilograms divided by the square of the height in meters.

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Table 2. Vaccine Efficacy against Covid-19 from 7 Days after Receipt of the Second Dose during the Blinded, Placebo-Controlled Follow-up Period.*

Efficacy End Point	BNT162b2			Placebo			Vaccine Efficacy (95% CI)‡
	No. of Cases	Surveillance Time†	No. at Risk	No. of Cases	Surveillance Time†	No. at Risk	
		1000 person-yr			*1000 person-yr*		*percent*
		(N=20,998)			**(N=21,096)**		
First occurrence of Covid-19 from 7 days after receipt of the second dose among participants without evidence of previous infection	77	6.247	20,712	850	6.003	20,713	91.3 (89.0–93.2)
		(N=22,166)			**(N=22,320)**		
First occurrence of Covid-19 from 7 days after receipt of the second dose among participants with or without evidence of previous infection	81	6.509	21,642	873	6.274	21,689	91.1 (88.8–93.0)

* This analysis included participants who had no serologic or virologic evidence (within 7 days after receipt of the second dose) of previous SARS-CoV-2 infection (i.e., negative N-binding antibody [serum] test at visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at visits 1 and 2) and had a negative NAAT at any unscheduled visit up to 7 days after receipt of the second dose.

† The surveillance time is the total time (in 1000 person-years) at risk for the given end point across all participants within each group. The time period for the accrual of Covid-19 cases was from 7 days after the second dose to the end of the surveillance period.

‡ Vaccine efficacy was calculated as 100×(1−IRR), where IRR (incidence rate ratio) is the ratio of the rate (number per 1000 person-years of follow-up) of confirmed cases of Covid-19 in the BNT162b2 group to the corresponding rate in the placebo group. The 95% confidence interval for vaccine efficacy was derived with the use of the Clopper–Pearson method, with adjustment for surveillance time.

identified in earlier reports included decreased appetite, lethargy, asthenia, malaise, night sweats, and hyperhidrosis. Few participants had serious adverse events or adverse events that led to trial withdrawal. No new serious adverse events were considered by the investigators to be related to BNT162b2 after the data cutoff date of the previous report.[9]

During the combined blinded and open-label periods, cumulative safety data during follow-up were available through 6 months after the second dose for 12,006 participants who were originally randomly assigned to the BNT162b2 group. No new safety signals relative to the previous report were observed during the longer follow-up period in the current report, which included open-label observation of the original BNT162b2 recipients and placebo recipients who received BNT162b2 after unblinding.[9]

During the blinded, placebo-controlled period, 15 participants in the BNT162b2 group and 14 in the placebo group died; during the open-label period, 3 participants in the BNT162b2 group and 2 in the original placebo group who received BNT162b2 after unblinding died. None of these deaths were considered to be related to BNT162b2 by the investigators. Causes of death were balanced between BNT162b2 and placebo groups (Table S4).

Safety monitoring will continue according to the protocol for 2 years after the second dose for participants who originally received BNT162b2 and for 18 months after the second BNT162b2 dose for placebo recipients who received BNT162b2 after unblinding.

EFFICACY

Among 42,094 participants 12 years of age or older who could be evaluated and had no evidence of previous SARS-CoV-2 infection, Covid-19 with an onset of 7 days or more after the second dose was observed in 77 vaccine recipients and in 850 placebo recipients up to the data cutoff date (March 13, 2021), corresponding to a vaccine efficacy of 91.3% (95% confidence interval [CI], 89.0 to 93.2) (Table 2). Among 44,486 participants

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with or without evidence of previous infection who could be evaluated, cases of Covid-19 were observed in 81 vaccine recipients and in 873 placebo recipients, corresponding to a vaccine efficacy of 91.1% (95% CI, 88.8 to 93.0).

Among the participants with evidence of previous SARS-CoV-2 infection based on a positive baseline N-binding antibody test, Covid-19 was observed in 2 vaccine recipients after the first dose and in 7 placebo recipients. Among the participants with evidence of previous SARS-CoV-2 infection based on a positive nucleic acid amplification test at baseline, cases of Covid-19 were observed in 10 vaccine recipients and in 9 placebo recipients (Table S5). Covid-19 was less common among the placebo recipients with positive N-binding antibodies at trial entry (7 of 542 participants, for an incidence of 1.3%) than among those without evidence of infection at trial entry (1015 of 21,521, for an incidence of 4.7%); these findings indicate that previous infection conferred approximately 72.6% protection.

Among the participants with or without evidence of previous infection, cases of Covid-19 were observed in 46 vaccine recipients and in 110 placebo recipients from receipt of the first dose up to receipt of the second dose, corresponding to a vaccine efficacy of 58.4% (95% CI, 40.8 to 71.2) (Fig. 2). During the interval from the approximate start of observed protection at 11 days after receipt of the first dose up to receipt of the second dose, vaccine efficacy increased to 91.7% (95% CI, 79.6 to 97.4). From its peak after the second dose, observed vaccine efficacy declined. From 7 days to less than 2 months after the second dose, vaccine efficacy was 96.2% (95% CI, 93.3 to 98.1); from 2 months to less than 4 months after the second dose, vaccine efficacy was 90.1% (95% CI, 86.6 to 92.9); and from 4 months after the second dose to the data cutoff date, vaccine efficacy was 83.7% (95% CI, 74.7 to 89.9).

Severe Covid-19, as defined by the Food and Drug Administration,[13] with an onset after receipt of the first dose occurred in 31 participants, of whom 30 were placebo recipients; this finding corresponds with a vaccine efficacy of 96.7% (95% CI, 80.3 to 99.9) against severe Covid-19 (Fig. 2 and Table S6). Although the trial was not powered to definitively assess efficacy according to subgroup, supplemental analyses indicated that vaccine efficacy after the second dose in subgroups defined according to age, sex, race, ethnic group, presence or absence of coexisting medical conditions, and country was generally consistent with that observed in the overall population (Table 3 and Table S7).

Given the concern about the SARS-CoV-2 B.1.351 (or beta) variant, which appears to be neutralized less efficiently by BNT162b2-immune sera than many other lineages,[14] whole-viral-genome sequencing was performed on midturbinate samples from Covid-19 cases observed in South Africa, where this lineage was prevalent. Nine cases of Covid-19 were observed in South African participants without evidence of previous SARS-CoV-2 infection, all of whom were placebo recipients; this finding corresponds with a vaccine efficacy of 100% (95% CI, 53.5 to 100) (Table 3). Midturbinate specimens from 8 of 9 cases contained sufficient viral RNA for whole-genome sequencing. All viral genomes were the beta variant (Global Initiative on Sharing All Influenza Data accession codes are provided in the Supplementary Appendix).

DISCUSSION

In this update to the preliminary safety and efficacy report of two 30-μg doses, at 21 days apart, of BNT162b2, 91.1% vaccine efficacy against Covid-19 was observed from 7 days to 6 months after the second dose in participants 12 years of age or older. Vaccine efficacy against severe disease with an onset after receipt of the first dose was approximately 97%. This finding, combined with the totality of available evidence, including real-world effectiveness data,[15-18] alleviates theoretical concerns over potential enhancement of vaccine-mediated disease.[19]

The benefit of BNT162b2 immunization started approximately 11 days after receipt of the first dose, with 91.7% vaccine efficacy from 11 days after receipt of the first dose up to receipt of the second dose. The trial cannot provide information on persistence of protection after a single dose, because 99% of the participants received the second dose as scheduled during the blinded trial period. A recent trial showed that although nonneutralizing viral antigen–binding antibody levels rise between the first and second BNT162b2 dose, serum neutralizing titers are low or undetectable during this interval.[20] Early protection against Covid-19 without strong serum neutral-

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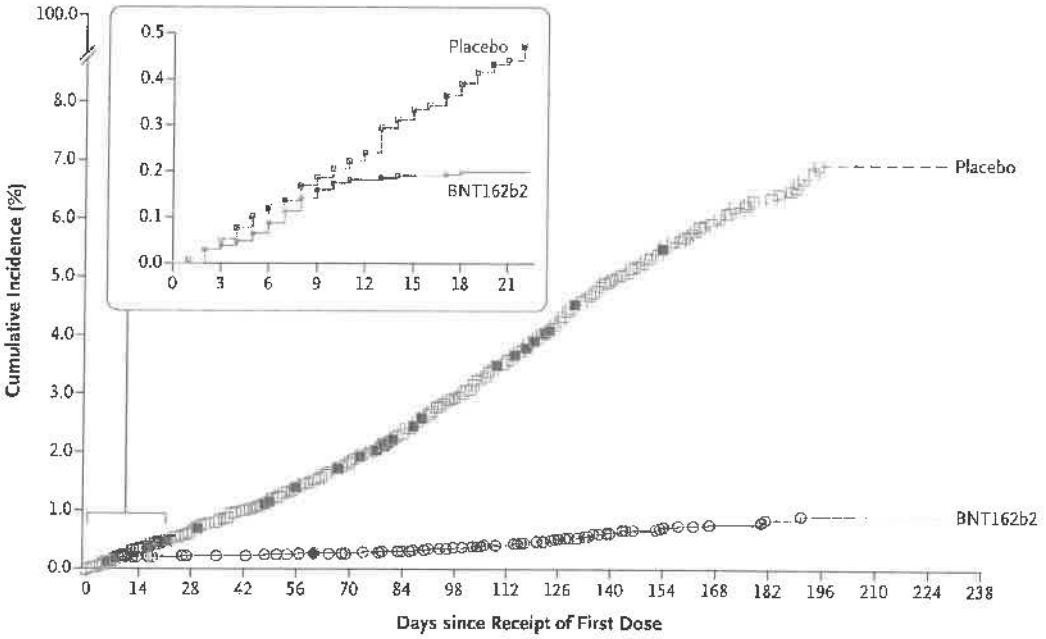

Efficacy End Point	BNT162b2 (N=23,040)			Placebo (N=23,037)			Vaccine Efficacy
	No. of cases	Surveillance time	No. at risk	No. of cases	Surveillance time	No. at risk	
		1000 person-yr			*1000 person-yr*		*% (95% CI)*
Overall: first occurrence of Covid-19 after receipt of first dose	131	8.412	22,505	1034	8.124	22,434	87.8 (85.3 to 89.9)
After receipt of first dose up to receipt of second dose	46	1.339	22,505	110	1.331	22,434	58.4 (40.8 to 71.2)
<11 Days after receipt of first dose	41	0.677	22,505	50	0.675	22,434	18.2 (−26.1 to 47.3)
≥11 Days after receipt of first dose up to receipt of second dose	5	0.662	22,399	60	0.656	22,369	91.7 (79.6 to 97.4)
After receipt of second dose to <7 days after	3	0.424	22,163	35	0.422	22,057	91.5 (72.9 to 98.3)
≥7 Days after receipt of second dose	82	6.649	22,132	889	6.371	22,001	91.2 (88.9 to 93.0)
≥7 Days after receipt of second dose to <2 mo after	12	2.923	22,132	312	2.884	22,001	96.2 (93.3 to 98.1)
≥2 Mo after receipt of second dose to <4 mo after	46	2.696	20,814	449	2.593	20,344	90.1 (86.6 to 92.9)
≥4 Mo after receipt of second dose	24	1.030	12,670	128	0.895	11,802	83.7 (74.7 to 89.9)

Figure 2. Efficacy of BNT162b2 against Covid-19 after Receipt of the First Dose (Blinded Follow-up Period).

The top of the figure shows the cumulative incidence curves for the first occurrence of coronavirus disease 2019 (Covid-19) after receipt of the first dose (efficacy analysis population of participants ≥12 years of age who could be evaluated). Each symbol represents Covid-19 cases starting on a given day, and filled symbols represent severe Covid-19 cases. Because of overlapping dates, some symbols represent more than one case. The inset shows the same data on an enlarged y axis through 21 days. The bottom of the figure shows the time intervals for the first occurrence of Covid-19 in the efficacy analysis population, as well as the surveillance time, which is given as the total time (in 1000 person-years) at risk for the given end point across all participants within each group. The time period for the accrual of Covid-19 cases was from after receipt of the first dose to the end of the surveillance period for the overall row and from the start to the end of the range stated for each time interval. Vaccine efficacy was calculated as 100×(1−IRR), where IRR (incidence rate ratio) is the ratio of the rate (number per 1000 person-years of follow-up) of confirmed cases of Covid-19 in the BNT162b2 group to the corresponding rate in the placebo group. The 95% confidence interval for vaccine efficacy was derived with the use of the Clopper–Pearson method, with adjustment for surveillance time.

ization indicates that neutralizing titers alone do not appear to explain early BNT162b2-mediated protection from Covid-19. Other immune mechanisms (e.g., innate immune responses, CD4+ or CD8+ T-cell responses, B-cell memory responses, and antibody-dependent cytotoxicity) may contribute to protection.[21-26]

Efficacy peaked at 96.2% during the interval from 7 days to less than 2 months after the second dose and declined gradually to 83.7% from

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Table 3. Vaccine Efficacy against Covid-19 up to 7 Days after Receipt of the Second Dose among Participants without Evidence of Infection.*

First Occurrence of Covid-19 after Receipt of the First Dose	BNT162b2 (N=20,998)			Placebo (N=21,096)			Vaccine Efficacy (95% CI)‡
	No. of Cases	Surveillance Time†	No. at Risk	No. of Cases	Surveillance Time†	No. at Risk	
		1000 person-yr			*1000 person-yr*		*percent*
Overall population	77	6.247	20,712	850	6.003	20,713	91.3 (89.0 to 93.2)
Age group — yr							
16 or 17	0	0.061	342	10	0.057	331	100 (58.2 to 100)
16 to 55	52	3.593	11,517	568	3.439	11,533	91.2 (88.3 to 93.5)
≥55	25	2.499	8,194	266	2.417	8,208	90.9 (86.3 to 94.2)
≥65	7	1.233	4,192	124	1.202	4,226	94.5 (88.3 to 97.8)
≥75	1	0.239	842	26	0.237	847	96.2 (76.9 to 99.9)
Sex							
Male	42	3.246	10,637	399	3.047	10,433	90.1 (86.4 to 93.0)
Female	35	3.001	10,075	451	2.956	10,280	92.4 (89.2 to 94.7)
Race or ethnic group§							
White	67	5.208	17,186	747	5.026	17,256	91.3 (88.9 to 93.4)
Black or African American	4	0.545	1,737	48	0.527	1,737	91.9 (78.0 to 97.9)
Asian	3	0.260	946	23	0.248	934	87.6 (58.9 to 97.6)
American Indian or Alaska Native	0	0.041	186	3	0.037	176	100 (−119.0 to 100)
Native Hawaiian or other Pacific Islander	0	0.015	54	1	0.008	30	100 (−1961.2 to 100)
Multiracial	3	0.151	518	22	0.128	476	88.5 (61.6 to 97.8)
Not reported	0	0.026	85	6	0.030	104	100 (2.8 to 100)
Ethnicity§							
Hispanic or Latinx	29	1.786	5,161	241	1.711	5,120	88.5 (83.0 to 92.4)
Non-Hispanic and non-Latinx	47	4.429	15,449	609	4.259	15,484	92.6 (90.0 to 94.6)
Not reported	1	0.032	102	0	0.033	109	NA
Country							
Argentina	15	1.012	2,600	108	0.986	2,586	86.5 (76.7 to 92.7)
Brazil	12	0.406	1,311	80	0.374	1,293	86.2 (74.5 to 93.1)
Germany	0	0.047	236	1	0.048	242	100 (−3874.2 to 100)
South Africa	0	0.080	291	9	0.074	276	100 (53.5 to 100)
Turkey	0	0.027	228	5	0.025	222	100 (−0.1 to 100)
United States	50	4.674	16,046	647	4.497	16,046	92.6 (90.1 to 94.5)

* This analysis of vaccine efficacy during the blinded, placebo-controlled follow-up period included all participants who had undergone randomization and were 12 years of age or older without baseline evidence of previous infection who had undergone randomization. NA denotes not applicable.

† Surveillance time is the total time (in 1000 person-years) at risk for the given end point across all participants within each group. The time period for the accrual of Covid-19 cases was from 7 days after the second dose to the end of the surveillance period.

‡ Vaccine efficacy was calculated as 100×(1−IRR). The 95% confidence interval for vaccine efficacy was derived with the use of the Clopper–Pearson method, with adjustment for surveillance time.

§ Race and ethnicity were reported by the participants. The categories shown are those that were used to collect the data.

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4 months after the second dose to the data cutoff date — an average decline of approximately 6% every 2 months. Ongoing follow-up is needed to understand persistence of the vaccine effect over time, the need for booster dosing, and timing of such a dose. Most participants who initially received placebo have now been immunized with BNT162b2, ending the placebo-controlled period of the trial. Nevertheless, ongoing observation of participants through 2 years in this trial, together with real-world effectiveness data,[15-18] will determine whether a booster is likely to be beneficial after a longer interval. Booster trials to evaluate safety and immunogenicity of BNT162b2 are under way to prepare for this possibility.

From 7 days after the second dose, 86 to 100% efficacy was observed across diverse demographic profiles, including age, sex, race or ethnic group, and factors that increase the risk of Covid-19, such as high body-mass index and other coexisting medical conditions. BNT162b2 was also highly efficacious in various geographic regions including North America, Europe, South Africa, and Latin America. Although vaccine efficacy was slightly lower in Latin American countries, BNT162b2 had a high efficacy of approximately 86% in Argentina and Brazil. Circulation of SARS-CoV-2 variants — some of which are associated with more rapid transmission and potentially greater pathogenicity[27] — has raised concerns that such variants could evade vaccine-mediated protection. Our studies of in vitro neutralization of a variety of SARS-CoV-2 variants have, to date, showed that all tested BNT162b2-immune sera neutralize all tested variants.[14,28-32] The beta variant, which has shown the greatest reduction in neutralization and was the dominant strain in South Africa during the reported observation period, is still neutralized at serum titers higher than those observed at the onset of protection against Covid-19 after the first vaccine dose.[9,14,20] We found that BNT162b2 had an observed efficacy of 100% (95% CI, 53.5 to 100) against Covid-19 in South Africa (9 cases occurred in the placebo recipients and 0 cases in the BNT162b2 recipients), and 8 of 9 cases for which sequence information could be obtained involved the beta variant of SARS-CoV-2.

Safety data are now available for approximately 44,000 participants 16 years of age or older; 12,006 participants have at least 6 months of safety follow-up data after a second BNT162b2 dose. The safety profile observed at a median of 2 months after immunization was confirmed through 6 months after immunization in the current analysis. No cases of myocarditis were noted.

Before immunization, 3% of the participants 16 years of age or older had evidence of SARS-CoV-2 infection. Although this group had a slightly higher incidence of systemic reactogenicity events after receipt of the first dose than those without evidence of previous infection, the group had a slightly lower incidence of reactogenicity events after the second dose than those without previous infection. Thus, there was minimal observed difference in the overall reactogenicity profile on the basis of infection status at baseline. Nine cases of Covid-19 were observed among participants with previous serologically defined natural infection: two cases were observed among the vaccine recipients and seven among the placebo recipients. These data support the current practice of immunizing without screening for evidence of previous infection.

This report has several limitations. Duration of protection and safety data that could be collected in a blinded, placebo-controlled manner were limited by the ethical and practical need to immunize eligible initial placebo recipients under emergency use authorization and according to the recommendations of public health authorities. The data presented here do not address whether vaccination prevents asymptomatic infection; however, evaluation of that question is ongoing in this trial, and real-world data suggest that BNT162b2 prevents asymptomatic infection.[33,34] Preliminary analyses of breakthrough cases have not yet identified a correlate of protection, since vaccine protection rates remain high. This report does not address vaccine efficacy and safety in pregnant women and in children younger than 12 years of age. Studies evaluating BNT162b2 in these populations are ongoing.

The data in this report show that BNT162b2 prevents Covid-19 effectively for up to 6 months after the second dose across diverse populations, despite the emergence of SARS-CoV-2 variants, including the beta variant, and the vaccine continues to show a favorable safety profile.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Manning, Mary Beth	Velocity Clinical Research	Cleveland, OH, USA
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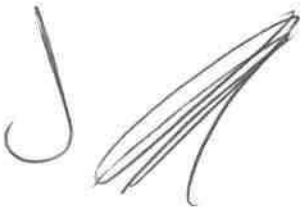

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Tran, Van	Ventavia Research Group	Houston, TX, USA
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Williams, Hayes	Achieve Clinical Research	Birmingham, AL, USA
Wilson, Jonathan	Piedmont Medical Research of Winston-Salem	Winston-Salem, NC, USA
Winkle, Peter	Anaheim Clinical Trials	Anaheim, CA, USA
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Ethical Conduct of the Study

The trial was conducted in accordance with the protocol, the ethical principles derived from international guidelines including the International Council for Harmonisation Good Clinical Practice Guidelines, the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, and applicable laws and regulations (including applicable privacy laws). An independent data monitoring committee reviewed efficacy and unblinded safety data.

Study Responsibilities

Pfizer was responsible for the design, study conduct, data collection, data analysis, data interpretation, and writing of this manuscript. Both Pfizer and BioNTech manufactured clinical trial material. BioNTech was the sponsor of the study and contributed to data interpretation and writing of the manuscript. All study data were available to all authors who vouch for its accuracy and adherence of the study to the protocol.

Testing for SARS-CoV-2 Virus and Antibodies

Testing for SARS-CoV-2 virus was conducted using the Cepheid Xpert Xpress SARS-CoV-2 RT-PCR test. Testing for SARS-CoV-2 antibodies was conducted using the Roche Elecsys® Anti-SARS-CoV-2 antibody test.

Determination of SARS-CoV-2 Lineage

For determination of SARS-CoV-2 lineage, nucleic acid extraction of midturbinate swab specimens was performed using the MagMAX™ Viral/Pathogen Ultra Nucleic Acid Isolation Kit processed on a KingFisher™ Presto.

SARS-CoV-2 viral genome sequencing was performed using the Ion Torrent and Illumina NextSeq platforms. For the Ion Torrent sequencing platform, the Ion AmpliSeq™ SARS-CoV-2 Research Panel was used, which consists of 2 primer pools targeting a total of 237 PCR amplicons specific to SARS-CoV-2 and 5 human expression controls in each pool. Oligonucleotide primers based on available SARS-CoV-2 nucleotide sequences direct the amplification of the viral genome with amplicon lengths of 125–275 bp. The panel provides >99% coverage of the SARS-CoV-2 genome (~30 kb). To determine the optimal number of target amplification cycles, SARS-CoV-2 viral RNA content in the nucleic acid purified from the midturbinate specimens was quantified using the TaqMan™ 2019-nCoV Assay Kit v1, the TaqMan™ 2019-nCoV Control Kit v1, and TaqPath™ 1-Step RT-qPCR Master Mix, CG. cDNA was synthesized with the SuperScript VILO cDNA synthesis kit. Libraries were prepared using the Ion AmpliSeq™ Library Kit plus the Ion AmpliSeq™ SARS-CoV-2 Research Panel according to the manufacturer's instructions (ThermoFisher. Ion AmpliSeq™ Library Kit Plus USER GUIDE. Publication MAN0017003 version C.0.). Libraries underwent template preparation with Ion Chef according to the manufacturer's instructions. Prepared templates were loaded onto an Ion 530 chip for semiconductor sequencing on the Ion GeneStudio™ S5 plus sequencer according to the manufacturer's instructions. Raw sequencing reads generated by the Ion Torrent sequencer were quality and adaptor trimmed by Ion

Torrent Suite and the resulting reads were then mapped to the complete genome of the SARS-CoV-2 Wuhan-Hu-1 isolate (GenBank accession number MN908947.3) using TMAP 5.14.0. Variant calling was carried out with the Torrent Variant Caller using the BAM file from the mapping of the cleaned sequence reads onto the reference sequence of SARS-CoV-2.

SARS-CoV-2 viral genome sequencing performed using the Illumina NextSeq platform used the AmpliSeq for Illumina SARS-CoV-2 panel of PCR primers to enrich for SARS-CoV-2 in the biological specimen. This was a 2-pool design, containing a total of 237 SARS-CoV-2 specific amplicon/primer pairs plus 5 human expression controls in each pool. Oligonucleotide primers based on available SARS-CoV-2 nucleotide sequences directed the amplification of overlapping amplicons with lengths of 125–275 bp that cover >99% of the viral genome. Nucleic acid extracted from the midturbinate specimens was digested initially with DNase (Invitrogen TURBO DNA-free™ Kit, AM1907), and RNA was purified using MagMAX™ beads before cDNA synthesis. Synthesis of cDNA using random sequence primers and downstream steps were as described by the manufacturer. SARS-CoV-2 amplicons were generated from the cDNA, followed by ligation of Universal Next Generation Sequencing Adaptors to the ends of the amplicons. Amplicon libraries were purified with magnetic beads and loaded onto a flow cell for sequence determination using the Illumina NextSeq instrument, according to the manufacturer's instructions. Sequences with ≥30-fold coverage across the entire spike gene were advanced for viral lineage assignment. Single nucleotide variants were called using the "Low Frequency Variant Detection" function with the cut-off for sequence heterogeneity set at >10%.

SARS-CoV-2 lineage assignment was based on Pangolin 2.0 software, which runs a multinomial logistic regression model trained against lineage assignments based on isolate data from the Global Initiative on Sharing All Influenza Data (GISAID), a global science initiative established in 2008 that provides open-access to genomics data of influenza virus and SARS-CoV-2.

Definitions of Confirmed and Severe COVID-19 Cases

The definition of SARS-CoV-2-related cases was the presence of ≥1 of the following symptoms and SARS-CoV-2-NAAT positivity during or within 4 days before or after the symptomatic period: fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhea, and/or vomiting. The onset date of the case was the date that symptoms were first experienced by the participant. If new symptoms were reported ≤4 days after resolution of all previous symptoms, they were considered part of a single illness.

Confirmed severe COVID-19 required confirmation of COVID-19 and the presence of ≥1 of the following: clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths per minute, heart rate ≥125 beats per minute, SpO_2 ≤93% on room air at sea level, or PaO_2/FiO_2 <300 mmHg); respiratory failure (defined as needing high-flow oxygen, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation); evidence of shock (systolic blood pressure <90 mmHg, diastolic blood pressure <60 mmHg, or requiring vasopressors); significant acute renal, hepatic, or neurologic dysfunction; intensive care unit admission; and/or death (https://www.fda.gov/media/137926/download).

Figure/Table Number	Figure/Table Title	Population(s)/Sample Size	Explanation
Figure 1	Disposition of Participants	All enrolled safety population ≥16 years of age N=44,165	Per protocol
Figure 2	Efficacy of BNT162b2 against COVID-19 Occurrence after Dose 1 During the Placebo-controlled Follow-up Period	N=46,077 (all available)	All randomized participants ≥12 years of age
Table 1	Demographics	Participants ≥16 years of age N=44,047	Includes HIV-infected individuals
Table 2	Vaccine Efficacy against COVID-19 from 7 Days after Dose 2 During the Blinded Placebo Controlled Follow-up Period (Evaluable Efficacy Population, ≥12 Years Old)	a. Efficacy endpoint including individuals **without** evidence of prior infection (N=42,094) b. Efficacy endpoint including individuals **with and those without** evidence of prior infection (N=44,486)	Evaluable population: • received 2 vaccinations as randomized • no major protocol deviations Excludes HIV+ participants
Table 3	Vaccine Efficacy Overall and by Subgroup in Participants Without Evidence of Infection Prior to 7 Days After Dose 2 During the Blinded Placebo Controlled Follow-up Period	N=42,094 (same as efficacy endpoint in Table 2, participants ≥12 years of age)	
Table S2	Baseline Comorbidities in Participants ≥16 Years of Age	N=44,047	Includes HIV-infected individuals
Table S3	Participants Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 During the Blinded Follow-up Period	Participants ≥16 years of age N=43,847	Vaccinated minus 200 HIV-infected participants
Table S4	Causes of Death from Dose 1 to Unblinding (Safety Population, ≥16 Years Old)	Participants ≥16 years of age N=43,847	Vaccinated minus 200 HIV-infected participants
Table S5	Vaccine Efficacy Overall and by Subgroup after Dose 1 During the Blinded Placebo Controlled Follow-up Period (All-Available Population)	N=46,077 (all available)	
Table S6	Vaccine Efficacy against Severe COVID-19 Occurrence after Dose 1 (All-Available Population)	N=46,077 (all available, participants ≥12 years of age)	
Table S7	Vaccine Efficacy from 7 Days after Dose 2 by Underlying Comorbidities (Risk Status) among Participants without Evidence of Infection Prior to 7 Days after Dose 2 (Evaluable Efficacy Population)	N=42,094 (same as efficacy endpoint in Table 2, participants ≥12 years of age)	
Figure S1	Local Reactions and Systemic Events Reported within 7 Days after Receipt of BNT162b2 or Placebo by Baseline SARS-CoV-2 Status	Reactogenicity subset of participants ≥16 years of age (ie, participants who used an electronic diary for reporting local reactions and systemic events) N=9839	Per protocol

Table S1 | Explanation of the Changes in Denominator Numbers in Various Analyses.

Charlson Comorbidity Index Category	BNT162b2 (N[a]=22,026)	Placebo (N[a]=22,021)	Total (N[a]=44,047)
	n[b] (%)	n[b] (%)	n[b] (%)
Participants with any Charlson comorbidity	4628 (21.0)	4511 (20.5)	9139 (20.7)
AIDS/HIV	100 (0.5)	100 (0.5)	200 (0.5)
Any malignancy	812 (3.7)	757 (3.4)	1569 (3.6)
Cerebrovascular disease	227 (1.0)	198 (0.9)	425 (1.0)
Chronic pulmonary disease	1783 (8.1)	1775 (8.1)	3558 (8.1)
Congestive heart failure	109 (0.5)	102 (0.5)	211 (0.5)
Dementia	7 (0.0)	11 (0.0)	18 (0.0)
Diabetes with chronic complication	116 (0.5)	130 (0.6)	246 (0.6)
Diabetes without chronic complication	1700 (7.7)	1699 (7.7)	3399 (7.7)
Hemiplegia or paraplegia	15 (0.1)	25 (0.1)	40 (0.1)
Leukemia	14 (0.1)	11 (0.0)	25 (0.1)
Lymphoma	26 (0.1)	36 (0.2)	62 (0.1)
Metastatic solid tumor	4 (0.0)	3 (0.0)	7 (0.0)
Mild liver disease	152 (0.7)	115 (0.5)	267 (0.6)
Moderate or severe liver disease	2 (0.0)	3 (0.0)	5 (0.0)
Myocardial infarction	225 (1.0)	218 (1.0)	443 (1.0)
Peptic ulcer disease	63 (0.3)	84 (0.4)	147 (0.3)
Peripheral vascular disease	144 (0.7)	139 (0.6)	283 (0.6)
Renal disease	140 (0.6)	153 (0.7)	293 (0.7)
Rheumatic disease	75 (0.3)	71 (0.3)	146 (0.3)

Table S2 | Baseline Comorbidities in Participants ≥16 Years of Age. Baseline comorbid conditions are classified according to the Charlson Comorbidity Index (Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol 1994;47:1245-51.). a. N=number of participants in the specified group. This value is the denominator for the percentage calculations. b. n=number of participants with the specified characteristic. Participants with multiple occurrences within each category are counted only once. For 'Participants with any Charlson comorbidity', n=number of participants reporting ≥1 occurrence of any Charlson comorbidity.

Adverse Event	BNT162b2 (N[a]=21,926) n[b] (%)	Placebo (N[a]=21,921) n[b] (%)
Any event	6617 (30.2)	3048 (13.9)
Related[c]	5241 (23.9)	1311 (6.0)
Severe	262 (1.2)	150 (0.7)
Life-threatening	21 (0.1)	26 (0.1)
Any serious adverse event	127 (0.6)	116 (0.5)
Related[c,d]	3 (0.0)	0
Severe	71 (0.3)	66 (0.3)
Life-threatening	21 (0.1)	26 (0.1)
Any adverse event leading to withdrawal	32 (0.1)	36 (0.2)
Related[c]	13 (0.1)	11 (0.1)
Severe	10 (0.0)	10 (0.0)
Life-threatening	3 (0.0)	7 (0.0)
Death	3 (0.0)	5 (0.0)

Table S3 | Participants Reporting at Least 1 Adverse Event from Dose 1 to 1 Month After Dose 2 During the Blinded Follow-up Period. The population included all ≥16-year-old participants who received ≥1 dose of vaccine irrespective of follow-up time. a. N=number of participants in the specified group. This value is the denominator for the percentage calculations. b. n=Number of participants reporting ≥1 occurrence of the specified event category. For 'any event', n=number of participants reporting ≥1 occurrence of any event. c. Assessed by the investigator as related to investigational product. d. Shoulder injury related to vaccine administration, right axillary lymphadenopathy, and paroxysmal ventricular arrhythmia (as previously reported). Adverse events for 12–15-year-old participants were reported previously.[11]

Reported Cause of Death[a]	BNT162b2 (N=21,926) n	Placebo (N=21,921) n
Deaths	15	14
Acute respiratory failure	0	1
Aortic rupture	0	1
Arteriosclerosis	2	0
Biliary cancer metastatic	0	1
COVID-19	0	2
COVID-19 pneumonia	1	0
Cardiac arrest	4	1
Cardiac failure congestive	1	0
Cardiorespiratory arrest	1	1
Chronic obstructive pulmonary disease	1	0
Death	0	1
Dementia	0	1
Emphysematous cholecystitis	1	0
Hemorrhagic stroke	0	1
Hypertensive heart disease	1	0
Lung cancer metastatic	1	0
Metastases to liver	0	1
Missing	0	1
Multiple organ dysfunction syndrome	0	2
Myocardial infarction	0	2
Overdose	0	1
Pneumonia	0	2
Sepsis	1	0
Septic shock	1	0
Shigella sepsis	1	0
Uncvaluable event	1	0

Table S4 | Causes of Death from Dose 1 to Unblinding (Safety Population, ≥16 Years Old). a. Multiple causes of death could be reported for each participant. There were no deaths among 12–15-year-old participants.

First COVID-19 Occurrence after Dose 1	BNT162b2 (N[a]=23,040) n1[b]	BNT162b2 (N[a]=23,040) Surveillance Time[c] (n2[d])	Placebo (N[a]=23,037) n1[b]	Placebo (N[a]=23,037) Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Overall (≥12 years old)	131	8.412 (22,505)	1034	8.124 (22,434)	87.8	(85.3, 89.9)
Efficacy endpoint by subgroup						
Select age groups (years)						
16 to 17	3	0.094 (373)	19	0.090 (370)	84.8	(48.4, 97.1)
16 to 55	95	4.845 (12,645)	693	4.669 (12,626)	86.8	(83.6, 89.5)
>55	33	3.310 (8740)	306	3.204 (8689)	89.6	(85.0, 92.9)
≥65	12	1.645 (4455)	138	1.596 (4437)	91.6	(84.8, 95.7)
≥75	2	0.326 (905)	26	0.310 (877)	92.7	(70.7, 99.2)
Sex						
Male	70	4.355 (11,560)	500	4.115 (11,312)	86.8	(83.0, 89.9)
Female	61	4.057 (10,945)	534	4.009 (11,122)	88.7	(85.3, 91.5)
Race						
White	115	6.957 (18,538)	916	6.719 (18,479)	87.9	(85.3, 90.1)
Black or African American	6	0.783 (2042)	53	0.770 (2063)	88.9	(74.1, 96.1)
American Indian or Alaska Native	1	0.061 (216)	7	0.055 (209)	86.9	(–1.6, 99.7)
Asian	4	0.348 (995)	26	0.337 (990)	85.1	(57.0, 96.2)
Native Hawaiian or other Pacific Islander	0	0.021 (58)	1	0.011 (32)	100.0	(–2000.0, 100.0)
Multiracial	5	0.208 (565)	25	0.190 (546)	81.8	(51.6, 94.6)
Not reported	0	0.035 (91)	6	0.042 (115)	100.0	(–0.7, 100.0)
Ethnicity						
Hispanic/Latinx	52	2.351 (5701)	302	2.282 (5673)	83.3	(77.5, 87.8)
Non-Hispanic/non-Latinx	78	6.018 (16,692)	730	5.799 (16,647)	89.7	(87.0, 92.0)
Not reported	1	0.043 (112)	2	0.043 (114)	49.4	(–872.9, 99.1)
Country						
Argentina	32	1.282 (2846)	146	1.269 (2840)	78.3	(68.0, 85.7)
Brazil	14	0.554 (1430)	95	0.520 (1420)	86.1	(75.6, 92.7)
Germany	2	0.067 (246)	1	0.069 (250)	–104.5	(–11,965.9, 89.4)
South Africa	0	0.128 (367)	11	0.125 (365)	100.0	(61.1, 100.0)
Turkey	3	0.048 (246)	12	0.045 (244)	76.4	(12.4, 95.7)
USA	80	6.333 (17,370)	769	6.095 (17,315)	90.0	(87.4, 92.1)
Baseline SARS-CoV-2 status						
Positive[f]	13	0.250 (692)	17	0.265 (736)	19.2	(–76.6, 63.9)
Positive N-binding only	2	0.192 (521)	7	0.198 (542)	70.5	(–54.7, 97.0)

Positive NAAT only	10	0.020 (66)	9	0.020 (69)	–10.5	(–207.3, 59.7)
Positive NAAT and N-binding	1	0.038 (105)	1	0.046 (124)	–20.5	(–9359.2, 98.5)
Negative[g]	116	8.101 (21,615)	1015	7.804 (21,521)	89.0	(86.6, 91.0)
Unknown	2	0.061 (198)	2	0.055 (177)	9.7	(–1145.4, 93.5)

Table S5 | Vaccine Efficacy Overall and by Subgroup after Dose 1 During the Blinded Placebo Controlled Follow-up Period (All-Available Population). Efficacy data are presented for participants ≥12 years old. a. N=number of participants in the specified group. b. n1=Number of participants meeting the endpoint definition. c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from dose 1 to the end of the surveillance period. d. n2=number of participants at risk for the endpoint. e. CI for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time. f. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19. g. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.

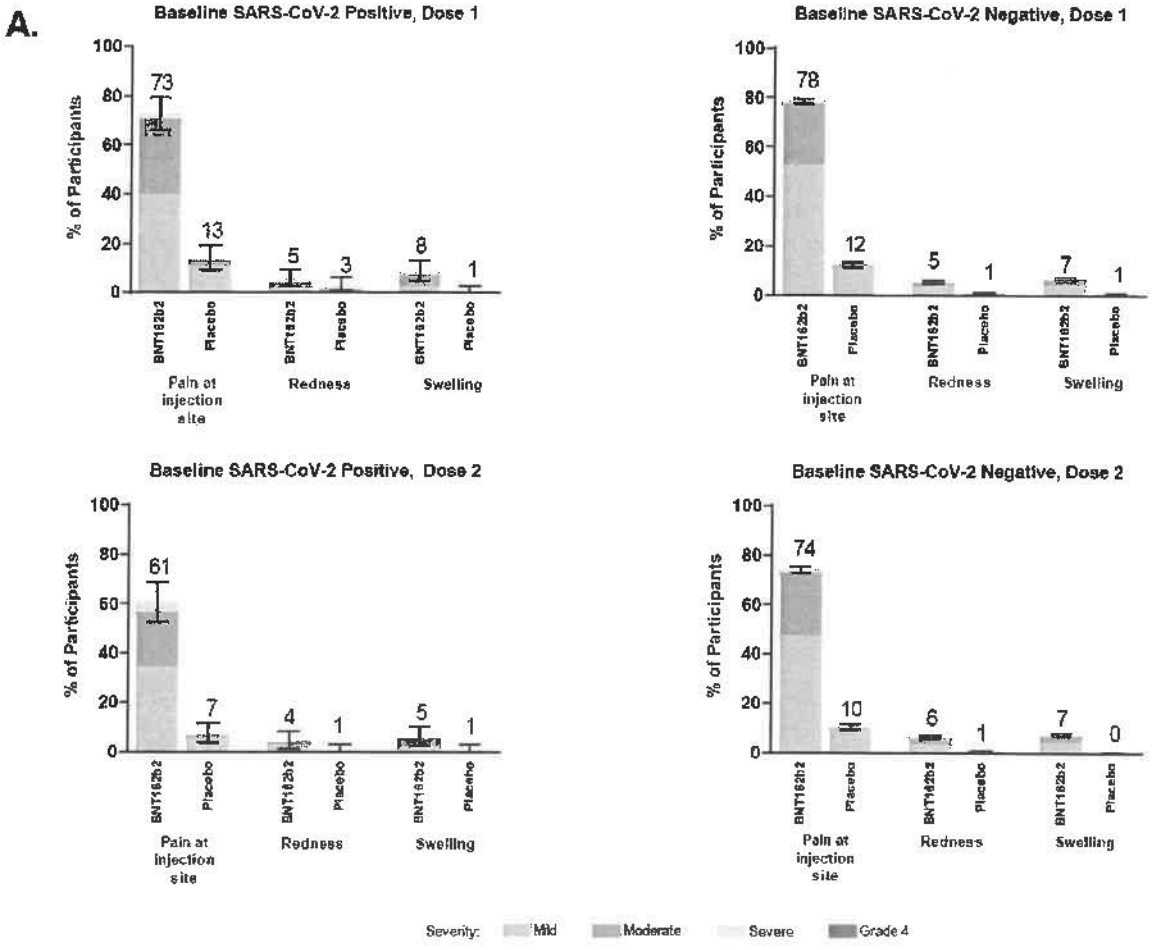
Efficacy Endpoint Subgroup	BNT162b2 (N[a]=23,040) n1[b]	BNT162b2 (N[a]=23,040) Surveillance Time[c] (n2[d])	Placebo (N[a]=23,037) n1[b]	Placebo (N[a]=23,037) Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First severe COVID-19 occurrence after dose 1	1	8.439 (22,505)	30	8.288 (22,435)	96.7	(80.3, 99.9)
After dose 1 to before dose 2	0	1.351 (22,505)	6	1.360 (22,435)	100.0	(14.5, 100.0)
Dose 2 to 7 days after dose 2	0	0.425 (22,170)	1	0.423 (22,070)	100.0	(–3783.5, 100.0)
≥7 Days after dose 2	1	6.663 (22,142)	23	6.505 (22,048)	95.7	(73.9, 99.9)

Table S6 | Vaccine Efficacy against Severe COVID-19 Occurrence after Dose 1 (All-Available Population). Efficacy data are presented for participants ≥12 years old. a. N=number of participants in the specified group. b. n1=number of participants meeting the endpoint definition. c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for severe COVID-19 case accrual is from dose 1 to the end of the surveillance period for the overall row, and from the start to the end of the range stated for each time interval. d. n2=number of participants at risk for the endpoint. [e]. CI for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time. Severe COVID-19 as defined by the US FDA [https://www.fda.gov/media/137926/download]).

Efficacy Endpoint Subgroup	BNT162b2 (N[a]=20,998) n1[b]	BNT162b2 (N[a]=20,998) Surveillance Time[c] (n2[d])	Placebo (N[a]=21,096) n1[b]	Placebo (N[a]=21,096) Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
First COVID-19 occurrence from 7 days after dose 2						
Overall (≥12 years old)	77	6.247 (20,712)	850	6.003 (20,713)	91.3	(89.0, 93.2)
At risk[f]						
Yes	35	2.797 (9167)	401	2.681 (9136)	91.6	(88.2, 94.3)
No	42	3.450 (11,545)	449	3.322 (11,577)	91.0	(87.6, 93.6)
Age group (years) and at risk						
16–64 and at risk	29	2.083 (6632)	325	1.993 (6629)	91.5	(87.5, 94.4)
≥65 and at risk	6	0.680 (2322)	71	0.656 (2304)	91.8	(81.4, 97.1)
Obese[g]						
Yes	27	2.103 (6796)	314	2.050 (6875)	91.6	(87.6, 94.6)
No	50	4.143 (13,911)	536	3.952 (13,833)	91.1	(88.1, 93.5)
Age group (years) and obese						
16–64 and obese	24	1.680 (5303)	266	1.624 (5344)	91.3	(86.7, 94.5)
≥65 and obese	3	0.404 (1370)	45	0.410 (1426)	93.2	(78.9, 98.7)

Table S7 | Vaccine Efficacy from 7 Days after Dose 2 by Underlying Comorbidities (Risk Status) among Participants Without Evidence of Infection Prior to 7 Days after Dose 2 (Evaluable Efficacy Population). Efficacy data are presented for participants ≥12 years old. a. N=number of participants in the specified group. b. n1=number of participants meeting the endpoint definition. c. Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after dose 2 to the end of the surveillance period. d. n2=number of participants at risk for the endpoint. e. CI for vaccine efficacy is derived based on the Clopper and Pearson method adjusted for surveillance time. f. Includes participants who had ≥1 Charlson Comorbidity Index (CMI) category or obesity (body mass index [BMI] ≥30 kg/m^2 [≥16 years old] or BMI ≥95th percentile [12–15 years old]). g. Participants who had BMI ≥30 kg/m^2 (≥16 years old) or BMI ≥95th percentile (12–15 years old; refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm).

Figure S1 | Local Reactions and Systemic Events Reported within 7 Days after Receipt of BNT162b2 or Placebo by Baseline SARS-CoV-2 Status. Local reactions and systemic events and medication use were collected with electronic diaries for 7 days after each vaccination from ≥16-year-old participants in the reactogenicity subset (n=9839; ie, participants who used an electronic diary for reporting local reactions and systemic events). **A.** Solicited injection-site (local) reactions. Pain at the injection site scale: mild, does not interfere with activity; moderate: interferes with activity; severe, prevents daily activity; Grade 4, emergency room visit or hospitalization). Redness and swelling scale: mild, 2.0 to 5.0 cm in diameter; moderate, >5.0 to 10.0 cm in diameter; severe, >10.0 cm in diameter; Grade 4, necrosis or exfoliative dermatitis for redness and necrosis for swelling. **B.** Systemic events and medication use. Fever scale as indicated in the key. Medication use is not graded. Fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain scale: mild, does not interfere with activity; moderate, some interference with activity; severe, prevents daily activity; Grade 4, emergency room visit or hospitalization. Vomiting scale: mild, 1 to 2 times in 24 hours; moderate, >2 times in 24 hours; severe, requires intravenous hydration; Grade 4, emergency room visit or hospitalization. Diarrhea scale: mild, 2 to 3 loose stools in 24 hours; moderate, 4 to 5 loose stools in 24 hours; severe, 6 or more loose stools in 24 hours; Grade 4, emergency room visit or hospitalization. Whiskers represent 95% CIs. Numbers above the whiskers are the overall percentage of participants in each group reporting the specified local reaction or systemic event. One participant who received BNT162b2 reported a fever of >40.0°C, but this is not visible on the graph. Local reactions and systemic events for 12-15-year-old participants have been reported previously (Frenck RW, et al. *N Engl J Med* 2021;385(3):239-250).



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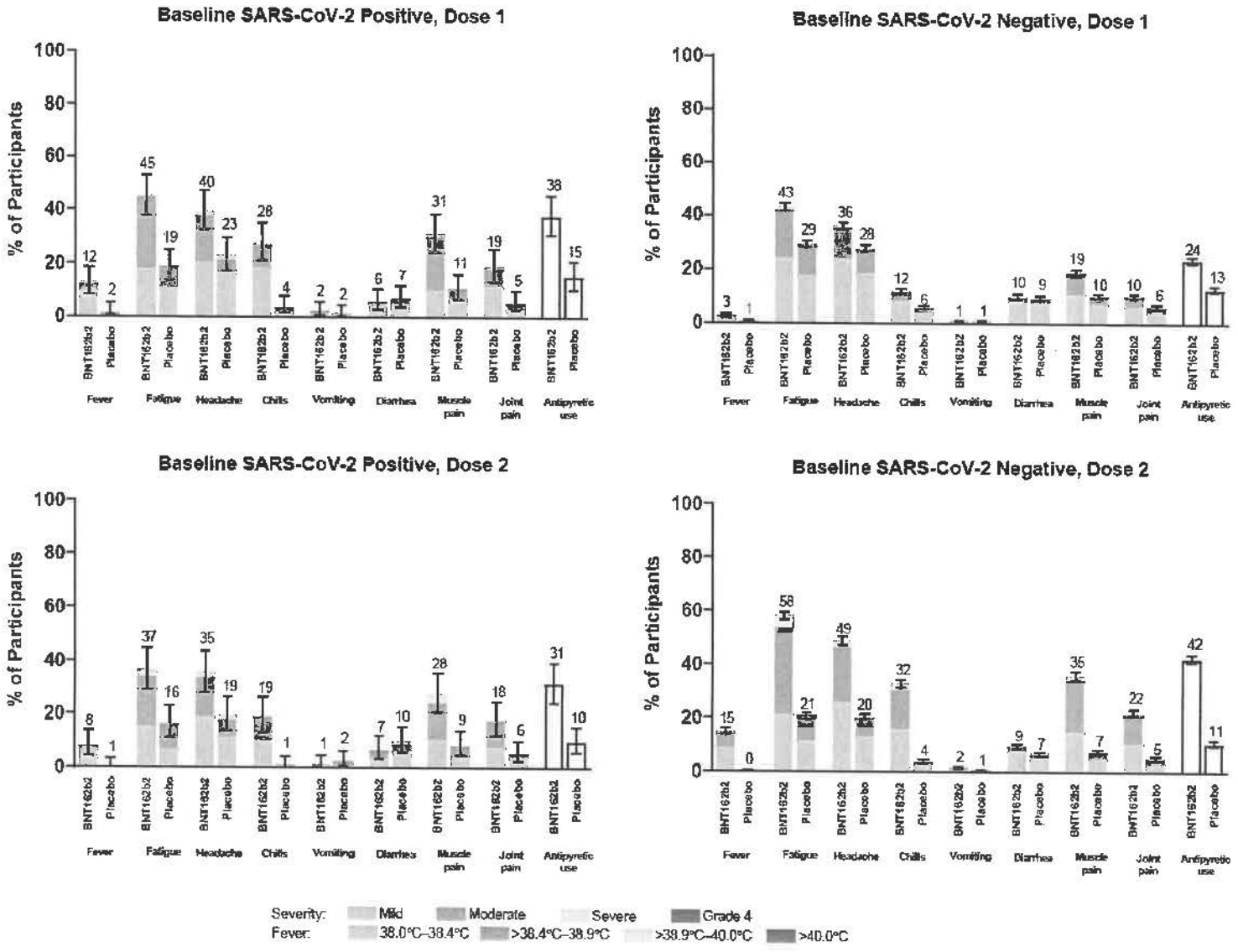
Baseline SARS-CoV-2 Positive, Dose 1
Baseline SARS-CoV-2 Negative, Dose 1
Baseline SARS-CoV-2 Positive, Dose 2
Baseline SARS-CoV-2 Negative, Dose 2
% of Participants
BNT162b2
Placebo
Fever
Fatigue
Headache
Chills
Vomiting
Diarrhea
Muscle pain
Joint pain
Antipyretic use
Severity: Mild Moderate Severe Grade 4
Fever: 38.0°C–38.4°C >38.4°C–38.9°C >38.9°C–40.0°C >40.0°C

"HE30"

Cause of Death Certification:
A guide for completing the Notice of Death/Stillbirth (DHA-1663)

Pali Lehohla
Statistician-General
Statistics South Africa, 2012

tenth revision which is currently in use. In order to ensure the comparability of mortality data between places and over time, the International Classification of Diseases (ICD) provides rules and guidelines for mortality coding (assigning an ICD code to a cause of death) and classification (selecting or identifying the single underlying cause of death from those listed on the medical certificate of death). In a large proportion of deaths, a sequence of morbid events will have led to death. From the standpoint of prevention, the objective is to break the sequence as early as possible. Thus, the underlying cause of death, rather than the immediate cause, is of particular interest from a public health point of view.

According to the ICD-10:

- The **Immediate Cause** is the final disease, injury or complication directly causing the death. It should be noted that the mechanism of death or terminal event (for example, heart failure, cardiac arrest, respiratory arrest) is not considered to be a valid underlying cause of death and should not be reported on the death certificate without stating the preceding disease or injury.

- The **Underlying Cause of Death** is the disease or injury that started the sequence of events leading directly to death or the circumstances of the accident or violence that produced the fatal injury. In the case of a violent death, the form of external violence or accident is antecedent to the injury entered, although the two events may be almost simultaneous.

- **Contributing causes** are other significant conditions contributing to the death, but not part of the direct causal sequence.

1.4 ICD coding and classification of mortality data

The purpose of the ICD is to permit the systematic recording, analysis, interpretation and comparison of mortality data collected in different geographic areas and at different times. It was originally developed to classify the causes of mortality recorded at the registration of death but its scope has been extended to include diagnoses in morbidity. The ICD is a variable-axis classification which groups statistical data on diseases in the following structure:

- Epidemic diseases
- Constitutional or general diseases
- Local diseases arranged by site
- Developmental diseases
- Injuries

The basic ICD is a single coded list of three-character categories which can each be divided up into ten four-character subcategories using a decimal point system. It uses an alphanumeric code with a letter in the first position and numbers in the rest. The 10th revision of ICD (ICD-10) comprises three volumes: Volume 1 contains the main classifications; Volume 2 contains instructions on how to use the classification; and Volume 3 contains an alphabetical index to the classification and should always be used with Volume 1 when coding as it contains many terms that are not included in Volume 1.

"HE31"

SAHPRA
South African Health Products Regulatory Authority

MEDIA RELEASE

SAHPRA and the Pfizer/Biontech Comirnaty Vaccine

Embargo: Immediate release

Pretoria, 16 March 2021 – SAHPRA has approved the Section 21 application for the Pfizer/Biontech Comirnaty Vaccine.

Issued by:

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About SAHPRA:

SAHPRA is tasked with regulating (monitoring, evaluating, investigating, inspecting and registering) all health products. This includes clinical trials, complementary medicines, medical devices and in-vitro diagnostics (IVDs). Furthermore, SAHPRA has the added responsibility of overseeing radiation control in South Africa. SAHPRA's mandate is outlined in the Medicines and Related Substances Act (Act No 101 of 1965 as amended) as well as the Hazardous Substances Act (Act No 15 of 1973).

SAHPRA has three pillars to ensure that medicines, medical devices and IVDs meet the requisite standards to protect the health and well-being of all who reside in South Africa:

- Safety
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- Quality

It is these three pillars that define the ethos of SAHPRA.

"HE32"

SAHPRA
South African Health Products Regulatory Authority

MEDIA RELEASE

SAHPRA approval of booster dosing with the Pfizer (Comirnaty®) COVID-19 vaccine

Embargo: Immediate release

Pretoria, 8 December 2021- The South African Health Products Authority (SAHPRA) initially approved the use of Pfizer's Comirnaty® COVID-19 vaccine on 16 March 2021, in terms of section 21 of the Medicines and Related Substance Act (Act 101 of 1965).

On 17 November 2021, SAHPRA received an application from Pfizer to amend the dosing schedule for the Comirnaty® COVID-19 vaccine, allowing an optional third (booster) dose. Following evaluation of the data submitted, SAHPRA has approved the following options:

- A third dose of the the Comirnaty® COVID-19 vaccine in individuals aged 18 years and older, to be administered at least 6 months after the second dose.
- A third dose of the the Comirnaty® COVID-19 vaccine in individuals aged 12 years and older who are severely immunocompromised, to be administered at least 28 days after the second dose.

The data provided only dealt with the situation of homologous boosting, where the third dose is of the same vaccine as the initial course (in this case, two doses). SAHPRA is aware of the keen interest in the efficacy and safety of heterologous boosting regimens (so-called "mix-and-match" approaches), and invites submission of supportive data in this regard.

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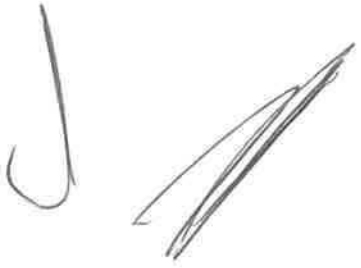

"HE33"

SAHPRA
South African Health Products Regulatory Authority

MEDIA RELEASE

SAHPRA registers two COVID-19 vaccines

Embargo: Immediate release

Pretoria, 7 February 2022 – SAHPRA registered two COVID-19 vaccines: the COMIRNATY vaccine by Pfizer Laboratories (Pty) Ltd on 25 January 2022, and the COVID-19 VACCINE MC PHARMA by MC Pharma (Pty) Ltd. on 31 January 2022. Both vaccines have been registered in terms of section 15 of the Medicines and Related Substance Act (Act 101 of 1965 as Amended), with conditions.

COMIRNATY vaccine

COMIRNATY is an mRNA vaccine, indicated for active immunisation to prevent COVID-19 in individuals 12 years of age and older. COMIRNATY is administered intramuscularly after dilution as a course of 2 doses (0,3 mL each). It is recommended that the second dose is administered three weeks after the initial dose.

This authorisation is based on acceptable safety, quality and efficacy data submitted by Pfizer Laboratories (Pty) Ltd to SAHPRA as a rolling submission over the period 3 February 2021 to 17 January 2022. The authorisation is, however, subject to a number of conditions which includes that the vaccine is supplied and administered in accordance with the National COVID-19 vaccination programme and applicable guidelines. Further conditions relate to the reporting of the results of ongoing studies and conformance with pharmacovigilance activities as outlined in the approved risk management plan, including the submission of periodic safety updates.

The adverse effects of the COMIRNATY vaccine, as outlined in the clinical trial evidence submitted by the applicant, were usually mild or moderate and cleared within a few days of vaccination. The most common adverse effects reported were pain at the injection site, headache, tiredness, muscle pain and chills. Very rare cases of myocarditis and pericarditis have been observed following vaccination with COMIRNATY. These cases have primarily

occurred within 14 days following vaccination, more often after the second vaccination, and more often in younger men. Available data suggest that the course of these conditions following vaccination is not different from that seen with myocarditis or pericarditis from other causes.

COVID-19 VACCINE MC PHARMA

The COVID-19 VACCINE MC PHARMA is an inactivated Vero Cell vaccine, indicated for immunisation against SARS-CoV-2 in those aged 18 years and older. initially developed by the Beijing Institute of Biological Products Co., Ltd, this product has also been referred to as the Sinopharm/BBIBP vaccine indicated for immunisation against SARS-CoV-2. The COVID-19 VACCINE MC PHARMA is administered as two doses by intramuscular injection at an interval of 2-4 weeks and each dose is 0.5ml.

This authorisation is based on acceptable safety, quality and efficacy data submitted by MC Pharma Pty (Ltd) to SAHPRA as a rolling submission over the period 23 July 2021 to 22 December 2021. The authorisation is, however, subject to a number of conditions which includes that the vaccine is supplied and administered in accordance with the National COVID-19 vaccination programme. Further conditions relate to the reporting of the results of ongoing studies and conformance with pharmacovigilance activities as outlined in the approved risk management plan, including the submission of periodic safety updates.

The adverse effects of the COVID-19 VACCINE MC PHARMA, as outlined in the clinical trial evidence submitted by the applicant, were usually mild or moderate and cleared within a few days of vaccination. The most common adverse effects reported were pain at the injection site, headache, tiredness, muscle pain and nausea.

"The registration of these vaccines is a vast stride in vaccine registration as SAHPRA plays its role in the fight against COVID-19. SAHPRA will continue to play its part in ensuring the quality, safety and efficacy of all health products, including all vaccines to ensure that the South African public is protected at all times," indicates SAHPRA CEO, Dr Boitumelo Semete-Makokotlela.

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Notes to Editors:

SAHPRA will post this media release on our website. Navigate to the News section on the website.

A podcast will be recorded and posted on the home page. Scroll down the home page to "**SAHPRA TV and Podcasts**". Podcasts appear on the right-hand side.

Should you request an interview for television, please send your request to media@sahpra.org.za and copy yuveng@sahpra.org.za. Include your discussion points in your request.

Updates on vaccine registration can be accessed here:

Vaccines - News and updates (sahpra.org.za)

Please also note that all queries related to the rollout of these vaccines should be addressed with the National Department of Health (NDoH)

"HE34"

SAHPRA
South African Health Products Regulatory Authority

MEDIA RELEASE

SAHPRA registers COMIRNATY's paediatric and adult vaccines

Embargo: Immediate release

Pretoria, 22 November 2022 – The South African Health Products Regulatory Authority (SAHPRA) has registered Pfizer's COMIRNATY Ready To Use (RTU) ADULT VACCINE and Dilute To Use (DTU) PAEDIATRIC VACCINE on 15 November 2022. The RTU vaccine, as the name suggests, is a formulation that does not require reconstitution in any way. The DTU vaccine must be reconstituted and cannot be used directly.

Both vaccines have been registered in terms of Section 15 (6a) of the *Medicines and Related Substance Act (Act 101 of 1965 as amended), with conditions*. This means that these products are not under Emergency Use Authorisation but have a full registration.

The current assigned shelf-life of the frozen vial for both vaccines is nine (9) months when stored at -90 °C to -60 °C. The thawed vial has 10 weeks storage and transportation at 2 °C to 8 °C within the nine (9) months shelf life.

COMIRNATY RTU ADULT VACCINE

The COMIRNATY RTU ADULT VACCINE is an mRNA vaccine indicated for active immunisation to prevent COVID-19 in individuals 12 years and above for this new ready to use formulation.

The RTU adult vaccine is administered intramuscularly as a primary course of two (2) doses (0,3 mL each). It is recommended to administer the second dose three (3) weeks after the first dose.

For severely immunocompromised individuals aged 12 years and older, a third primary course dose may be administered intramuscularly at least 28 days after the second dose. Please note that this formulation has not been approved for boosting at this stage.

COMIRNATY DTU PAEDIATRIC VACCINE

The COMIRNATY DTU PAEDIATRIC VACCINE is an mRNA vaccine indicated for active immunisation against SARS-CoV-2 and may contribute to protection against COVID-19 in individuals 5 - 11 years of age, that is, it is for the paediatric population.

The DTU paediatric vaccine's 10 micrograms/dose is administered intramuscularly after dilution as a primary course of two (2) doses (0,2 mL each). It is recommended to administer the second dose three (3) weeks after the first dose.

For severely immunocompromised individuals aged five (5) years and older, a third primary course dose may be administered intramuscularly at least 28 days after the second.

"These authorisations are based on acceptable safety, quality and efficacy data submitted by Pfizer Laboratories (Pty) Ltd to SAHPRA as a full submission. The authorisation is, however, subject to a number of conditions which includes that the vaccine is supplied and administered in accordance with the National COVID-19 vaccination programme and applicable guidelines. Further conditions relate to the reporting of the results of ongoing monitoring and conformance with pharmacovigilance activities as outlined in the approved risk management plan, including the submission of periodic safety updates", indicates SAHPRA CEO, Dr Boitumelo Semete-Makokotlela.

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- Quality

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"HE35"

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FREQUENTLY ASKED QUESTIONS: VACCINE SAFETY AND ADVERSE EVENTS

Aug 25th, 2021 | Tool Kits

FREQUENTLY ASKED QUESTIONS
VACCINE SAFETY AND ADVERSE EVENTS

What is the difference between registered vaccines and "emergency use" vaccines?
In normal times, you can only use a vaccine if it is registered with the South African Health Products Regulatory Authority (SAHPRA). SAHPRA will only register a vaccine if:

- all the clinical trials are done, and
- they have studied all the information from the trials to see if it is safe, good quality and effective

In an emergency like the COVID-19 pandemic, SAHPRA can approve an unregistered vaccine to be used for a certain time (emergency use authorisation). This happens when there is enough information that SAHPRA can be confident that the vaccine is safe and effective, but the information is not yet enough to meet all the requirements for full registration.

Is the J&J vaccine still a clinical trial?
No. The clinical trials for the J&J vaccine are done and it is now registered with SAHPRA. J&J will continue to do studies and submit the information to SAHPRA to monitor the safety of the vaccine.

had to complete their phase 3 clinical trial before it could be approved. SAHPRA is independent from government. Only vaccines that are approved by SAHPRA can be used, but government is responsible for deciding which vaccine/s will be provided as part of vaccination programmes.

Which vaccine (J&J or Pfizer) is the best?

Both vaccines are safe and will protect you from getting very sick, going to the hospital or dying from COVID19. The side effects from J&J and Pfizer are similar. They are mild and will go away within three days. Therefore, the best vaccine is the vaccine that is available and offered to you first.

Do I need to be vaccinated if I have previously recovered from COVID-19? Can my body not fight the disease on its own, without suffering the side effects of the vaccine?

Evidence shows that your body's response when you are sick from COVID-19 is much weaker and shorter than the response to the vaccine. Getting the vaccine will give you a much stronger and longer-lasting immune response. The side effects of the vaccine are mild and do not last more than a day or two, while getting sick from COVID-19 can cause hospitalisation or death.

Why was the time between the two doses of Pfizer extended?

The time between the Pfizer doses was extended because there is now evidence that if you get the second dose 42 days after the first dose, your body's response is much stronger and lasts longer than when the time is shorter.

Can people with chronic diseases, such as high blood pressure, get the vaccine?

People with chronic diseases such as high blood pressure, heart disease and diabetes are at higher risk of getting severe COVID-19. Therefore, they will benefit the most from getting the vaccine. They should also make sure that their condition is controlled, go for regular check-ups with their healthcare practitioner and take their chronic medication. If you are unsure about your condition, consult with your healthcare practitioner.

I have COVID-19 symptoms – is it safe to get vaccinated?

You should not get the vaccine if you have symptoms of COVID-19 and should rather be tested. If you have COVID-19, you should wait at least 30 days after you have recovered from COVID-19 before you get your vaccine.

How dangerous is an allergic reaction to the vaccine?

Severe allergic reactions to the vaccine are very rare. An allergic reaction usually happens within seconds or minutes after getting the vaccine. This is why ALL people must wait in the observation area for 15 minutes after getting the vaccine to make sure they do not have a major allergic reaction.

3) Anyone who had a severe allergic reaction after the first dose should not get the second dose of that vaccine.
If you previously had an allergic reaction to a medication or vaccine, but are unsure what specific ingredient caused it, please speak to your healthcare practitioner before getting the vaccine.

For people with allergies, who should speak to their health practitioner before getting the vaccine?
Anyone with a history of allergic reactions to other vaccines or medicines should first speak to their health practitioner to find out which ingredient caused the allergic reaction. The healthcare practitioner will tell you whether it is safe to get the vaccine. If your healthcare practitioner says you can get the vaccine, but your previous reaction to a vaccine or medication was severe, you should be vaccinated in a hospital and be observed for 30 minutes after vaccination. If your previous reaction was not severe, you can get the vaccine at a normal vaccination site, but you must wait in the observation area for 30 minutes after getting the vaccine to make sure there is no allergic reaction.

Is it safe to get the vaccine if you are allergic to eggs?
Yes. None of the COVID-19 vaccines have any egg proteins. However, you will have to stay in the observation area for 30 minutes after getting the vaccine, instead of the standard 15 minutes, because you have a history of allergies.

I have heard of elderly people dying shortly after getting the vaccine. Is the vaccine safe for the elderly?
The vaccine is both safe and highly effective to prevent severe COVID-19 disease and death. Through the use of the vaccine we are seeing a huge drop in deaths from COVID-19 in the elderly in several countries.

Why do some people still get COVID-19 within two weeks after getting the vaccine?
It takes at least two weeks for the body to develop immunity after getting the vaccine. You are only 'fully vaccinated' 30 days after getting the J&J vaccine or two weeks after the second dose of the Pfizer vaccine. If you are exposed to the virus before you are 'fully vaccinated', you may get the disease. Also, if you get COVID-19 within a few days after being vaccinated, it means you were already infected before getting the vaccine.

The vaccine also does not completely prevent COVID-19 infection, even after you are 'fully vaccinated' but reduces the risk of severe COVID-19 infection, hospitalisation or death from COVID-19.

Can the vaccine cause COVID-19 disease?
None of the vaccines used in South Africa contains the live virus that causes COVID-19. The vaccine can therefore not make you sick with COVID-19.

Can the Pfizer vaccine cause heart inflammation? Is it safe to give the vaccine to elderly people?
In a very few cases, doctors found heart inflammation in young men who got the Pfizer vaccine. This is a very rare effect, usually seen within two weeks after the second dose of the vaccine. Common symptoms are chest pa shortness of breath and an abnormal heartbeat (fast, pounding or fluttering). These symptoms are mostly mild and can

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Should I get vaccinated?

Should I get vaccinated?

Modified on: Tue, 20 Dec, 2022 at 6:48 PM

Two key reasons to get vaccinated are to protect ourselves and to protect those around us. Because not everyone can be vaccinated – including very young babies, those who are seriously ill or have certain allergies – they depend on others being vaccinated to ensure they are also safe from vaccine-preventable diseases.

Related Articles

- How should I prepare to get vaccinated?
- Should I still wear a mask after I have been vaccinated?
- Will I get proof that I have been vaccinated?
- Why should my child get vaccinated?
- Where can I get vaccinated?
- Could a child still get measles if he/she is fully vaccinated?
- Can children get vaccinated?
- Should I isolate even if I am vaccinated?
- Do I need to take time off work after being vaccinated?
- Do I need to take time off work to get vaccinated?

"HE36"

South African Govern... · 2021/05/30

South Africa government organization

#COVID19SA | "Each **and** every one of us can help our parents, our grandparents, or the elderly people in our community to register on the system **and** get protected. All of the vaccines that are approved for use in SA are **safe and effective.**" - President Ramaphosa #Level2 #StaySafe

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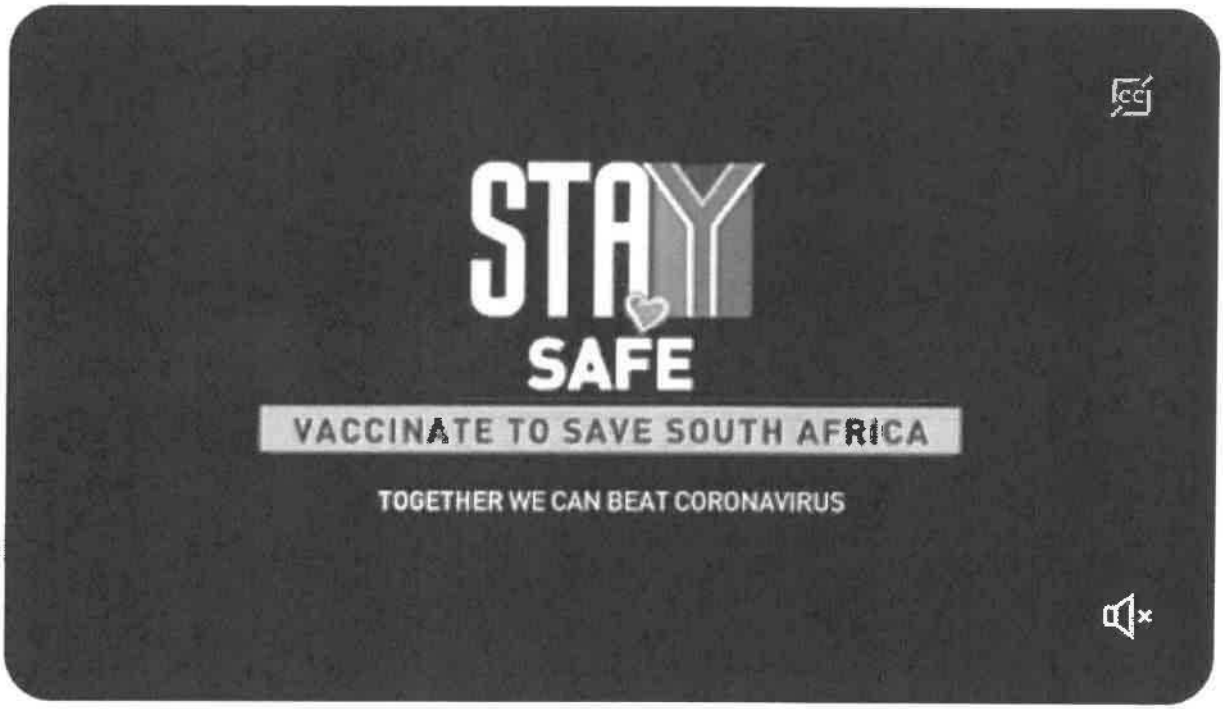
South African Govern... · 2021/07/22

South Africa government organization

The coronavirus vaccines are **safe and effective**. They provide protection against #COVID19 #StaySafe #IChooseVaccination



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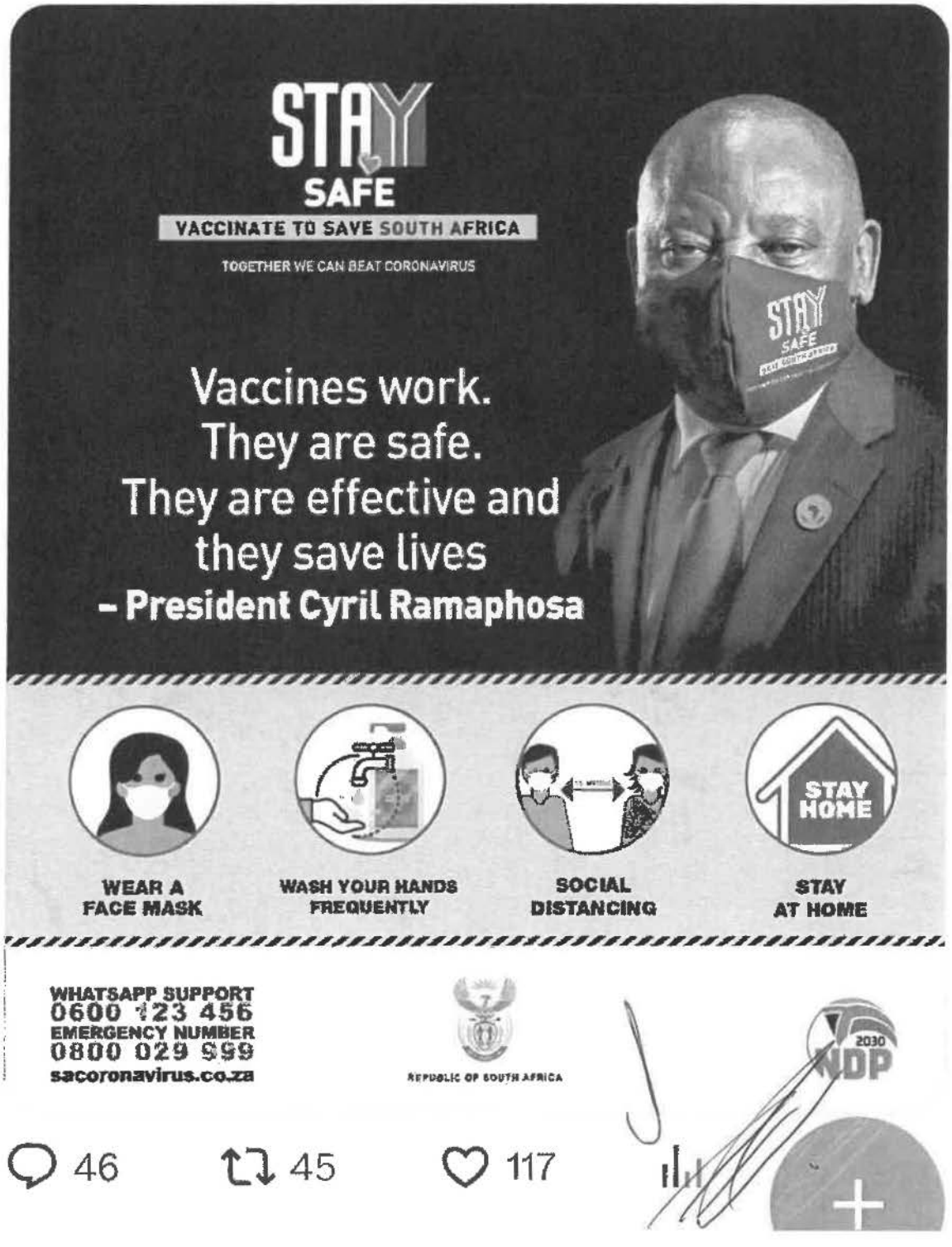
South African Govern... · 2021/07/09

South Africa government organization

Vaccines are **safe**, reliable **and effective**. The vaccines that we are currently using in the rollout do work against the variant we are dealing with. - Dr Nicholas Crisp

#IChooseVaccination #VaccineRollOutSA



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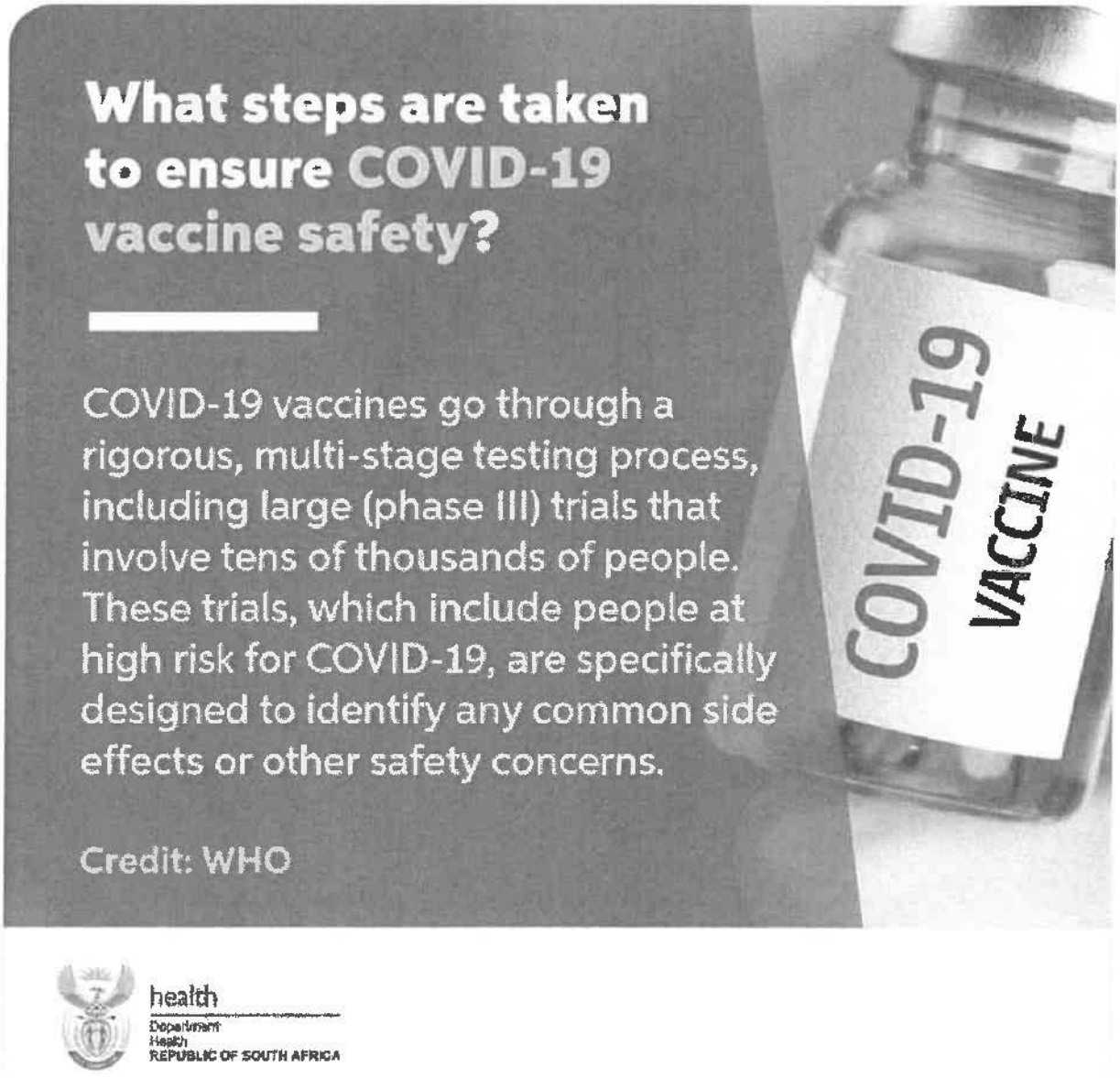
South African Govern... · 2021/08/10

South Africa government organization

#COVID19 vaccines undergo rigorous trials to ensure they are **safe and effective.**

#IChooseVaccination #StaySafe



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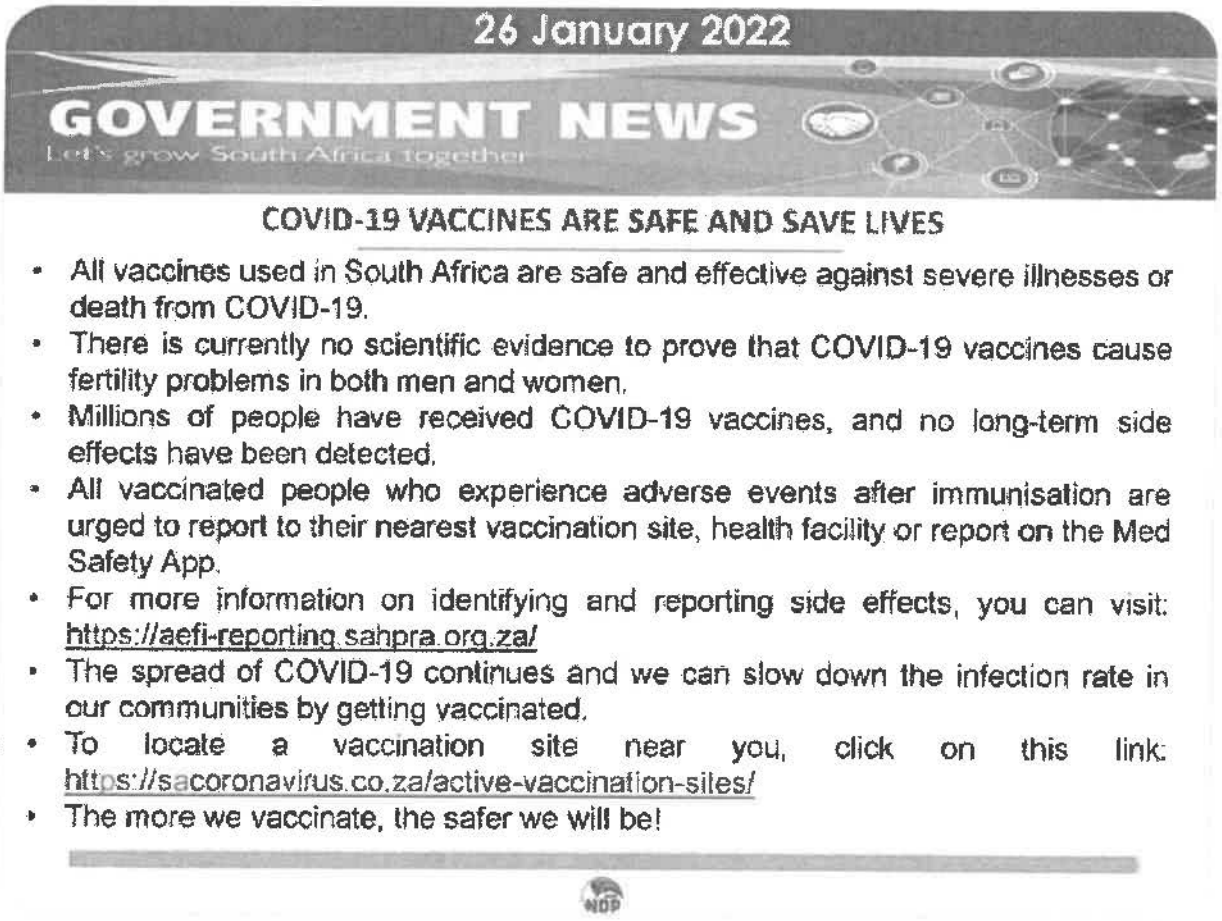
South African Govern... · 2022/01/26

South Africa government organization

We are spreading the message in all languages to ensure that people understand that these vaccines are **safe, effective and** free. #VaccinateToSaveSA #VaccinesWork



26 January 2022

GOVERNMENT NEWS

Let's grow South Africa together

COVID-19 VACCINES ARE SAFE AND SAVE LIVES

- All vaccines used in South Africa are safe and effective against severe illnesses or death from COVID-19.
- There is currently no scientific evidence to prove that COVID-19 vaccines cause fertility problems in both men and women.
- Millions of people have received COVID-19 vaccines, and no long-term side effects have been detected.
- All vaccinated people who experience adverse events after immunisation are urged to report to their nearest vaccination site, health facility or report on the Med Safety App.
- For more information on identifying and reporting side effects, you can visit: https://aefi-reporting.sahpra.org.za/
- The spread of COVID-19 continues and we can slow down the infection rate in our communities by getting vaccinated.
- To locate a vaccination site near you, click on this link: https://sacoronavirus.co.za/active-vaccination-sites/
- The more we vaccinate, the safer we will be!

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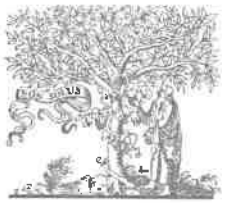

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Serious adverse events of special interest following mRNA COVID-19 vaccination in randomized trials in adults

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ABSTRACT

Introduction: In 2020, prior to COVID-19 vaccine rollout, the Brighton Collaboration created a priority list, endorsed by the World Health Organization, of potential adverse events relevant to COVID-19 vaccines. We adapted the Brighton Collaboration list to evaluate serious adverse events of special interest observed in mRNA COVID-19 vaccine trials.

Methods: Secondary analysis of serious adverse events reported in the placebo-controlled, phase III randomized clinical trials of Pfizer and Moderna mRNA COVID-19 vaccines in adults (NCT04368728 and NCT04470427), focusing analysis on Brighton Collaboration adverse events of special interest.

Results: Pfizer and Moderna mRNA COVID-19 vaccines were associated with an excess risk of serious adverse events of special interest of 10.1 and 15.1 per 10,000 vaccinated over placebo baselines of 17.6 and 42.2 (95 % CI −0.4 to 20.6 and −3.6 to 33.8), respectively. Combined, the mRNA vaccines were associated with an excess risk of serious adverse events of special interest of 12.5 per 10,000 vaccinated (95 % CI 2.1 to 22.9); risk ratio 1.43 (95 % CI 1.07 to 1.92). The Pfizer trial exhibited a 36 % higher risk of serious adverse events in the vaccine group; risk difference 18.0 per 10,000 vaccinated (95 % CI 1.2 to 34.9); risk ratio 1.36 (95 % CI 1.02 to 1.83). The Moderna trial exhibited a 6 % higher risk of serious adverse events in the vaccine group: risk difference 7.1 per 10,000 (95 % CI −23.2 to 37.4); risk ratio 1.06 (95 % CI 0.84 to 1.33). Combined, there was a 16 % higher risk of serious adverse events in mRNA vaccine recipients: risk difference 13.2 (95 % CI −3.2 to 29.6); risk ratio 1.16 (95 % CI 0.97 to 1.39).

Discussion: The excess risk of serious adverse events found in our study points to the need for formal harm-benefit analyses, particularly those that are stratified according to risk of serious COVID-19 outcomes. These analyses will require public release of participant level datasets.

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1. Introduction

In March 2020, the Brighton Collaboration and the Coalition for Epidemic Preparedness Innovations partnership, Safety Platform for Emergency vACcines (SPEAC), created and subsequently updated a "priority list of potential adverse events of special interest relevant to COVID-19 vaccine trials." [1] The list comprises adverse events of special interest (AESIs) based on the specific vaccine platform, adverse events associated with prior vaccines in general, theoretical associations based on animal models, and COVID-19 specific immunopathogenesis. [1] The Brighton Collaboration is a global authority on the topic of vaccine safety and in May 2020, the World Health Organization's Global Advisory Committee on Vaccine Safety endorsed and recommended the reporting of AESIs based on this priority list. To our knowledge, however, the list has not been applied to serious adverse events in randomized trial data.

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We sought to investigate the association between FDA-authorized mRNA COVID-19 vaccines and serious adverse events identified by the Brighton Collaboration, using data from the phase III randomized, placebo-controlled clinical trials on which authorization was based. We consider these trial data against findings from post-authorization observational safety data. Our study was not designed to evaluate the overall harm-benefit of vaccination programs so far. To put our safety results in context, we conducted a simple comparison of harms with benefits to illustrate the need for formal harm-benefit analyses of the vaccines that are stratified according to risk of serious COVID-19 outcomes. Our analysis is restricted to the randomized trial data, and does not consider data on post-authorization vaccination program impact. It does however show the need for public release of participant level trial datasets.

2. Methods

Pfizer and Moderna each submitted the results of one phase III randomized trial in support of the FDA's emergency use authorization of their vaccines in adults. Two reviewers (PD and RK) searched journal publications and trial data on the FDA's and Health Canada's websites to locate serious adverse event results tables for these trials. The Pfizer and Moderna trials are expected to follow participants for two years. Within weeks of the emergency authorization, however, the sponsors began a process of unblinding all participants who elected to be unblinded. In addition, those who received placebo were offered the vaccine. These self-selection processes may have introduced nonrandom differences between vaccinated and unvaccinated participants, thus rendering the post-authorization data less reliable. Therefore, to preserve randomization, we used the interim datasets that were the basis for emergency authorization in December 2020, approximately 4 months after trials commenced.

The definition of a serious adverse event (SAE) was provided in each trial's study protocol and included in the supplemental material of the trial's publication. [2–4] Pfizer and Moderna used nearly identical definitions, consistent with regulatory expectations. An SAE was defined as an adverse event that results in any of the following conditions: death; life-threatening at the time of the event; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant disability/incapacity; a congenital anomaly/birth defect; medically important event, based on medical judgment.

In addition to journal publications, we searched the websites of the FDA (for advisory committee meeting materials) and Health Canada (for sections of the dossier submitted by sponsors to the regulator). [5] For the FDA website, we considered presentations by both the FDA and the sponsors. [6] Within each of these sources, we searched for SAE results tables that presented information by specific SAE type; we chose the most recent SAE table corresponding to the FDA's requirement for a safety median follow-up time of at least 2 months after dose 2.

For each trial, we prepared blinded SAE tables (containing SAE types without results data). Using these blinded SAE tables, two clinician reviewers (JF and JE) independently judged whether each SAE type was an AESI. SAE types that matched an AESI term verbatim, or were an alternative diagnostic name for an AESI term, were included as an AESI. For all other SAE types, the reviewers independently judged whether that SAE type was likely to have been caused by a vaccine-induced AESI, based on a judgment considering the disease course, causative mechanism, and likelihood of the AESI to cause the SAE type. Disagreements were resolved through consensus; if consensus could not be reached, a third clinician reviewer (PW) was used to create a majority opinion. For each included SAE, we recorded the corresponding Brighton Collaboration AESI category and organ system. When multiple AESIs could potentially cause the same SAE, the reviewers selected the AESI that they judged to be the most likely cause based on classical clinical presentation of the AESI.

We used an AESI list derived from the work of Brighton Collaboration's Safety Platform for Emergency vACcines (SPEAC) Project. This project created an AESI list which categorizes AESIs into three categories: those included because they are seen with COVID-19, those with a proven or theoretical association with vaccines in general, and those with proven or theoretical associations with specific vaccine platforms. The first version was produced in March 2020 based on experience from China. Following the second update (May 2020), the WHO Global Advisory Committee on Vaccine Safety (GACVS) adopted the list, and Brighton commenced a systematic review process "to ensure an ongoing understanding of the full spectrum of COVID-19 disease and modification of the AESI list accordingly." [7] This resulted in three additional AESIs being added to the list in December 2020. The subsequent (and most recent fourth) update did not result in any additional AESIs being added to the list. [1].

We matched SAEs recorded in the trial against an expanded list of AESIs created by combining Brighton's SPEAC COVID-19 AESI list with a list of 29 clinical diagnoses Brighton identified as "known to have been reported but not in sufficient numbers to merit inclusion on the AESI list." [7] Sensitivity analysis was used to determine whether use of the original versus expanded list altered our results.

Risk ratios and risk differences between vaccine and placebo groups were calculated for the incidence of AESIs and SAEs. We excluded SAEs that were known efficacy outcomes (i.e. COVID-19), consistent with the approach Pfizer (but not Moderna) used in recording SAE data. The Pfizer study trial protocol states that COVID-19 illnesses and their sequelae consistent with the clinical endpoint definition were not to be reported as adverse events, "even though the event may meet the definition of an SAE." [8] For unspecified reasons, Moderna included efficacy outcomes in their SAE tables, effectively reporting an all-cause SAE result. Because we did not have access to individual participant data, to account for the occasional multiple SAEs within single participants, we reduced the effective sample size by multiplying standard errors in the combined SAE analyses by the square root of the ratio of the number of SAEs to the number of patients with an SAE. This adjustment increased standard errors by 10 % (Pfizer) and 18 % (Moderna), thus expanding the interval estimates. We estimated combined risk ratios and risk differences for the two mRNA vaccines by averaging over the risks using logistic regression models which included indicators for trial and treatment group.

We used a simple harm-benefit framework to place our results in context, comparing risks of excess serious AESIs against reductions in COVID-19 hospitalization.

3. Results

Serious adverse event tables were located for each of the vaccine trials submitted for EUA in adults (age 16 + for Pfizer, 18 + for Moderna) in the United States: Pfizer-BioNTech COVID-19 vaccine BNT162b2 (NCT04368728) [2,9,10] and Moderna COVID-19 vaccine mRNA-1273 (NCT04470427). [3,11,12] (Table 1).

3.1. Reporting windows and serious adverse events

Moderna reported SAEs from dose 1 whereas Pfizer limited reporting from dose 1 to 1 month after dose 2. Both studies

Table 1
Data sources for phase III trials.

Trial	Data cutoff date	Journal articles	FDA sources	Health Canada sources
Pfizer trial in ages 16 and above (NCT04368728)	14 Nov 2020 (supported Dec 2020 EUA)	Aggregate data only	**Table 23 in sponsor briefing document**	**Table 55 in sponsor document C4591001 Final Analysis Interim Report Body**
Moderna trial in ages 18 and above (NCT04470427)	25 Nov 2020 (supported Dec 2020 EUA)	Table S11 in publication	Table 27 in sponsor briefing document	**Table 14.3.1.13.3 in sponsor document mRNA-1273-P301 Unblinded Safety Tables Batch 1 (DS2)**

Note: bolded font indicates dataset chosen for analysis; EUA = Emergency Use Authorization.

reported all data at the time of data cutoff (14 Nov 2020 for Pfizer, 25 Nov 2020 for Moderna). 17 SAEs that were efficacy endpoints were removed from the Moderna trial (16 "COVID-19" SAEs and 1 "COVID-19 pneumonia" SAE). One such efficacy endpoint meeting the definition of a SAE was removed from the Pfizer trial ("SARS-CoV-2 test positive" SAE).

The Pfizer trial exhibited a 36 % higher risk of serious adverse events in vaccinated participants in comparison to placebo recipients: 67.5 per 10,000 versus 49.5 per 10,000; risk difference 18.0 per 10,000 vaccinated participants (95 % compatibility[1] interval 1.2 to 34.9); risk ratio 1.36 (95 % CI 1.02 to 1.83). The Moderna trial exhibited a 6 % higher risk of SAEs in vaccinated individuals compared to those receiving placebo: 136 per 10,000 versus 129 per 10,000; risk difference 7.1 per 10,000 (95 % CI −23.2 to 37.4); risk ratio 1.06 (95 % CI 0.84 to 1.33). Combined, there was a 16 % higher risk of SAEs in mRNA vaccine recipients than placebo recipients: 98 per 10,000 versus 85 per 10,000; risk difference 13.2 (95 % CI −3.2 to 29.6); risk ratio 1.16 (95 % CI 0.97 to 1.39). (Table 2).

3.2. Serious adverse events of special interest

Regarding whether each SAE type was included on the SPEAC derived AESI list, agreement between the two independent clinician reviewers was 86 % (281/325); 40 of the 44 disagreements were resolved through consensus, and only four disagreements necessitated a third clinician reviewer. **Supplemental** Table 1 includes a full list of included and excluded SAEs across both trials.

In the Pfizer trial, 52 serious AESI (27.7 per 10,000) were reported in the vaccine group and 33 (17.6 per 10,000) in the placebo group. This difference corresponds to a 57 % higher risk of serious AESI (RR 1.57 95 % CI 0.98 to 2.54) and a risk difference of 10.1 serious AESI per 10,000 vaccinated participants (95 % CI −0.4 to 20.6). In the Moderna trial, 87 serious AESI (57.3 per 10,000) were reported in the vaccine group and 64 (42.2 per 10,000) in the placebo group. This difference corresponds to a 36 % higher risk of serious AESI (RR 1.36 95 % CI 0.93 to 1.99) and a risk difference of 15.1 serious AESI per 10,000 vaccinated participants (95 % CI −3.6 to 33.8). Combining the trials, there was a 43 % higher risk of serious AESI (RR 1.43; 95 % CI 1.07 to 1.92) and a risk difference of 12.5 serious AESI per 10,000 vaccinated participants (95 % CI 2.1 to 22.9). (Table 2).

Of the 236 serious AESIs occurring across the Pfizer and Moderna trials, 97 % (230/236) were adverse event types included as AESIs because they are seen with COVID-19. In both Pfizer and Moderna trials, the largest excess risk occurred amongst the Brighton category of coagulation disorders. Cardiac disorders have been of central concern for mRNA vaccines; in the Pfizer trial more cardiovascular AESIs occurred in the vaccine group than in the placebo group, but in the Moderna trial the groups differed by only 1 case. (Tables 3 and 4).

[1] A compatibility interval is identical to a confidence interval, but relabeled to emphasize that it is not a Bayesian posterior interval (as is improperly suggested by the "confidence" label).[13,14]

3.3. Sensitivity analysis

As a sensitivity analysis, we restricted the serious AESI analysis to those AESIs listed in SPEAC's COVID-19 AESI list (i.e. separating out Brighton's list of 29 clinical diagnoses "known to have been reported but not in sufficient numbers to merit inclusion on the AESI list.") This reduced the total number of AESIs across the two trials by 48 (35 vaccine group, 13 placebo group). There was still a higher risk of serious AESI when limited to the SPEAC COVID-19 AESI list, but the magnitude of the excess (in both relative and absolute terms) was smaller than when using the larger AESI list. **(Supplemental** Table 2).

3.4. Harm-benefit considerations

In the Moderna trial, the excess risk of serious AESIs (15.1 per 10,000 participants) was higher than the risk reduction for COVID-19 hospitalization relative to the placebo group (6.4 per 10,000 participants). [3] In the Pfizer trial, the excess risk of serious AESIs (10.1 per 10,000) was higher than the risk reduction for COVID-19 hospitalization relative to the placebo group (2.3 per 10,000 participants).

4. Comparison with FDA reviews

In their review of SAEs supporting the authorization of the Pfizer and Moderna vaccines, the FDA concluded that SAEs were, for Pfizer, "balanced between treatment groups," [15] and for Moderna, were "without meaningful imbalances between study arms." [16] In contrast to the FDA analysis, we found an excess risk of SAEs in the Pfizer trial. Our analysis of Moderna was compatible with FDA's analysis, finding no meaningful SAE imbalance between groups.

The difference in findings for the Pfizer trial, between our SAE analysis and the FDA's, may in part be explained by the fact that the FDA analyzed the total number of participants experiencing any SAE, whereas our analysis was based on the total number of SAE events. Given that approximately twice as many individuals in the vaccine group than in the placebo group experienced multiple SAEs (there were 24 more events than participants in the vaccine group, compared to 13 in the placebo group), FDA's analysis of only the incidence of participants experiencing any SAE would not reflect the observed excess of multiple SAEs in the vaccine group.

A more important factor, however, may be that FDA's review of non-fatal SAEs used a different analysis population with different follow-up windows. The FDA reported 126 of 21,621 (0.6 %) of vaccinated participants experienced at least one SAE at data cutoff compared to 111 of 21,631 (0.5 %) of placebo participants. In contrast, our analysis found 127 SAEs among 18,801 vaccine recipients versus 93 SAEs among 18,785 placebo recipients. [15] While summary results for the population we analyzed was provided in a table, FDA did not report an analysis of them. The substantially larger denominators in FDA's analysis (5,666 more participants) reflect the fact that their analysis included all individuals receiving at least one dose (minus 196 HIV-positive participants), irrespec-

Table 2
Serious adverse events.

Trial	Total events (events per 10,000 participants)[a] Vaccine	Placebo	Risk difference per 10,000 participants (95 % CI)[e]	Risk ratio (95 % CI)[e]
Serious adverse events				
Pfizer[b]	127 (67.5)	93 (49.5)	18.0 (1.2 to 34.9)	1.36 (1.02 to 1.83)
Moderna[c,d]	206 (135.7)	195 (128.6)	7.1 (−23.2 to 37.4)	1.06 (0.84 to 1.33)
Combined[f]	333 (98.0)	288 (84.8)	13.2 (−3.2 to 29.6)	1.16 (0.97 to 1.39)
Serious adverse events of special interest				
Pfizer	52 (27.7)	33 (17.6)	10.1 (−0.4 to 20.6)	1.57 (0.98 to 2.54)
Moderna	87 (57.3)	64 (42.2)	15.1 (−3.6 to 33.8)	1.36 (0.93 to 1.99)
Combined	139 (40.9)	97 (28.6)	12.5 (2.1 to 22.9)	1.43 (1.07 to 1.92)

[a] Denominators for Pfizer were 18,801 in the vaccine group and 18,785 in the placebo group, and for Moderna were 15,185 in the vaccine group and 15,166 in the placebo group.

[b] Pfizer excluded efficacy outcomes from its SAE table (COVID-19 illnesses and their sequelae meeting the definition of an SAE). However, at least one SAE appears to have been inadvertently included, which we removed from our calculations ("SARS-CoV-2 test positive": 0 vaccine group; 1 placebo group).

[c] Moderna included efficacy outcomes in its SAE table (COVID-19 illnesses and their sequelae meeting the definition of an SAE). We removed efficacy SAEs outcomes that could be identified: "COVID-19" and "COVID-19 pneumonia." Lacking access to participant level data, SAEs that were sequelae of serious COVID-19 could not be identified and therefore remain included in this analysis.

[d] "All SAEs" for Moderna was calculated using the "Number of serious AEs" row in Moderna's submission to FDA.[11].

[e] Standard errors used to estimate 95% CIs were inflated by the factor $\sqrt{[\#SAE]/[\#patients\ with\ SAE]}$ to account for multiple SAE within patients.

[f] The combined risk differences and risk ratios were computed from the fitted logistic regression models and so may not exactly equal comparisons computed from the first two columns.

Table 3
Serious AESIs, Pfizer trial.

Brighton category	Vaccine	Placebo	Vaccine events per 10,000	Placebo events per 10,000	Difference in events per 10,000	Risk ratio
Association with immunization in general						
Anaphylaxis	1	1	0.5	0.5	0.0	1.00
Association with specific vaccine platform(s)						
Encephalitis/encephalomyelitis	0	2	0.0	1.1	1.1	0.00
Seen with COVID-19						
Acute kidney injury	2	0	1.1	0.0	1.1	N/A
Acute liver injury	0	1	0.0	0.5	−0.5	0.00
Acute respiratory distress syndrome	2	1	1.1	0.5	0.5	2.00
Coagulation disorder	16	10	8.5	5.3	3.2	1.60
Myocarditis/pericarditis	2	1	1.1	0.5	0.5	2.00
Other forms of acute cardiac injury	16	12	8.5	6.4	2.1	1.33
Subtotal	39	28	20.7	14.9	5.8	1.39
Brighton list of 29 clinical diagnoses seen with COVID-19						
Abscess	4	1	2.1	0.5	1.6	4.00
Cholecystitis	4	2	2.1	1.1	1.1	2.00
Colitis/Enteritis	1	1	0.5	0.5	0.0	1.00
Diarrhea	1	0	0.5	0.0	0.5	N/A
Hyperglycemia	1	1	0.5	0.5	0.0	1.00
Pancreatitis	1	0	0.5	0.0	0.5	N/A
Psychosis	1	0	0.5	0.0	0.5	N/A
Subtotal	13	5	6.9	2.7	4.3	2.60
Total	**52**	**33**	**27.7**	**17.6**	**10.1**	**1.57**

tive of the duration of post-injection follow-up time. In contrast, our analysis was based on the study population with median follow-up ≥ 2 months after dose 2 (minus 120 HIV-positive participants), of which 98.1 % had received both doses. [2,17] The FDA's analysis of SAEs thus included thousands of additional participants with very little follow-up, of which the large majority had only received 1 dose.

4.1. Comparison with post-authorization studies

Although the randomized trials offer high level evidence for evaluating causal effects, the sparsity of their data necessitates that harm-benefit analyses also consider observational studies. Since their emergency authorization in December 2020, hundreds of millions of doses of Pfizer and Moderna COVID-19 vaccines have been administered and post-authorization observational data offer a complementary opportunity to study AESIs. Post-authorization observational safety studies include cohort studies (which make use of medical claims or electronic health records) and disproportionality analyses (which use spontaneous adverse event reporting systems). In July 2021, the FDA reported detecting four potential adverse events of interest: pulmonary embolism, acute myocardial infarction, immune thrombocytopenia, and disseminated intravascular coagulation following Pfizer's vaccine based on medical claims data in older Americans. [18] Three of these four serious adverse event types would be categorized as coagulation disorders, which is the Brighton AESI category that exhibited the largest excess risk in the vaccine group in both the Pfizer and Moderna trials. FDA stated it would further investigate the findings but at the time of our writing has not issued an update. Similarly, spontaneous-reporting systems have registered serious adverse reactions including anaphylaxis (all COVID-19 vaccines), thrombocytopenia syndrome among premenopausal females (Janssen vaccine), and myocarditis and pericarditis among younger males (Pfizer and Moderna vaccines). [19,20].

Using data from three postmarketing safety databases for vaccines (VAERS, EudraVigilance, and VigiBase), disproportionality studies have reported excess risks for many of the same SAE types as in

Table 4
Serious AESIs, Moderna trial.

Brighton category	Vaccine	Placebo	Vaccine events per 10,000	Placebo events per 10,000	Difference in events per 10,000	Risk ratio
Association with specific vaccine platform(s)						
Bell's Palsy	1	0	0.7	0.0	0.7	N/A
Encephalitis/encephalomyelitis	1	0	0.7	0.0	0.7	N/A
Seen with COVID-19						
Acute kidney injury	1	3	0.7	2.0	−1.3	0.33
Acute liver injury	1	0	0.7	0.0	0.7	N/A
Acute respiratory distress syndrome	7	4	4.6	2.6	2.0	1.75
Angioedema	0	2	0.0	1.3	−1.3	0.00
Coagulation disorder	20	13	13.2	8.6	4.6	1.54
Generalized Convulsions	2	0	1.3	0.0	1.3	N/A
Myelitis	0	1	0.0	0.7	−0.7	0.00
Myocarditis/pericarditis	4	5	2.6	3.3	−0.7	0.80
Other forms of acute cardiac injury	26	26	17.1	17.1	0.0	1.00
Other rash	1	1	0.7	0.7	0.0	1.00
Rhabdomyolysis	0	1	0.0	0.7	−0.7	0.00
Single Organ Cutaneous Vasculitis	1	0	0.7	0.0	0.7	N/A
Subtotal	65	56	42.8	36.9	5.9	1.16
Brighton list of 29 clinical diagnoses seen with COVID-19						
Abscess	1	0	0.7	0.0	0.7	N/A
Arthritis	3	1	2.0	0.7	1.3	3.00
Cholecystitis	4	0	2.6	0.0	2.6	N/A
Colitis/Enteritis	6	3	4.0	2.0	2.0	2.00
Diarrhea	2	1	1.3	0.7	0.7	2.00
Hyperglycemia	1	0	0.7	0.0	0.7	N/A
Hyponatremia	1	1	0.7	0.7	0.0	1.00
Pancreatitis	2	0	1.3	0.0	1.3	N/A
Pneumothorax	0	1	0.0	0.7	−0.7	0.00
Psychosis	1	1	0.7	0.7	0.0	1.00
Thyroiditis	1	0	0.7	0.0	0.7	N/A
Subtotal	22	8	14.5	5.3	9.2	2.75
Total	**87**	**64**	**57.3**	**42.2**	**15.1**	**1.36**

the present study. [21–23] For example, a study using VAERS and EudraVigilance comparing the disproportionality of adverse event reports between the influenza vaccine versus the mRNA COVID-19 vaccines reported excess risks for the following Brighton AESIs: cardiovascular events, coagulation events, hemorrhages, gastrointestinal events, and thromboses. [22] While CDC published a protocol[24] in early 2021 for using proportional reporting ratios for signal detection in the VAERS database, results from the study have not yet been reported. [25] Among self-controlled case series, one reported a rate ratio of 1.38 (95 % CI 1.12–1.71) for hemorrhagic stroke following Pfizer vaccine, [26] another reported 0.97 (95 % CI 0.81–1.15), [27] while a cohort study[28] reported 0.84 (95 % CI 0.54–1.27).

5. Discussion

Using a prespecified list of AESI identified by the Brighton Collaboration, higher risk of serious AESI was observed in the mRNA COVID-19 vaccine group relative to placebo in both the Pfizer and Moderna adult phase III trials, with 10.1 (Pfizer) and 15.1 (Moderna) additional events for every 10,000 individuals vaccinated. Combined, there was a risk difference of 12.5 serious AESIs per 10,000 individuals vaccinated (95 % CI 2.1 to 22.9). These results raise concerns that mRNA vaccines are associated with more harm than initially estimated at the time of emergency authorization. In addition, our analysis identified a 36 % higher risk of serious adverse events in vaccinated participants in the Pfizer trial: 18.0 additional SAEs per 10,000 vaccinated (95 % CI 1.2 to 34.9). Consistent with the FDA evaluation, our analysis found no clear difference in SAEs between groups in the Moderna trial.

Results between the Pfizer and Moderna trials were similar for the AESI analysis but exhibited substantial variation in the SAE analysis. Caution is needed in interpreting this variation as it may be substantially explained by differences in SAE recording practices in the trials rather than differences in actual vaccine harm profiles. For reasons that are not documented in the trial protocol, Moderna included efficacy outcomes in its SAE tabulations, while Pfizer excluded them. As a result, Moderna's SAE table did not present a traditional SAE analysis but rather an all-cause SAE analysis. The FDA analysis of the Moderna trial presented an all-cause SAE analysis, which estimates total vaccine effects on SAEs, including effects transmitted via effects on COVID-19. It did not however present a traditional SAE analysis with efficacy endpoints removed, which attempts to estimate only the direct effects on SAEs. While our analysis attempted to perform a traditional SAE analysis by excluding efficacy SAEs (serious COVID-19 and its sequelae), our effort was hindered because we did not have access to patient level data. Easily recognizable efficacy SAEs ("COVID-19", "COVID-19 pneumonia," and "SARS-CoV-2 test positive") could be removed, but many participants who experienced a COVID-19 SAE likely experienced multiple other SAEs (e.g. pneumonia, hypoxia, and thrombotic events) which could not be identified and therefore remain included in our analysis. Of 17 total efficacy SAEs (16 "COVID-19" and 1 "COVID-19 pneumonia") removed from our analysis of the Moderna trial, 16 were in the placebo arm. As a consequence, the background SAE risk (risk in absence of COVID-19) would be overestimated by the Moderna placebo group, resulting in underestimation of the actual risk of SAEs and AESIs attributable to the vaccine in the Moderna comparisons as well as in the combined analysis. Access to patient-level data would allow adjustments for this problem.

Rational policy formation should consider potential harms alongside potential benefits. [29] To illustrate this need in the present context, we conducted a simple harm-benefit comparison using the trial data comparing excess risk of serious AESI against reductions in COVID-19 hospitalization. We found excess risk of serious AESIs to exceed the reduction in COVID-19 hospitalizations in both Pfizer and Moderna trials.

This analysis has the limitations inherent in most harm-benefit comparisons. First, benefits and harms are rarely exact equivalents, and there can be great variability in the degree of severity within both benefit and harm endpoints. For example, intubation and short hospital stay are not equivalent but both are counted in "hospitalization"; similarly, serious diarrhea and serious stroke are not equivalent but both are counted in "SAE." Second, individuals value different endpoints differently. Third, without individual participant data, we could only compare the number of individuals hospitalized for COVID-19 against the number of serious AESI events, not the number of participants experiencing any serious AESI. Some individuals experienced multiple SAEs whereas hospitalized COVID-19 participants were likely only hospitalized once, biasing the analysis towards exhibiting net harm. To gauge the extent of this bias, we considered that there were 20 % (Pfizer) and 34 % (Moderna) more SAEs than participants experiencing any SAE. As a rough sensitivity calculation, if we divide the Pfizer excess serious AESI risk of 10.1 by 1.20 it becomes 8.4 compared to a COVID-19 hospitalization risk reduction of 2.3; if we divide the Moderna excess serious AESI risk of 15.1 by 1.34 it becomes 11.3 compared to a COVID-19 hospitalization risk reduction of 6.4.

Harm-benefit ratios will be different for populations at different risk for serious COVID-19 and observation periods that differ from those studied in the trials. Presumably, larger reductions in COVID-19 hospitalizations would have been recorded if trial follow-up were longer, more SARS-CoV-2 was circulating, or if participants had been at higher risk of serious COVID-19 outcomes, shifting harm-benefit ratios toward benefit. Conversely, harm-benefit ratios would presumably shift towards harm for those with lower risk of serious COVID-19 outcomes—such as those with natural immunity, younger age or no comorbidities. Similarly, waning vaccine effectiveness, decreased viral virulence, and increasing degree of immune escape from vaccines might further shift the harm-benefit ratio toward harm. Large, randomized trials in contemporary populations could robustly answer these questions. Absent definitive trials, however, synthesis of multiple lines of evidence will be essential. [30,48,49].

Adverse events detected in the post-marketing period have led to the withdrawal of several vaccines. An example is intussusception following one brand of rotavirus vaccine: around 1 million children were vaccinated before identification of intussusception, which occurred in around 1 per 10,000 vaccinees. [31] Despite the unprecedented scale of COVID-19 vaccine administration, the AESI types identified in our study may still be challenging to detect with observational methods. Most observational analyses are based on comparing the risks of adverse events "observed" against a background (or "expected") risk, which inevitably display great variation, by database, age group, and sex. [32] If the actual risk ratio for the effect was 1.4 (the risk ratio of the combined AESI analysis), it could be quite difficult to unambiguously replicate it with observational data given concerns about systematic as well as random errors. [33–35].

In addition, disproportionality analyses following COVID-19 vaccination also have limitations, particularly with respect to the type of adverse events seen in our study. The majority of SAEs that contributed to our results are relatively common events, such as ischemic stroke, acute coronary syndrome, and brain hemorrhage. This complicates signal detection because clinical suspicion of an adverse vaccine reaction following an event commonly seen in clinical practice will be lower than for SAEs like myocarditis.[50] For this reason, clinical suspicion leading to the filing of an individual case safety report--may be far less common in the post-authorization setting than in the trials. At the same time, heightened awareness about COVID-19 vaccine SAEs can result in under and overreporting. Public health messages assuring vaccine safety may lower clinical suspicion of potential causal relationships, whereas messages about potential harms can conversely stimulate reports that otherwise may not have been made. These factors can lead to bias both directions, further complicating interpretation. In contrast to these problems, in the randomized trials used in this analysis, all SAEs were to be recorded, irrespective of clinical judgment regarding potential causality.

Although our analysis is secondary, reanalyses of clinical trial data have led to the detection of adverse events well after the market entry of major drugs such as rofecoxib and rosiglitazone. [36,37] Our analysis has an advantage over postmarketing observational studies in that the data are from blinded, placebo-controlled randomized trials vetted by the FDA, which were matched against a list of adverse events created before the availability of the clinical-trial results and designed for use in COVID-19 vaccine trials.

Our study has several important limitations. First, Pfizer's trial did not report SAEs occurring past 1 month after dose 2. This reporting threshold may have led to an undercounting of serious AESIs in the Pfizer trial. Second, for both studies, the limited follow up time prevented an analysis of harm-benefit over a longer period. Third, all SAEs in our analysis met the regulatory definition of a serious adverse event, but many adverse event types which a patient may themselves judge as serious may not meet this regulatory threshold. Fourth, decisions about which SAEs to include or exclude as AESIs requires subjective, clinical judgements in the absence of detailed clinical information about the actual SAEs. We encourage third party replication of our study, with access to complete SAE case narratives, to determine the degree to which these decisions affected our findings. For additional sensitivity analyses, such replication studies could also make use of other AESI lists, such as those prepared by FDA, [38–41] CDC, [24], Pfizer, [42], or a *de novo* AESI list derived from a list of COVID-19 complications understood to be induced via SARS-CoV-2's spike protein. [43,44].

A fifth important limitation is our lack of access to individual participant data, which forced us to use a conservative adjustment to the standard errors. The 95 % CIs[13,14] calculated are therefore only approximate because we do not know which patients had multiple events. Finally, as described above, in the Moderna analysis, the SAEs that were sequelae of serious COVID-19 could not be identified and therefore remain included in our calculations. Because the vaccines prevent SAEs from COVID-19 while adding SAE risks of their own, this inclusion makes it impossible to separately estimate SAEs due to the vaccine from SAEs due to COVID-19 in the available Moderna data, as must be done to extrapolate harm-benefit to other populations. These study limitations all stem from the fact that the raw data from COVID-19 vaccine clinical trials are not publicly available. [45,46].

We emphasize that our investigation is preliminary, to point to the need for more involved analysis. The risks of serious AESIs in the trials represent only group averages. SAEs are unlikely to be distributed equally across the demographic subgroups enrolled in the trial, and the risks may be substantially less in some groups compared to others. Thus, knowing the actual demographics of those who experienced an increase in serious AESI in the vaccine group is necessary for a proper harm-benefit analysis. In addition, clinical studies are needed to see if particular SAEs can be linked to particular vaccine ingredients as opposed to unavoidable consequences of exposure to spike protein, as future vaccines could then be modified accordingly or sensitivities can be tested for in advance. In parallel, a systematic review and meta-analysis using individual participant data should be undertaken to address questions of harm-benefit in various demographic subgroups, particularly in those at low risk of serious complications from COVID-19. Finally, there is a pressing need for comparison of SAEs and harm-benefit for different vaccine types; some initial work has already begun in this direction. [47].

Full transparency of the COVID-19 vaccine clinical trial data is needed to properly evaluate these questions. Unfortunately, as we approach 2 years after release of COVID-19 vaccines, participant level data remain inaccessible. [45,46].

Author contributions

All authors had full access to all of the data in the study (available at https://doi.org/10.5281/zenodo.6564402), and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: All authors.
Acquisition of data: Doshi.
Analysis and interpretation: All authors.
Statistical analysis: Jones, Greenland.
Drafting of the manuscript: Fraiman, Doshi.
Critical revision of the manuscript for important intellectual content: All authors.

Data availability

All of the data in the study is available at https://doi.org/10.5281/zenodo.6564402

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethical review statement

This research was confirmed to be Not Human Subjects Research (NHSR) by University of Maryland, Baltimore (HP-00102561).

Conflicts of interest

JF, JE, MJ, SG, PW, RK: none to declare. PD has received travel funds from the European Respiratory Society (2012) and Uppsala Monitoring Center (2018); grants from the FDA (through University of Maryland M-CERSI; 2020), Laura and John Arnold Foundation (2017-22), American Association of Colleges of Pharmacy (2015), Patient-Centered Outcomes Research Institute (2014-16), Cochrane Methods Innovations Fund (2016-18), and UK National Institute for Health Research (2011-14); was an unpaid IMEDS steering committee member at the Reagan-Udall Foundation for the FDA (2016-2020) and is an editor at The BMJ. The views expressed here are those of the authors and do not necessarily reflect those of their employers.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.08.036.

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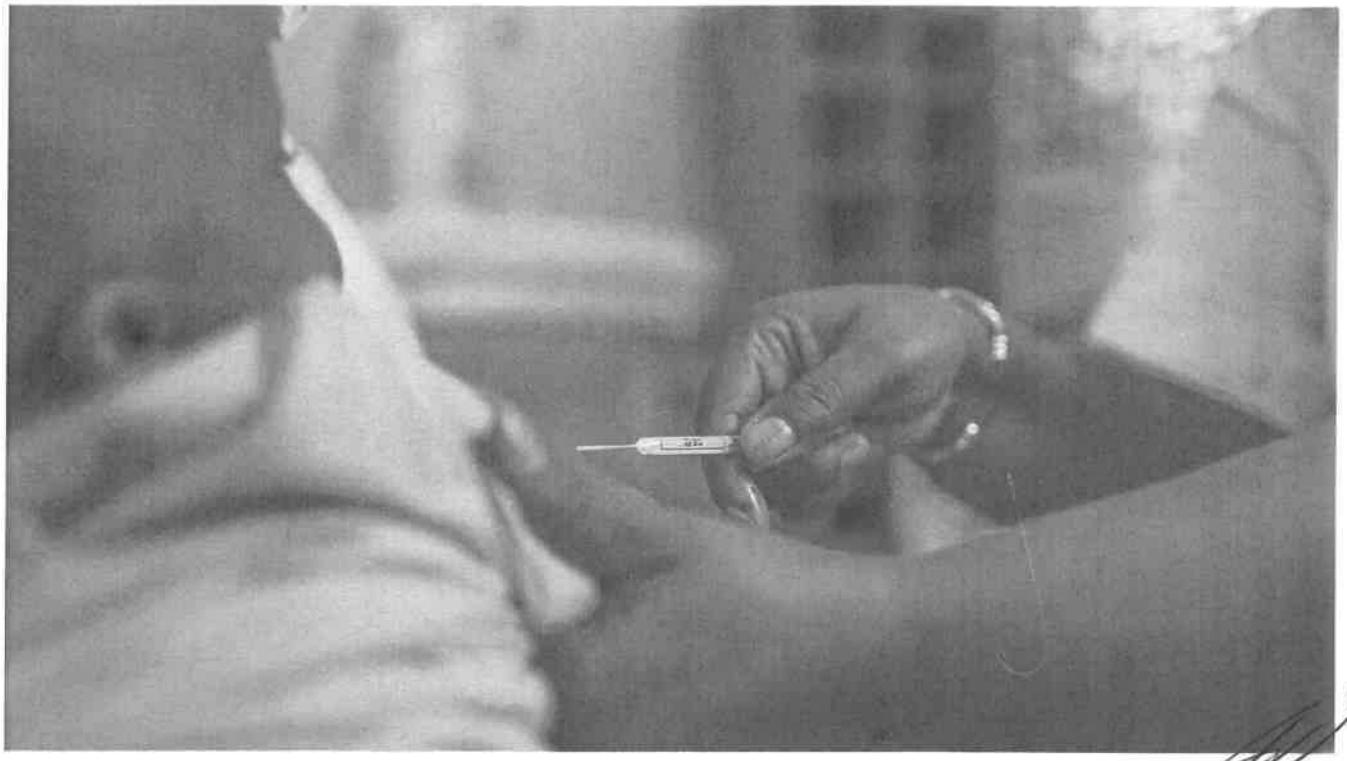
VaccinesWork

The science behind COVID-19 COVID-19 Explainer

What is the difference between efficacy and effectiveness?

The two terms used to describe how well a drug or vaccine works are often used interchangeably, but they are not actually the same thing – here's why.

18 November 2020 3 min read **by** Priya Joi



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Efficacy is the degree to which a vaccine prevents disease, and possibly also transmission, under ideal and controlled circumstances – comparing a vaccinated group with a placebo group. Effectiveness meanwhile refers to how well it performs in the real world. Although a vaccine that has high efficacy – such as Moderna's COVID-19 vaccine with 94.5% efficacy and Pfizer's with 90% efficacy – would be expected to be highly effective in the real world, it is unlikely to translate into the same effectiveness in practice.

What is efficacy?

A vaccine with an efficacy of 90% in a trial, for instance, means there was a 90% reduction in cases of disease in the vaccinated group compared to the unvaccinated (or placebo) group. But efficacy in laboratory conditions does not always translate to effectiveness, and so an efficacy trial can overestimate a vaccine's impact in practice.

In clinical trials, the conditions under which a participant is taking a vaccine are carefully designed – people are often not included in trials if they have underlying health issues, or are taking medication – and side effects are closely monitored.

Moreover, participants in the trial represent a subsection of the full age range of a population. For example, not many COVID-19 vaccine trials have included young children, even though they may also need to receive the vaccine when one is ready.

How do we measure effectiveness?

When a vaccine is given to the population, factors, such as the medication people are taking, underlying chronic illnesses, age, and how the vaccine is stored and administered under everyday conditions, can reduce how effective the vaccine is at preventing disease.

Once the efficacy of a vaccine has been determined, measuring its effectiveness is critical to ensuring uptake of the vaccine and to understand how to develop better vaccines. Surveillance data is vital to understanding effectiveness, as is immunisation data – capturing data, for example, on when people get the vaccine and what proportion of the population in a given country is covered.

Effectiveness of a vaccine is measured in what epidemiologists call observational studies because participants are not randomly assigned to a treatment versus a placebo group. For example, case-control studies assess effectiveness by comparing the vaccination status of individuals who develop the disease (cases) with a group of individuals without the disease (controls) who are also representative of the population from which the cases arise. If the vaccine is effective, the cases are more likely to be the unvaccinated individuals.

Vaccines do not always need to have an exceptionally high effectiveness to be useful, for example the influenza vaccine is 40-60% effective yet saves thousands of lives every year.

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CLINICAL/NARRATIVE REVIEW

A Primer on Effectiveness and Efficacy Trials

Amit G. Singal, MD, MS[1,2], Peter D.R. Higgins, MD, PhD[3] and Akbar K. Waljee, MD, MS[3,4]

Although efficacy and effectiveness studies are both important when evaluating interventions, they serve distinct purposes and have different study designs. Unfortunately, the distinction between these two types of trials is often poorly understood. In this primer, we highlight several differences between these two types of trials including study design, patient populations, intervention design, data analysis, and result reporting.

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INTRODUCTION

Intervention studies can be placed on a continuum, with a progression from efficacy trials to effectiveness trials. Efficacy can be defined as the performance of an intervention under ideal and controlled circumstances, whereas effectiveness refers to its performance under 'real-world' conditions.[1] However, the distinction between the two types of trial is a continuum rather than a dichotomy, as it is likely impossible to perform a pure efficacy study or pure effectiveness study.[2]

There are several steps that must occur for an efficacious intervention to be effective in clinical practice; therefore, an efficacy trial can often overestimate an intervention's effect when implemented in clinical practice. An efficacious intervention must be readily available, providers must identify the target population and recommend the intervention, and patients must accept and adhere to the intervention.[3] For example, several studies highlight how underutilization of colorectal cancer and hepatocellular carcinoma screening contribute to poor effectiveness in clinical practice.[4–8] In fact, poor access, recommendation, acceptance, and adherence rates can lead to highly efficacious interventions being less effective in practice than less-efficacious interventions. For example, ultrasound has a sensitivity of 63% for detecting hepatocellular carcinoma at an early stage in prospective efficacy studies and is regarded as being more efficacious that alpha fetoprotein. However, in a recent effectiveness study, ultrasound only had a sensitivity of 32%, comparable to that of alpha fetoprotein (sensitivity 46%).[9,10] This gap was related to the low utilization rates of ultrasound and its operator-dependent nature. Similarly, hepatitis C and hepatocellular carcinoma therapy can also be highly efficacious in reducing morbidity and mortality but are limited by low rates of access, recommendation, and acceptance.[11–14]

Although efficacy research maximizes the likelihood of observing an intervention effect if one exists, effectiveness research accounts for external patient-, provider-, and system-level factors that may moderate an intervention's effect. Therefore, effectiveness research can be more relevant for health-care decisions by both providers in practice and policy-makers.[15] The distinction between these two types of trials is important but often poorly understood. In fact, an analysis of product evaluations for Health Technology Assessments found that efficacy data is often assumed to be effectiveness data.[16] The aim of this primer is to highlight differences between these two types of trials (Table 1) and how these differences affect study design.

STUDY DESIGN

Efficacy studies investigate the benefits and harms of an intervention under highly controlled conditions. Although this has multiple methodologic advantages and creates high internal validity, it requires substantial deviations from clinical practice, including restrictions on the patient sample, control of the provider skill set and limitations on provider actions, and elimination of multimodal treatments.[2] A placebo-controlled randomized controlled trial (RCT) design is ideal for efficacy evaluation because it minimizes bias through multiple mechanisms, such as standardization of the intervention and double blinding. RCTs generally eliminate issues of access (intervention is provided free), provider recommendation, and patient acceptance and adherence.

Effectiveness studies (also known as pragmatic studies) examine interventions under circumstances that more closely approach real-world practice, with more heterogeneous patient populations, less-standardized treatment protocols, and delivery in routine clinical settings. Effectiveness studies may also use a RCT design; however, the intervention is more often compared with usual care, rather than placebo. Minimal restrictions are placed on the provider actions in modifying dose, the dosing regimen, or co-therapy, allowing tailored therapy for each subject. Although effectiveness studies

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sacrifice some internal validity, they have higher external validity than efficacy studies.[2] Effectiveness trials without a witnessed effect may be related to one of several factors including an ineffective intervention, poor implementation, lack of provider acceptance, or lack of patient acceptance and adherence.

PATIENT POPULATION

Efficacy trials use strict inclusion and exclusion criteria to enroll a defined, homogenous patient population. Inclusion criteria confirm that patients truly have the disease of interest, whereas exclusion criteria exclude those who are unlikely to respond to the intervention. For example, efficacy studies may exclude patients who are at low risk for the primary outcome, those who are deemed likely to be non-compliant, or those with significant comorbid medical conditions. However, these strict inclusion and exclusion criteria can limit the generalizability of the results to patients seen in clinical practice. Effectiveness trials typically have limited exclusion criteria and involve a more heterogeneous population, including higher rates of non-compliant patients and more subjects with significant comorbid conditions.[17] However, effectiveness trials can still exclude patients for safety concerns, as these patients would not be expected to get the intervention in usual practice.[18] For example, a recent RCT demonstrated that rectal indomethacin significantly reduced the risk of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis; however, only high-risk patients, such as those with sphincter of Oddi dysfunction, were included.[19] Effectiveness studies would help clarify if these results can be generalized to low-risk and medium-risk patients undergoing ERCP in everyday practice.

THE INTERVENTION

In efficacy trials, interventions are delivered in a highly standardized way, including timing and dosage of medications and perhaps even the associated patient education. The use of concurrent medications or interventions is often restricted, so any witnessed effect can be attributed to the intervention of interest. Furthermore, efficacy trials are conducted with top-quality equipment and highly experienced providers, who are often provided training in the intervention and measurement of outcomes prior to the study. Finally, intensive resources are often dedicated to maximize provider uptake and patient compliance with the intervention.[17] Research assistants can provide intense counseling, education, and even reminders for scheduled medications or clinic appointments. This intensive attention can in part explain the high placebo effect seen in some trials, such as those in irritable bowel syndrome and inflammatory bowel disease.[20,21]

Effectiveness trials standardize the availability of the intervention in the study sample but do not go to extremes to reinforce implementation by providers or participation by patients. There are no requirements regarding provider expertise, and equipment quality may be variable. Similarly, providers are not restricted in terms of offering concurrent therapies or crossing over patients on-and-off therapy, which can lead to higher rates of drug–drug interactions and make it less clear if any effect was truly related to the intervention of interest. Finally, additional study resources, such as reminder phone calls or study coordinators, are not available to augment provider and/or patient compliance.

ANALYSIS

Both efficacy and effectiveness trials typically use an intention-to-treat approach for statistical analysis. However, given that efficacy trials aim to address if interventions work under ideal circumstances, secondary analyses using a per-protocol approach may be informative. Alternative techniques that have been proposed to account for differences between efficacy and effectiveness include contaminated adjustment intention to treat and voting with their feet analyses.[22–24] Effectiveness trials often have higher rates of missing data than efficacy trials.[17,18] There are several methods for handing missing data, with details beyond the scope of this primer.[25–27]

REPORTING DATA

The applicability of results from both efficacy and effectiveness studies depend on the context of the trial and the situation to which the data are being applied. It is crucial for any study to provide sufficient data regarding the trial's setting, participants, and intervention. A trial with an insufficient description regarding the intervention is effectively rendered useless, as external implementation and validation is impossible. Guidelines for reporting results of efficacy and effectiveness studies should be followed to standardize reporting of results.[28,29]

Table 1 Differences between efficacy and effectiveness studies

	Efficacy study	Effectiveness study
Question	Does the intervention work under ideal circumstance?	Does the intervention work in real-world practice?
Setting	Resource-intensive 'ideal setting'	Real-world everyday clinical setting
Study population	Highly selected, homogenous population Several exclusion criteria	Heterogeneous population Few to no exclusion criteria
Providers	Highly experienced and trained	Representative usual providers
Intervention	Strictly enforced and standardized No concurrent interventions	Applied with flexibility Concurrent interventions and cross-over permitted

COMPARATIVE EFFECTIVENESS RESEARCH

Clinicians have historically been frustrated by the lack of consideration of external validity in RCTs, other efficacy studies, and guidelines.[30] Accordingly, there has been a call for studies whose results can be more readily applied to everyday clinical practice.[15] This culminated in the American Recovery and Reinvestment Act, which allotted more than $1 billion to support comparative effectiveness research (CER). The Institute of Medicine has defined CER as "the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition, or to improve the delivery of care."[31] The purpose of CER is to assist patients, providers, and policy-makers in making informed decisions that can improve health care both at the individual and population levels. As suggested by the name, CER places an emphasis on effectiveness studies, conducted in settings similar to real-world clinical practice, to maximize external validity of any results. With increased funding support for effectiveness research, the number of effectiveness studies will likely increase over the next several years.

CONCLUSION

An understanding of the distinction between efficacy and effectiveness research is not only crucial when conducting research but also interpreting results from studies and deciding how applicable it may be to clinical practice and patients who may have less access and less adherence to medications. Given a growing focus on evidence-based medicine and pay-for-performance measures, providers must base clinical decisions on the best available evidence. However, defining the best available evidence may not always be clear. Although some prioritize efficacy data from RCTs, others view effectiveness data as more pertinent to real-world clinical practice decisions.[2] There are at least two tools, which can help clinicians judge where a trial may lie on the efficacy–effectiveness continuum.[18,32] Gartlehner and colleagues identified criteria to distinguish efficacy and effectiveness studies, with a sensitivity and specificity of 72% and 83%, respectively. Similarly, PRECIS is a tool with 10 domains (for example, sample exclusion criteria, intervention flexibility, and follow-up intensity) that can help categorize studies as efficacy or effectiveness trials. Although both types of studies are important when evaluating interventions, they serve different purposes and provide different data.

CONFLICT OF INTEREST

Guarantors of the article: Amit G. Singal, MD, MS and Akbar K. Waljee, MD, MS.

Specific author contributions: Study concept and design, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and study supervision: Amit G. Singal and Akbar K. Waljee; critical revision of the manuscript for important intellectual content: Peter D.R. Higgins.

Financial support: None.

Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- Although efficacy and effectiveness studies are both important when evaluating interventions, they serve distinct purposes and provide different data.

WHAT IS NEW HERE

- Efficacy research maximizes the likelihood of observing an intervention effect, whereas effectiveness research better accounts for external patient-, provider-, and system-level factors that may moderate an intervention's effect in clinical practice.
- Tools exist to help clinicians judge where a trial may lie on the efficacy–effectiveness continuum.

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"HE40"

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 20-F

(Mark One)

☐ REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR (g) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2021

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

OR

☐ SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Commission file number: 001-39081

BioNTech SE

(Exact name of Registrant as specified in its charter)

Federal Republic of Germany
(Jurisdiction of incorporation or organization)

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(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered, pursuant to Section 12(b) of the Act

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
American Depositary Shares, each Representing one ordinary share	BNTX	The Nasdaq Stock Market LLC
Ordinary shares, no par value, with a notional amount attributable to each ordinary share of €1*	—	The Nasdaq Stock Market LLC*

Securities registered or to be registered pursuant to Section 12(g) of the Act: None

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act: None

Indicate the number of outstanding shares of each of the issuer's classes of capital stock or common stock as of the close of business covered by the annual report.

Ordinary shares, no par value, with a notional amount attributable to each share of €1 outstanding as of March 30, 2022, no par value: 246,807,808

diminish our own rights or economic opportunities with respect to our COVID-19 vaccine. Our current and potential third-party service providers may be impacted by government entities potentially invoking the Defense Production Act or other potential restrictions to all or a portion of services they might otherwise offer. The current presidential administration has communicated its intent to continue using the Defense Production Act to expand manufacturing capacity of vaccine and vaccine supplies as well as COVID-19 tests and testing supplies.

Additionally, we may need to, or we may be required by governmental or non-governmental authorities to, set aside specific quantities of doses of our COVID-19 vaccine for designated purposes or geographic areas. We face challenges related to the allocation of supply of our COVID-19 vaccine, particularly with respect to geographic distribution.

Furthermore, public sentiment regarding commercialization of a COVID-19 vaccine, the safety and efficacy of our COVID-19 vaccine, other COVID-19 vaccines and treatments, the COVID-19 pandemic generally, as well as public perception of the severity of SARS-CoV-2 virus may limit or negate our ability to generate income from sales of our COVID-19 vaccine. We believe that social media is increasingly being used to communicate information and misinformation about the COVID-19 pandemic and our and other COVID-19 vaccines. If social media posts and other communications contain negative, inaccurate or misleading information about our COVID-19 vaccine, demand for our COVID-19 vaccine may be diminished and we may suffer reputational damage.

The COVID-19 disease itself is very unpredictable, each variant comes with varying levels of transmissibilty and severity. Consequently, the burden of the disease may wane or dissipate such that our and other COVID-19 vaccines may be less essential from an individual and public health perspectives.

We face significant competition with other makers of COVID-19 vaccines and may be unable to maintain a competitive market share for our COVID-19 vaccine.

A large number of vaccine manufacturers, academic institutions and other organizations currently have programs to develop COVID-19 vaccine candidates and certain other vaccines have been authorized for emergency use or approved in various countries. For example, Moderna, Inc.'s and Johnson & Johnson's vaccine candidates have been approved for emergency use in the United States, United Kingdom, European Union and other countries and other vaccines have been approved for emergency use in other jurisdictions. While we are not aware of all of our competitors' efforts, other vaccine candidates developed by the Gamaleya Research Institute of Epidemiology and Microbiology, the University of Oxford/AstraZeneca plc, CanSino Biologics Inc., the Vector Institute, Novavax, Inc., China National Pharmaceutical Group (Sinopharm)/Beijing Institute of Biological Products and Wuhan Institute of Biological Products, Sinovac Biotech Ltd., Bharat Biotech International Limited and other companies are in late stages of clinical development or have been authorized for emergency use or approved in certain countries. Our competitors pursuing vaccine candidates may have greater financial, product candidate development, manufacturing and marketing resources than we do. Larger pharmaceutical and biotechnology companies have extensive experience in clinical testing and obtaining regulatory approval for their products, and may have the resources to invest heavily to accelerate discovery and development of their vaccine candidates.

Our efforts to successfully commercialize our COVID-19 vaccine may fail if competitors develop and commercialize COVID-19 vaccines that are safer, more effective, produce longer immunity against COVID-19, require fewer administrations, have fewer or less severe side effects, have broader market acceptance, are more convenient to administer or distribute or are less expensive than any vaccine candidate that we have developed or we may develop.

We may not be able to demonstrate sufficient efficacy or safety of our COVID-19 vaccine to obtain permanent regulatory approval in jurisdictions where it has been authorized for emergency use or granted conditional marketing approval.

Our COVID-19 vaccine has been granted full U.S. FDA approval for individuals 16 years and older, emergency or limited use authorization in a number of countries and approval for use in certain other countries. Our COVID-19 vaccine has not yet been approved by regulatory authorities in many of such countries. We and Pfizer intend to continue to observe our COVID-19 vaccine and other variants of a COVID-19 vaccine candidate in global clinical trials. It is possible that subsequent data from these clinical trials may not be as favorable as data we submitted to regulatory authorities to support our applications for emergency use authorization, marketing or conditional marketing approval or that concerns with the safety of our COVID-19 vaccine will arise from the widespread use of our COVID-19 vaccine outside of clinical trials. Our COVID-19 vaccine may not receive approval outside of the emergency use setting in the countries where it is not currently approved, which could adversely affect our business prospects.

"HE41"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF HEALTH	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: LIMPOPO DEPARTMENT OF HEALTH	Twelfth Respondent

MPUMALANGA DEPARTMENT OF HEALTH	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: MPUMALANGA DEPARTMENT OF HEALTH	Fourteenth Respondent
NORTHERN CAPE DEPARTMENT OF HEALTH	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTHERN CAPE DEPARTMENT OF HEALTH	Sixteenth Respondent
NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICA HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

SUPPORTING AFFIDAVIT

I, the undersigned

DR MARE OLIVIER

do hereby make oath and state that:-

1. I am an adult female general practitioner with my principal place of business at 12 Langverwacht Road, Kuilsrivier, Western Cape.

2. The facts in this affidavit are, to the best of my knowledge, both true and correct, and, unless the contrary appears from the context of this document, they fall within my personal knowledge and/or expertise. I ask the Court to note that I have no conflicts of interests that would in any way jeopardise or compromise my objectivity in diagnosing and handling my patients, or in presenting evidence to this Court. The opinions I have reached have been so reached based on my expertise and are wholly independent.

3. Herman Jacobus Edeling's ("Edeling") mentions me and my patients. Edeling reproduces the accounts of the vaccine injuries I have seen in my practice (as further detailed in this affidavit). I confirm the correctness thereof.

4. In this affidavit, I set out further information in relation to those cases in order to fully apprise to Court of the reasons for my diagnoses. I have obtained consent from my patients to disclose their information in this affidavit. This consent notwithstanding, I am withholding the patient's names at their requests. I will refer to the patients as "patient one", "patient two", "patient three", "patient four", "patient five", "patient six", and "patient seven". Should the Court require patient names, the patient files can be made available to the Court for inspection on the date of the hearing. It is important to note that, for the sake of not overburdening the Court, I am not detailing all cases of Pfizer vaccine injuries that I've diagnosed. I have selected only the seven most severe cases in which the patients have either died, been near death or have suffered life-altering injuries due to the Pfizer vaccines. I

do; however, annex as **"MO1"**, a copy of an spreadsheet listing the patient information of all two hundred and thirty nine (239) patient that were, in my opinion, injured by the vaccines.

5. The patients I have chosen to focus on in this affidavit were all healthy with no significant, relevant family medical histories and they all either died, or had severe, life-threatening or life-altering reactions within a short time frame after having received the Pfizer Comirnaty vaccine. The reason for selecting patients who were generally healthy prior to the vaccines, and with no relevant family medical history is that it makes the injury causality assessment more simple.

6. Further, I ask the Court to note that some of the conditions with which the below patients presented appear in the post-authorisation adverse event report ("the report") commissioned by Pfizer as "*adverse events of special interest*" potentially related to the Pfizer vaccine. The fact that these conditions appear in the report does not establish causation – but strongly suggests (at the very least) correlation between the relevant condition and the administration of the Comirnaty vaccine, and this was one of the factors I considered in reaching my diagnoses.

My qualifications

7. I hold an MBChB from the University of Stellenbosch (1993). I have been in private practice as a general practitioner for over 27 years and in private practice for 17 years. I do not have a full *curriculum vitae*, and was unable to prepare one under the strict timelines of this case. However, if the respondents contest my qualifications, I will annex evidence and my curriculum vitae in reply.

8. I now commence detailing my most severe patient cases.

Patient one

9. This patient was a previously healthy, fit 57-year-old. Prior to his death, he had been my patient for the past fifteen years, and I can attest to the fact of his health (prior to the Covid-19 vaccine) as well as his clean family medical history. It was a difficult journey watching this patient's deterioration after his Pfizer vaccine on 7 September 2021 to his ultimate and untimely death on 24 January 2023. This patient suffered enormous pain, physical degeneration, and a loss of dignity as he slowly died. This notwithstanding, he photographically documented his journey and gave me permission to share those photographs in legal proceedings (even after his death) if ever asked to do so.

10. This patient's first and only Pfizer injection was on 7 September 2021. He began presenting with symptoms a mere four days later. By 11 July 2021, he was presenting with pain in his right eye and temporal area. He saw a neurologist in November 2021, and she requested an MRI, the results of which came back as "normal". She made the diagnosis of Bell's Palsy and trigeminal neuralgia. She prescribed pain medication to manage the trigeminal neuralgia. I pause here to note that trigeminal neuralgia is listed as an adverse event of special interest in the Pfizer post-authorization report.

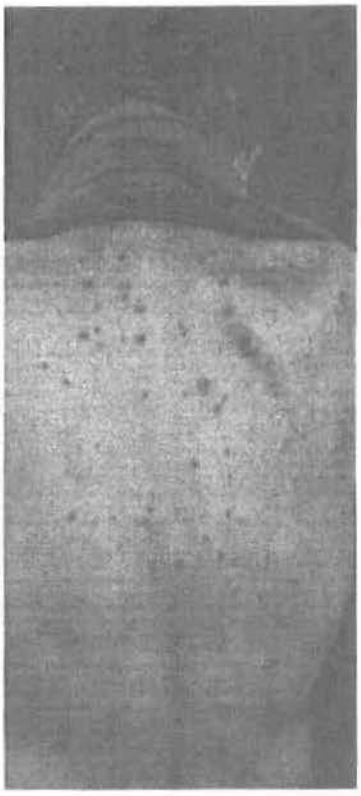
11. I saw the patient for the first time after his MRI, in February 2022. By this stage he told me that the pain tablets were not working adequately, and that his symptoms were worsening. At that point, he had spent in excess of ZAR 160 000 trying to find

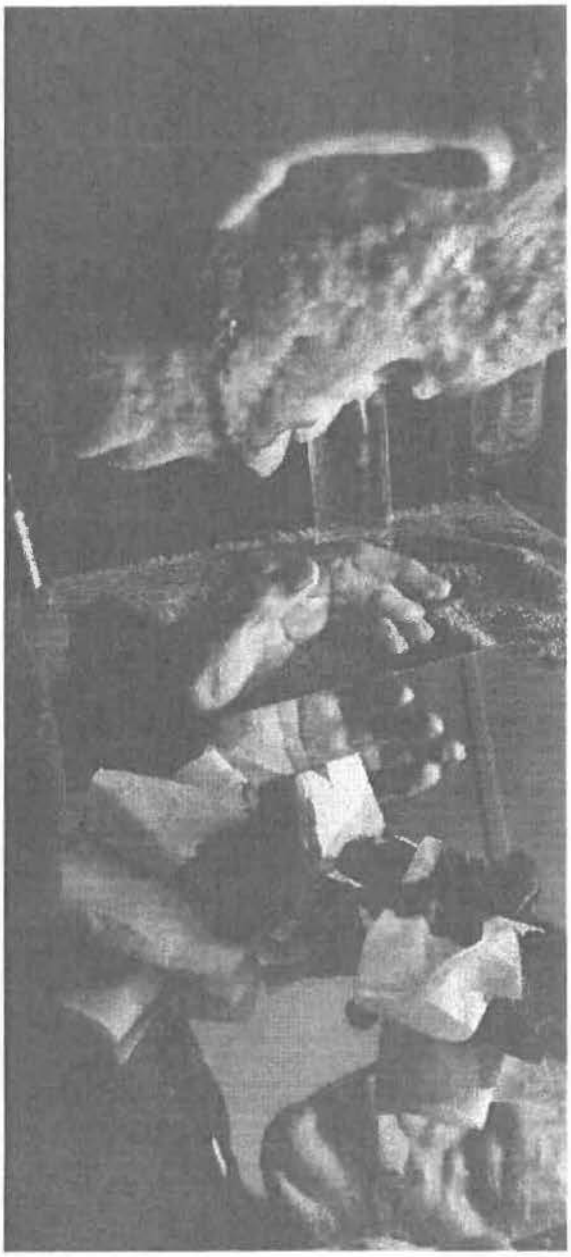
out what was wrong with him, and to procure effective treatment – but had thus far failed.

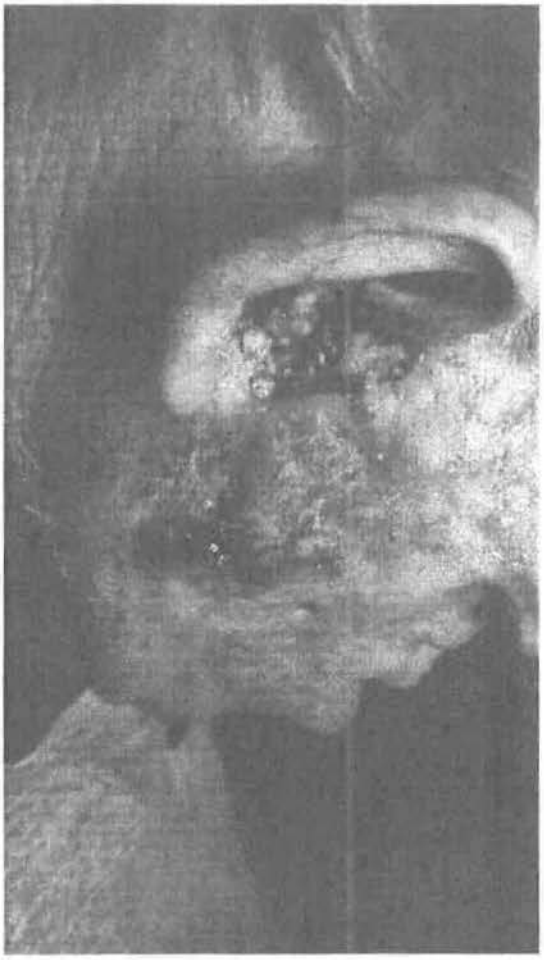
12. I saw him again in the beginning of August 2022. By this time, he had severe wasting, and he presented with a palpable hard mass in his right external ear channel. The hard mass obstructed his entire ear channel which, in turn, prevented a physical examination. I sent the patient for a CT scan which showed a mass in his parotid gland, spreading to different cranial nerves and facial muscles responsible for chewing. He then received a biopsy at Tygerberg hospital, and he was diagnosed with basaloid carcinoma of the parotid glad (Basaloid carcinoma is a type of cancer that affects the parotid gland, which is one of the major salivary glands located in the cheek near the jaw. It is a rare form of cancer that is often aggressive and tends to spread to other parts of the body).

13. He died from this cancer on 24 January 2023.

14. The sudden and unexplained onset of this patient's condition, together with its rapid progression, and the close temporal association to the vaccine led me to conclude that this patient was injured by the Pfizer vaccine. The fact that trigeminal neuralgia is listed in the Pfizer post-marketing adverse events report was a further factor that I considered in reaching my conclusion. Photographs of this patient until the month of his death appear immediately below.







Patient two

15. This patient was a previously healthy 74-year old woman. She was injected with 2 doses of the Pfizer vaccine. Her first dose was administered on 30 June 2021, and her second dose on 21 August 2021. At no stage had she contracted Covid-19.

16. Prior to her vaccination, her only health issue was mild hypertension (which was well-controlled under medication), and mild dementia.

17. I first consulted with her just prior to her second vaccination. At that stage, her dementia had visibly deteriorated, and she was exhibiting severe wasting (In medical terms, "wasting" refers to a reduction in muscle mass and strength, often accompanied by weight loss and decreased physical function). In addition, her hypertension condition deteriorated and became almost impossible to manage with any medical interventions.

18. By 8 September 2021 when I next saw her, she presented with a thrombosis (a thrombosis is the formation of a blood clot inside a blood vessel, obstructing the flow of blood) on the left forearm with increased D-dimers. It is important to understand what raised D-dimer levels mean. A D-dimer is a blood test that measures the level of a protein fragment that is produced when a blood clot breaks down. Elevated levels of D-dimers may indicate the presence of a clot or an increased tendency for clotting, which can be due to a variety of underlying medical conditions, such as deep vein thrombosis, pulmonary embolism, or stroke. I pause to mention that clotting disorders are also listed in the post-authorisation adverse event report.

19. By 17 September 2021, she had developed acute pulmonary tuberculosis ("**TB**"). At this juncture, her wasting was severe. She was admitted to hospital, where she subsequently died on 1 January 2022.

20. Due to the close temporal association between this patient's vaccines, the exacerbation of her pre-existing conditions and the onset of her TB (in circumstances where there no previous health markers for the development of this condition), I concluded that this patient's deterioration and death were linked to the Pfizer vaccine.

Patient three

21. This patient was a 43 year old previously healthy woman. Her only medical history was mild and well-controlled hypertension. She received two doses of the Pfizer vaccine. Her first dose was administered on 27 July 2021, and her second dose was administered on 11 September 2021.

22. On 20 June 2022, she consulted with one of my colleagues who diagnosed her with a urinary tract infection.

23. I then consulted with her on 14 July 2022. By that stage she was presenting with upper abdominal pain. Upon examination, I found an enlarged liver. She also had bilirubin in her urine (bilirubin is a yellow pigment that is produced when the body breaks down old red blood cells. It is processed and eliminated from the body by the liver, and excreted in the bile and feces. Elevated levels of bilirubin in the blood

(known as hyperbilirubinemia) can indicate a problem with the processing or elimination of bilirubin, such as liver disease).

24. My observations concerned me. I ran blood tests, and referred the patient for an urgent ultrasound. The results of the ultrasound showed severely raised liver function, and raised CEA. CEA stands for Carcinoembryonic Antigen. In the context of the liver, it's a protein marker that is sometimes used to monitor the progression of certain types of liver cancer or to monitor the effectiveness of treatment. However, it is not a specific marker for liver cancer and elevated levels can also be seen in other types of cancer or in non-cancerous conditions. I referred the patient to a surgeon who saw her on 18 July 2022. She was diagnosed with primary colon cancer.

25. The cancer progressed extremely rapidly, and killed her on the 5th of August 2022. She had no family history of colon cancer, and (prior to vaccine), no markers for the development of this conditions – let alone such a severe onset and rapid progression.

26. Due to the close temporal association between the administration of this patient's vaccines, the onset of her cancer, its rapid progression and her untimely death caused by the aggressive cancer, I concluded that her cancer was linked to the Pfizer vaccine.

Patient four

27. The fourth patient was a healthy 61 year old woman with mild, well-controlled hypertension. She was injected with two doses of the Pfizer vaccine. Her first administration was on 28 July 2021, and her second dose was administered on 8 September 2021.

28. On 30 November 2021, she had a mammogram which returned normal results. However, by March 2022, she had presented with a lump in her breast and had another mammogram which subsequently confirmed the presence of a carcinoma. On 11 April 2022, a biopsy confirmed the presence of breast cancer. The patient is currently receiving chemotherapy.

29. Due to the close temporal association between the administration of her vaccines, and the onset of her cancer considered together with the fact that she had no previous family history of breast cancer, I concluded that this patient's cancer was causally connected to the Pfizer vaccine.

Patient five

30. The fourth patient was a 67 year old healthy female with mild, well-controlled hypertension and mild osteoarthritis of the hands. She was thrice vaccinated with Pfizer vaccines. Her first vaccine was administered on 2 June 2021, her second vaccine was administered on 15 July 2021, and her final vaccine was administered on 18 January 2022.

31. On 8 February 2022, the patient consulted with me at my practice. She presented with a change in her stools and blood when defecating. I screened her for cancer. Both her CEA's and D-Dimer counts returned on the results as elevated. Because of this, I referred her for a colonoscopy which subsequently confirmed colon cancer. While she was in hospital for treatment of the cancer, she also suffered a heart attack. This patient had no family history of colon cancer, and there were no medical markers present for the development of this disease.

32. The patient is stable at present, and on treatment for her cancer

33. Due to the close temporal association between the vaccines and her cancer onset, together with an entirely absent family history of colon cancer, I concluded that the cancer was causally linked to administration of the Pfizer vaccines.

Patient six

34. This patient is an otherwise healthy, fit young boy aged 15 years. He has been my patient since birth. He had one Pfizer injection in January 2022.

35. He attended my practice on 6 April 2022 with abdominal complaints. He then presented with more abdominal complaints and complains about nausea on 16 May 2022. He then returned on 19 October 2022 at which point he presented with macroscopic haemorrhagic cystitis (this refers to the visible presence of red blood cells in the urine. Haemorrhagic cystitis is a condition in which the bladder becomes inflamed and experiences bleeding).

36. The important factor here was that the test I conducted showed a negative culture. Haemorrhagic cystitis with a negative culture refers to a situation where there is visible blood in the urine (macroscopic hematuria) but no bacterial or fungal growth is present in a urine culture. This suggests that the cause of the bladder inflammation and bleeding is not due to an infection, but may be due to other factors such as chemotherapy, radiation therapy, or an underlying medical condition or inflammation. The problem was, of course, that this young child had no such underlying causes that could have resulted in his condition. Over and above this, haemorrhagic cystitis is uncommon in healthy men – and particularly uncommon in young healthy adolescents.

37. Due to the close temporal association between the vaccines and the presentation of the haemorrhagic cystitis, the absence of any underlying conditions that could have caused the Haemorrhagic cystitis, and the rarity of this condition in his age demographic, I concluded that this patient was injured by the Pfizer vaccine.

Patient seven

38. This patient was a previously healthy 43 year old woman. At the beginning of 2021, she had two Pfizer vaccines, although she cannot recall the dates of those injections. Towards the end of the same year, and on 30 August 2021, she went for general check-up.

39. She presented with raised hypertension (which took three weeks to get under control), and severely raised D-dimer levels. By 10 October 2022, she presented

with abdominal pain and jaundice. An ultrasound showed gallstones, and a mass growing on her gallbladder. She received surgery and is presently stable.

40. I diagnosed this patient, too, as having been injured by the vaccine. The lack of any medical marker for the development of this condition together with the close temporal association between the commencement of the conditions, and the administration of the vaccine were sufficient to establish a probable causal link between the vaccines and the onset of the patient's condition.

Conclusion

41. It is my opinion, the Pfizer vaccine is unsafe, and should be recalled pending further investigation.

DR MARE OLIVIER

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me at [illegible] on this the 10 day of FEB 2023, the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

COMMISSIONER OF OATHS

Name: [illegible]

Address: [illegible]

Position: [illegible]

SUID-AFRIKAANSE POLISIEDIENS
10 FEB 2023
SOUTH AFRICAN POLICE SERVICE

"MO1"

— VACCIDENTS —

COVID POSITIVE AFTER VACCINE EVENTS

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK
1	[redacted]	[redacted]	30/5	Pfizer	8/6
2			4/6	J&J	15/6
3			24/6	Pfizer	6/7
4			1/7	Pfizer	8/7
5			26/5	Pfizer	8/7/2021
6			6/7	Pfizer	12/7
7			9/7	Pfizer	12/7
8			24/6	Pfizer	14/7
9			24/6	Pfizer	14/7
10			6/7	J&J	15/7
11			12/7	J&J	17/7
12			24/6	Pfizer	9/7
13			24/6	Pfizer	9/7
14			X2 (1sh)	Pfizer	10/7
15			Maart 21	J&J	21/7
16			20/7	Pfizer	23/7
17			23/7	J&J	25/7
18			20/7	Pfizer	27/7
19			13/7	Pfizer	25/7
20			7/7	Pfizer	29/7
21			30/6	Pfizer	1/8
22			30/6	Pfizer	1/8

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK
23	POSITIEF.				
24	POSITIEF (Hospitaal)				
25	POSITIEF (Hospitaal)				
26	POSITIEF.				
27	POSITIEF				
28	Sleg ds erg seer arm				
29	bai siek				
30	Siek				
31	Siek → Hospitaal — stelsel d/ oorlede (75 jaar oud)				
32	Siek !!!				
33	Siek !!				
34	oorlede				
35	oorlede				
36	Siek (beide JAB's)				
37	Siek				
38	siek				
39	Siek				
40	Siek				
41	Siek SAT 74%				
42	Siek				
43	Siek.				
44	Siek				

(2)

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES	
23	[redacted]	[redacted]	15/7	Pfizer	30/7	COVID (+) Siek	
24			17/6	Pfizer	30/7	COVID (+) Bed siek!!	80 jr
25			15/7	Pfizer	1/8	COVID (+) siek	51 jr
26			13/7	Pfizer	2/8	COVID (+) siek	51 jr
27			23/7	Pfizer	4/8	COVID (+) siek	47 jr
28			3/7	Pfizer	4/8	COVID (+) siek	80 jr
29			12/5	J&J	8/8	COVID (+) HCW	38 years
30			28/7	Pfizer	7/8	COVID (+) ++ siek	44 year
31			6/4	J&J	9/8	COVID (+)	48 years
32			7/7	Pfizer	8/8	COVID (+)	63 years.
33			17/7	Pfizer	11/8	COVID (+)	40 years
34			20/7	Pfizer	3/8 + 19/8	Hemorhagisse sustitis	57 years
35			17/7	Pfizer	18/8	Erge COVID	49 years
36			20/7	Pfizer	26/8	Erge COVID	
37			30/6	J&J	26/8	Erge COVID (87	2e pfizer 24/8)
38			24/8	2e Pfizer	27/8	Erge COVID	
39			21/6	1e Pfizer	6/8-4/8	Gehospitaliseer COVID	
40			10/8	1e Pfizer	31/8	Erge COVID	44 year.
41			10/8	1e Pfizer	3/9	Erge COVID	48 years
42			10/8	1e Pfizer	2/9	Erge angioedema	47 jaar
43			24/07	1e Pfizer	3/9	Erge COVID Sat 76°	48 year.
44			24/07	2e Pfizer	7/9	↑ Ferritin + Tired	

(3)

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES
45	[redacted]	[redacted]	6/21	Pfizer	7/21	TB
46			7/21	2e Pfizer	14/9	↑ BP.
47			7/2021	1e Pfizer	3/9	COVID ⊕
48			6/9/2021	1e Pfizer	17/9	CVA with aphasia
49			10/8/2021	2e Pfizer	10/9	↑ Ferritin ⊂ Malaise
50			10/8/2021	1e Pfizer	1/9	↑↑ Ferritin ⊂ Malaise
51			26/7/21	2e Pfizer	8/9	↑↑ BP
52			21/8/21	1e Pfizer	23/8	severe malaise / lymphadenopathy
53			16/8/21	21/9 2e Pf	2/9	Mamma Ca
54			20/9	1e Pfizer	22/9	Tachycardia / ↓ saturation
55			21/9	2e Pfizer	4/10	DVT ⊕ calf
56			16/8	2e Pfizer	10/9	DVT, Geneva vertico / TPA
57			Julie 21	2e Pfizer	1/10/2021	↑ van Hill / Fibromyalgia / Malaise
58			Julie 21	J&J	11/10/2021	DVT ⊕ been
59			Sept 21	2e Pfizer	end Sept	Herpes genitalis (flair up)
60			Julie 21	2e Pfizer	11/10	Hemorrhagrese. sishtro
61			4/10/21	2e Pfizer	11/10	COVID ⊕
62			8/21	2e Pfizer	9/21	Severe flair up of RA
63			16/9	1e Pfizer	19/9	COVID ⊕ / Bulkpyn / Absence
64			27/9	2e Pfizer	4/10	Multiple gum abscesses
65			16/8	1e Pfizer	20/8	CVA
66			7/2021	2e Pfizer	10/10	Cavernous thrombosis

52 year
71 year
48 years
66 years
81 years
↑↑ Ferritin ⊂ Malaise ↓ 6 y.
76 years
37 years
48 years.
4 / year.
D-Dimer 3500
72 years · D-Dimer 1600
Malaise 62 years
22 yr.
59 years.
75 years.
59 years ⊕ Glaucoma
58 years.
48 years
55 years
62 years

AB

(4)

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES
67	[redacted]	[redacted]	1/9/2021	2e Pfizer	sept.	Uncontrolled DM | Rash | Tired
68	[redacted]	[redacted]	16/8/2021	2e Pfizer	Sept	TB activation (1e coe)
69	[redacted]	[redacted]	10/8/2021	J&J	Sep 2021	Paralysis
70	[redacted]	[redacted]	27/9/2021	2e Pfizer	Oct-2021	Skinrash
71	[redacted]	[redacted]	10/8/2021	1e Pfizer	14/11/2021	DVT (R) baboon
72	[redacted]	[redacted]	6/9/2021	2e Pfizer	10/9/2021	Tachycardia (126) | HBP | Hgt
73	[redacted]	[redacted]	5/2021	J&J	end oct	↑ D-Dimer 830
74	[redacted]	[redacted]	8/2021	Pfizer	Nov 21	Multiple abcesses
75	[redacted]	[redacted]	21/9/21	2e Pfizer	22/10	Naar Hpt | Tachycardie (126)
76	[redacted]	[redacted]	20/8/2021	1e Pfizer	20/8	Palpitations | Chest-pain etc
77	[redacted]	[redacted]	22/10/21	2e Pfizer	middel Sep	Menometrorragia (Stukje)
78	[redacted]	[redacted]	1/11/21	1e Pfizer	28/11	CVA 2 multiple clots
79	[redacted]	[redacted]	8/11/21	2e Pfizer	25/11	Nuwe diabeet HGT
80	[redacted]	[redacted]	einde Aug	2e Pfizer	mid Oct.	Skyf | Rukkings | Dropree
81	[redacted]	[redacted]	Julie21	2e Pfizer	Okt 21	Enige Hpt BP 200/110
82	[redacted]	[redacted]	Aug 21	2e Pfizer	Oct 21	↑ BP | suiker | edeem
83	[redacted]	[redacted]	Aug 21	2e Pfizer	Nov 21	↓ WST ↓ neutrofiele
84	[redacted]	[redacted]	Sept 21	2e Pfizer	Nov 21	Terugkeer van Prostaat
85	[redacted]	[redacted]	Julie21	2e Pfizer	Julie21	↑ BP | chol | Braindas.
86	[redacted]	[redacted]	Aug 21	2e Pfizer		↑ glukose (RA uitbreke
87	[redacted]	[redacted]	Oktober	J&J	Nov.	COVID (+)
88	[redacted]	[redacted]	Julie21	2e Pfizer	Sept/Dec	↑ BP | cardiac arrhy

52 years
72 years
47 years
62 years
44 yr
Hgt 45
59 years
59 year
40 years
53 years old
25 years
66 years
65 years
60 jaar
51jr
53jr
75jr
52jr
65jr
63jr
50jr
77 year

↑↑ D-Dimer na 2 mnde covid

↑ D-Dimer

AB

(5)

VACCIDENTS

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES	
89	[redacted]	[redacted]	Sept 2021	J+J	9/12/2021	COVID (+)	
90			Julie	1e Pfizer	9/12/2021	COVID (+)	
91			June 21	J+J	7/2021	COVID (+) ↑ DM ± peripheral neuropathy	
92			Sept 21	1e Pfizer	12/12/2021	COVID (+)	47years
93			Sept'21	2e Pfizer	13/12/2021	COVID (+)	51 years
94			Nov 21	2e J+J	13/12/2021	COVID (+)	49
95			17/8/21	2e Pfizer	Aug 21	Erge ↑ van MS	66jr
96			Sept 21	2e Pfizer	12/12/21	COVID (+).	
97			Sep 21	2e Pfizer	13/12/21	COVID (+)	
98			Nov'21	2e J+J	14/12/21	COVID (+)	
99			Mei'21	2e Pfizer	12/2021	Leukemie ± Plaatje v. 16 → 76jr.	
100			Sep'21	2e Pfizer	9/2021	Chestpain/↑pulserate/Tired	39years
101			Julie'21	2e Pfizer	12/2021	COVID (+)	74years
102			Julie'21	J+J	12/2021	COVID (+)	47years
103			Nov 21	2e Pfizer	11/2021	Vestibulopatie Vertigo	58jaar
104			July 21	J+J	12/2021	COVID (+)	43 years
105			Mei 21	J+J	12/2021	COVID (+)	
106			Nov 21	2e Pfizer	11/2021	Severe uncontrolled DM	50years.
107			Aug 21	2e Pfizer	12/2021	↑ D-Dimer	54years
108			21/10/21	2e Pfizer	3/1/2022	Covid (+)	21 years
10			7/2022	2e Pfizer	7/2/2021	SVT	55 years
110			21/10/21	2e Pfizer	21/1/2022	COVID (+)	3 49 years

10/5/2022

AB

6

VACCIDENTS

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES	
111	[redacted]	[redacted]	1/7/2021	J+J	29/12/21	COVID (+).	
112			9/2021	J+J	22/12/21	COVID (+)	
113			8/2021	2e Pfizer	5/1/2022	New bm / ↑ Ferritin / ↑ D-dimer	67 years
114			8/2021	2e Pfizer	5/1/2022	↑ D-dimer + proBNP	
115			8/2021	2e Pfizer	8/1/2022	V/V/ niesta / ↑ CRP	88jr
116			5/8/2021	JJ	9/1/2022	Shingles body	48 years
117			15/10/2021	Pfizer 2e	11/1/2022	COVID (+)	34 years
118			9/2021	Pfizer 2e	11/1/2022	Sterf MI + comorbi	53 years
119			8/2021	2e Pfizer	14/1/2022	Severe Hpt. BP 190/110	51 years
120			10/2021	2e Pfizer	17/1/2022	COVID (+)	51
121			10/2021	2e Pfizer	19/1/2022	↑ D Dimer (x2)	49 years
122			7/2021	2e Pfizer	25/1/2022	COVID (+)	82 years
123			10/2021	2e Pfizer	23/1/2022	COVID (+)	48 years
124			9/2021	2e Pfizer	23/1/2022	Narcolepsie	85 jaar.
125			9/2021	2e Pfizer	24/1/2022	↑ D Dimer x3 / ↓ Plat	70 jaar.
126			8/2021	2e Pfizer	7/2/2022	D Dimer ↑ V. Sch na [illegible]	53 years. (Because COVID
127			7/2021	2e Pfizer	2/2022	Mass (C) kidney	60 years
128			12/2021	2e Pfizer	12/2021	Multiple bots	48 years
129			11/2021	2e Pfizer	2/2022	Hypothyroidism	58 years
130			10/2021	2e Pfizer	2/2022	New Hpt	42 years
181			8/2021	2e Pfizer	2/2022	↑↑ BP / ↓ ryter / HRBS	64 years.
132			8/2021	2e Pfizer	2/2022	↑↑ D Dimer met DVT	75 years.

2400

(A)

VACCIDENTS

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES
B3	[redacted]	[redacted]	2/2022	Booster Pfizer	2/2021	Blood PR / ↑D-Dimer / ↑CEA
B4			15/10/2021	1e Pfizer	2/2022	Bell's palsy
B5			5/2021	2e Pfizer	2/2022	D-Dimer 1970
B6			8/2021	2e Pfizer	2/2022	Shingles ○ not
B7			10/2021	2e Pfizer	2/2022	↓ Platelets
B8			8/2021	2e Pfizer	2/2022	↑ D-Dimer
B8			2/2022	3e Pfizer	2/2022	↑ D-Dimer (1900
B9			8/2021	2e Pfizer	1/2022	Necrotizing pneumonia/abcess
140			2/2022	3e Pfizer	2/2022	↑ D-Dimer
141			1/2022	3e Pfizer	2/2022	↑ D-Dimer / ↑ PSA.
142			10/2021	2e Pfizer	3/2022	COVID ⊕
143			2/2022	Booster	2/2022	Cardiac arrythmia/HBP
144			2/2022	2e Pfizer	3/2022	↑ D-Dimer
145			2/2022	Booster	3/2022	↑ D-Dimer
146			9/2021	2e Pfizer	3/2022	TIA's / D-Dimer 710000
147			1/2022	2e Pfizer	8/2022	↑↑ Plaketo 496 000
147			8/2021	1e Pfizer	3/2022	↑ vaw autoimmune hiroid
148			2/2022	Booster	3/2022	↑ D-Dimer 721
149			7/2021	2e Jab	3/2022	Stygende D-Dimer
150			2/2022	Booster	9/2021	Alopecia.
151			3/2022	Booster	3/2022	↑ D-Dimer
152			9/2022	2e Pfizer	3/2022	COVID ⊕

colonkanker

B3 — 65 years
55 years.
6 74 ya
68 years
67 years
57 years
91.
53 years.
63 years
70 jr.
43 years
79 years
56 years.
77 years
48 years.
20 years.
87 years
81 year
69 jar.
81 jaar.
75 jaar.
42 years

AB

(8)

VACCIDENTS

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES	
153	[redacted]	[redacted]	2/2022	Booster Pf	3/2022	↑ D-Dimer	75years
154			8/2021	2e Pfizer	3/2022	Raising D-Dimer	72years
155			7/2021	2e Pfizer	3/2022	BooCa	64years.
15			8/2021	2e Pfizer	9/2021-Nov	Cholecystitis, DM, ↑BP	67years
157			3/2022	Booster	4/2022	↑↑ D-Dimer - TTas	80.
158			8/2021	2e Pfizer	3/2022	↑D-Dimer, Hipochr mikrosite	48years
159			9/2021	2e Pfizer	4/2022	CVA	64 jar
160			8/2022	Booster	4/2022	↑D-Dimer, Abnle levels	74 year. @gallstones
161			10/2021	2e Pfizer	4/2022	(P) COVID	67years
162			9/2021	1e Pfizer	9/2021	(P) Bells Palsy/Shingles	55years
163			9/2021	2e Pfizer	3/2022	BooCa	59 year.
164			3/2022	Booster	4/2022	↓RBS ↑ferritin ↑D-Dimer	83years
165			3/2022	Booster Pfi	4/2022	↑D-Dimer (x2)	81years
166			3/2022	Booster Pfi	4/2022	↓ vision (P) ecg	70jr
167			8/2021	2e Pfizer	4/2022	Bronchospasm, D-Dimer	335 TTjr
168			8/2021	2e Pfizer	4/2022	Shingles	TTj
169			3/2022	Booster	4/2022	Worsening of psoriasis	54years
160			10/2021	2e Pfizer	4/2022	COVID (P)	50years
171			9/2021	2e Pfizer	5/2022	COVID (P)	59years
172			8/2021	1e Pfizer	4/2022	COVID (P)	34 years
173			5/2021-Jan	11/2021 Jan	-28/3	Pfizer — COVID (P)	33years.
174			4 10/2022	2e Pfizer	4/5/2022	COVID (P)	

(a)

VACCIDENTS

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES	
175	[redacted]	[redacted]	28/3/22	Pfizer booster	4/2022	Brainfog ↓ Visie met ligsensatief	70 years
176	[redacted]		10/2021	Pfizer 2e	5/2022	COVID(+)	42 years
177	[redacted]		5/2021	J&J	8/2022	COVID(+)	44 year
178	[redacted]		8/2022	2e Pfizer	5/2022	D-Dimer 71000 (+) abN	FBC 55year
179	[redacted]		3x Pfizer	Booster	5/2022	↓NaCl ↑ D-Dimer	78years
180	[redacted]		3x Pfizer	Maart22	5/2022	COVID(+)	47 years
181	[redacted]		3x Pfizer	Mei 2022	6/2022	↓ Plateletc / Hemorrhagie	47 years
182	[redacted]		2x Pfizer	6	na 2e Pfiz	borskramp / ↑ D-Dimer	48year
183	[redacted]		3x Pfizer	3/2022	Booster	COVID(+)	36 years
180	[redacted]		3x Pfizer	3/2022	Booster	COVID(+)	38year
185	[redacted]		(+) Booster	3/2022	Booster	Progressieve ↑ in D-Dimer	70year
186	[redacted]		2x Pfizer	8/2021	6/2022	COVID vir 2e keer	65years
187	[redacted]		1x P&J	3/2021	5/2022	Acute MI	52years
188	[redacted]		3x Pfizer	3/2022	6/2022	COVID(+)	3years
189	[redacted]		3x Pfizer	11/2021	6/2022	↑ D-Dimer	28year
190	[redacted]		2x Pfizer	10/2021	5/2022	Auto immune hepatitis	38years
191	[redacted]		2x Pfizer	10/2021	6/2022	↑ D-Dimer 25000	55years
192	[redacted]		2x Pfizer	7/2021	7/2022	↑ D-Dimer 1300	80 years
193	[redacted]		3x Pfizer	Pfizer	7/2022	Ves e / AV block / Hpt	75jr
194	[redacted]		1x J&J	Maart 2021	7/2022	Post menop bloeding ↑ D-Dimer	60jaar
195	[redacted]		Aug 2021	2e Pfizer	7/2022	Metastt. lever Ca / ↑ D-dimer	42jr
196	[redacted]		Nov 2021	2e Pfizer	7/2022	↑ LFT's / ↑ CRP	26 years

(10)

VACCIDENTS

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES	
197	[redacted]	[redacted]	13/10/2021	2e Pfizer	6/2022	Meningoencefalo-myelitis	40 jr
198			3/2022	Booster P	7/2022	D-Dimer > 4000	60 jr.
199			7/2021	2e Pfizer	7/2022	Swollen axillary nodes	76 years
200			3/2021	J & J	7/2022	COVID ⊕ ✕ 6 weeks	49 years
201			7/2021	2e Pfizer	07/22	COPLEDG	42
202			9/2021	1e Pfizer	9/2021	Bells palsy / Trigeminal neuralgia ↑D-Dimer	56 years
203			11/2022	2e Pfizer	8/2022	DVT ⊖ Been / ↑D-Dimer	56 years +
204			2021	2e Pfizer	8/2022	↑↑↑ D-Dimer 7000 / ↑CRP	→ Reported — 42 years ⊕ HPT
205			2021	2e Pfizer	8/2022	↑Fibromyalgia / ↑CRP / ↑D-Dimer	52 years.
206			5/2021	J & J	6/2021	Progressive general myalgia	Ths CRP 29 jaar
207			10/2021	2e Pfizer	8/2021	UTI's / ↑ van AS / hiatushernia	50 jr. Tagikardie
208			21/8/2021	J & J	5/2022	Repeated UTI's	27 years.
209			7/2021	2e Pfizer	6/2022	Colon Ca + metastasis to pancreas + lung	6 years
210				2e Pfizer	9/2022	Progressieve ↑↑ D. Dimer	66 jr.
211				2e Pfizer	9/2022	Malignant Hpt	61 years
212				3e Pfizer	1/2022 - 8/2022	Uveïtis / Chronic	47 years
213			6/2021	2e Pfizer	6/2022	Bone Ca	80 jaar.
214				2e Pfizer	9/2022	↑ D-Dimer	51 jaar
215				2e Pfizer	9/2022	Shingles ⊖ gesig	78 jr
216			IK JJ	2/8/21	2022	Repeated de UTI's	27 years
217				2e Pfizer	9/2022	New diabetic HgT - 30	82 years
218			2e Pfizer	—	9/2022	↑BP / ↑ HgT 21 / CVA ⊖	74 years.

VACCIDENTS

	PATIENT	FILE NO	DATE OF VACCINE	VACCINE NAME	DATE OF SICK	NOTES	
219	[redacted]	[redacted]	11/8/2021	2e Pfizer	5/2022	Shingles (post herpetic neuralgia)	47 years
220			21/8/2021	1e J&J	10/2022	Hemorrhagic cystitis	23 years.
221						Hemorrhagic cystitis	49 years
222			Dec 2021	2e J&J	3/2022	Chronic severe pain (RA new)	54 years
223			7/2021	Pfizers	10/2022	↑D-Dimer / Glucose ↑↑↑	68 years
224				Pfizers	10/2022	Granuloma annulêre	37 years
225			8/2021	2e Pfizer	10/2022	New thyroiditis / Osteoarthritis	52
226			10/2021	2e Pfizer	1-10/2022	Covid / ↑D-Dimer / ↓thyroid	46 years
227			1/2022	1x Pfizer	10/2022	Hemorrhagic cystitis	15 years
228			3/2022	3e Pfizer	9/2022	Uncontrolled Hpt	49 years
329 229			2x Pfizer (2021)		10/2022	2e Kear Covid	64 years
230			2x Pfizer	2021	11/2022	Hemorh cystitis / PSA	59 years
231			2x Pfizer	2021	11/2022	Hipertensão / 2x Covid / palpitações	38 years
232			2x Pfizer	2021	8/2021	Covid / ↑neurol dx / CVA / ↑D-dimer	53 years
233			3x Pfizer	2022	10/2022	↑ artrite / ↑↑D-dimer	67 years
234			1x J&J	2021		Repeated UTI's	22 years
235			3x Pfizer	2022	10/2021	Mass (R) parotid gland	51 years
236			2x Pfizer	2021	10/2022	Brain fog / ↑ D-Dimer	47 years
237			2x Pfizer	2021	12/2022	Covid (R)	43 years
238			2x Pfizer	2021	2022	Worsening of psoriasis	49 years
239			2x Pfizer	2021	2021	Severe arthralgia / Myalgia	39 year (abN menses)
240							

"HE42"

IN THE HIGH COURT OF SOUTH AFRICA
(GAUTENG LOCAL DIVISION, PRETORIA)

CASE NO.: _____

In the matter between:

FREEDOM ALLIANCE OF SOUTH AFRICA ("FASA")	Applicant
and	
THE MINISTER OF HEALTH	First Respondent
THE DEPARTMENT OF HEALTH	Second Respondent
EASTERN CAPE DEPARTMENT OF HEALTH	Third Respondent
MEMBER OF THE EXECUTIVE COUNCIL: EASTERN CAPE DEPARTMENT OF HEALTH	Fourth Respondent
FREE STATE DEPARTMENT OF HEALTH	Fifth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: FREE STATE DEPARTMENT OF HEALTH	Sixth Respondent
GAUTENG DEPARTMENT OF HEALTH	Seventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: GAUTENG DEPARTMENT OF HEALTH	Eighth Respondent
KWAZULU NATAL DEPARTMENT OF HEALTH	Ninth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: KWAZULU NATAL DEPARTMENT OF HEALTH	Tenth Respondent
LIMPOPO DEPARTMENT OF HEALTH	Eleventh Respondent
MEMBER OF THE EXECUTIVE COUNCIL: LIMPOPO DEPARTMENT OF HEALTH	Twelfth Respondent

MPUMALANGA DEPARTMENT OF HEALTH	Thirteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: MPUMALANGA DEPARTMENT OF HEALTH	Fourteenth Respondent
NORTHERN CAPE DEPARTMENT OF HEALTH	Fifteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTHERN CAPE DEPARTMENT OF HEALTH	Sixteenth Respondent
NORTH WEST DEPARTMENT OF HEALTH	Seventeenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: NORTH WEST DEPARTMENT OF HEALTH	Eighteenth Respondent
WESTERN CAPE DEPARTMENT OF HEALTH	Nineteenth Respondent
MEMBER OF THE EXECUTIVE COUNCIL: WESTERN CAPE DEPARTMENT OF HEALTH	Twentieth Respondent
THE PRESIDENT OF THE REPUBLIC OF SOUTH AFRICA	Twenty-first Respondent
SOUTH AFRICA HEALTH PRODUCTS REGULATORY AUTHORITY	Twenty-second Respondent
PFIZER	Twenty-third Respondent

SUPPORTING AFFIDAVIT

I, the undersigned

DR ANTON JANSE VAN RENSBURG

do hereby make oath and state that:-

1. I am an adult male general practitioner with my principal place of business at 92 Stella Street, Brooklyn, Pretoria.

2. The facts in this affidavit are, to the best of my knowledge, both true and correct, and, unless the contrary appears from the context of this document, they fall within my personal knowledge and/or expertise. I ask the Court to note that I have no conflicts of interests that would in any way jeopardise or compromise my objectivity in diagnosing and handling my patients, or in presenting evidence to this Court. The opinions I have reached have been so reached based on my expertise, and are wholly independent of any external influencing factors or conflicts of interest.

3. I have read the founding affidavit deposed to by Herman Jacobus Edeling ("Edeling"). I support the contents of that affidavit insofar as he concludes that the Pfizer Covid-19 vaccines are neither safe nor effective. That conclusion accords with the patient cases I have dealt with in my own practice. In his affidavit, Edeling summarises the vaccine injuries I have seen in my practice. I confirm the contents of his affidavit insofar as they pertain to me, and the vaccine injury diagnoses I have made in respect of the relevant patients.

4. In this affidavit, I set out further information in relation to those cases in order to fully apprise to Court of the reasons for my diagnoses. I have obtained consent from my patients to disclose their information in this affidavit. This consent notwithstanding, I am withholding the patient's names at their requests. I will refer to the patients as "patient one", "patient two", "patient three", "patient four", "patient five" and "patient six". Should the Court require patient names, the patient files can be made available to the Court for inspection on the date of the hearing. It is

J.S

important to note that, for the sake of not overburdening the Court, I am not detailing all cases of Pfizer vaccine injuries that I've diagnosed. I have selected only the six most severe cases in which the patients have either been near death or have suffered life-altering injuries due to the Pfizer vaccines. I do; however, annex as "**AJ1**", a copy of an excel spreadsheet listing the patient information of all patients that were, in my opinion, injured by the Pfizer vaccine.

5. The patients I have chosen to focus on in this affidavit were all healthy with no significant family medical histories and they all had severe, life-threatening or life-altering reactions within a short time frame after having received the Pfizer Comirnaty vaccine. The conditions with which the below patients presented (except for the conditions of one patient) are all listed in the post-authorisation adverse event report ("the report") commissioned by Pfizer as "*adverse events of special interest*" potentially related to the Comirnaty vaccine. Those conditions include – but are not limited to - motor-neurone disease, heart attacks, clots and clotting disorders, and neuropathy. The fact that these conditions appear in the report does not establish causation – but strongly suggests (at the very least) correlation between the relevant condition and the administration of the Comirnaty vaccine, and this was one of the factors I considered in reaching my diagnoses.

My qualifications

6. I hold an MBChB from the University of Pretoria (1997), and hold a Master's degree in nutrition from the same university (2012). I have been in private practice as a general practitioner for over 20 years, with a special interest in severe disease. I am also, and have been since 2010, a medical consultant and wellness coach to management in some of the country's most established companies including:

J.S

South African Reserve Bank, South African Revenue Service, Transnet, Department of Science and Technology, Auditor General, Nedbank, Standard Bank, ABSA, Ernst & Young, SASOL, TOTAL, DHL, Multichoice, Life Hospital Group, Barloworld, Adcock, SAPPI, Vodacom. My full curriculum vitae is annexed as "**AJ2**".

7. I now commence detailing my most severe, selected cases.

Patient one

8. This patient was a 39-year-old male. He had been injected with two doses of the Pfizer Comirnaty vaccine. His first vaccine dose was administered on 14 September 2021, and his second dose on 6 November 2021.

9. 24 days after his second Pfizer injection, the patient had a severe heart attack. He was hospitalised, and a clot was discovered in his coronary artery. The heart attack was of a level of severity that would have killed him but for the intervention of a cardiologist. He was treated by the placement of a stent in the affected artery, and is still recovering. Additionally, he now suffers from regular migraines.

10. An angiogram (which is used to view coronary arteries) demonstrated that the patient had no chronic pathology in coronary blood vessels. In lay terms that means that the patient had no underlying problems that would ordinarily result in a heart attack (such as cholesterol plaque or any other pathology like birth defects in the blood vessels). When I consulted with the patient on 7 December 2021, I ascertained that he was otherwise healthy, with no underlying health issues or

family history that would have suggested any reason for the sudden heart attack – especially one of such severity. I diagnosed the patent as having been injured and having suffered his heart attack due to the administration of the Pfizer vaccine. In reaching that diagnosis, I considered the close temporal relationship between the second administration of the Pfizer vaccine, and the heart attack as well as published peer-reviewed literature which was available at the time showing connections between clotting, heart attacks, and the Pfizer vaccine. My patient notes for patient one are annexed as "**AJ3**".

11. Due to the seriousness of his condition, I referred the patient for evaluation to a specialist physician, Dr Renier Van Tonder. Following his consultation with Dr van Tonder, I was sent Dr Van Tonder's report which is annexed as "**AJ4**". That report concludes that:

> *"In summary, this is a patient with an acute coronary syndrome [...] likely precipitated with [sic] Covid vaccines [...]"*

12. There was no medical reason for this patient's heart attack other than the Pfizer Comirnaty vaccine. I concluded, and maintain, that this patient was vaccine injured.

Patient two

13. This patient was a 53 year old previously healthy female. She had been injected with one dose of the Pfizer Comirnaty vaccine in September 2021. I consulted with the patient on 13 October 2022.

14. Within three days of having received the vaccine, the patient presented with vertigo, severe ear pain, diarrhoea, and vomiting. Her symptom persisted, untreated by doctors who refused to consider vaccine injury, until she came to see me in October 2022. In April 2022, she developed severe tinnitus, due to suspected vestibulocochlear neuropathy.

15. When I consulted with the patient, I ascertained that she was otherwise healthy, with no underlying health issues or family history that would have suggested any reason for the onset of these severe, life-changing conditions. I diagnosed the patient as having been vaccine injured by the Pfizer vaccine. In reaching that diagnosis, I considered the close temporal relationship between the second administration of the Pfizer vaccine, and the lack of any other medical causal factors. My patient notes for patient two are annexed as "**AJ5**".

Patient three

16. The third patient was a healthy 55 year old male . He had received two doses of the Pfizer Comirnaty vaccine. His first dose was administered in June 2021, and the second dose in August 2021.

17. Within 20 days of the administration of the second Pfizer vaccine, the patient was experiencing stiffness in his hands. By December 2021, the patient started losing sensation in his left leg. This was followed by a progressive loss of motor function in both legs, and he was ultimately diagnosed in March 2022 with motor neurone disease by a neurologist. He was referred to me for palliative care and management of his condition. It is a medical certainty that this condition will

eventually kill the patient, following a long period of muscular degeneration and horrendous suffering.

18. The patient had Covid-19 in December 2020 (eight months prior to his first administration of the Pfizer vaccine) but recovered fully with no post-infection sequelae. I am of the opinion that Covid-19 could not have been the cause of the motor neurone disease because there is currently no peer-reviewed literature of which I am aware linking Covid-19 to motor neurone disease.

19. This patient was completely healthy prior to this sudden onset of motor-neurone disease. He had no family history of motor neurone disease and no indicators,, either in himself or in his family that could have predisposed him to the condition.

20. Again, given the close temporal association between the administration of the Pfizer vaccine and the onset of the symptoms, I concluded that this patient was vaccine injured and that his motor-neurone disease was the result of the two doses of the Pfizer vaccine that he received. I attach as "**AJ6**" my patient notes for this patient.

Patient four

21. The fourth patient was a 73 year old healthy male patient. He had received only one dose of the Pfizer Comirnaty vaccine on 31 May 2021. I consulted with the patient on 19 September 2022.

22. Within five days of having received the Pfizer vaccine, the patient developed obstructive jaundice. Obstructive jaundice is a specific type of jaundice, where symptoms develop due to a narrowed or blocked bile duct or pancreatic duct, preventing the normal drainage of bile from the bloodstream into the intestines. It may be severe or even fatal. The patient has subsequently recovered from the liver related pathology.

23. He also developed hyper-coagulability, which is a high clotting risk, with clot formation, and reported developing abscesses in multiple sites of his body.

24. Further, he had pre-existing Parkinson's disease symptoms, which worsened significantly almost immediately after the vaccine. This related specifically to tremors in his legs which were significantly worse. The tremors have since started involving all the limbs in his body and they have become a major problem at night causing severe sleep deprivation. At time of visit to my practice, liver function and inflammatory markers were still abnormal.

25. By 25 June 2021 (less than a month after his vaccination), he was hospitalised at Kloof hospital because of the severity of the aforementioned liver-related symptoms, and his gallbladder had to be removed.

26. When I consulted with the patient, as my notes annexed as "**AJ7**" demonstrate, he presented with no health conditions that could have precipitated either the obstructive jaundice, the clotting or the immediate and severe worsening of Parkinson's symptoms. Likewise, there was nothing of medical significance in his family history that could have been causally related to these conditions and symptoms. I diagnosed the patient as having been injured by the Pfizer vaccine.

Patient five

27. This patient was a 55-year old healthy female. She had received two doses of the Pfizer Comirnaty vaccine. Her first dose was administered in June 2021 and the second dose in August 2021.

28. Within 24 hours after the first dose of the vaccine, the patient had an acute anaphylactic reaction, which is a severe, deadly allergic reaction. She was given injectable and oral cortisone by a general practitioner to manage the attack. Had it not been for that intervention, the patient could have died.

29. These issues notwithstanding, the patient chose to have the second Pfizer dose. After that, she developed chronic urticaria (which is an allergic skin rash) and asthma. Furthermore, she now suffers from allergies (which appear to be getting progressively worse) with which she had never previously presented and she gets repeated episodes of hives. She presented at my practice on 30 May 2022 with these symptoms which were still present. At the time she came to see me on 30 May 2022 (which was almost a year after her symptoms began), the patient was desperate. None of the doctors she had seen had been able to help her, inclusive of a specialist physician. The only interventions that are of any assistance are regular cortisone dosages, at least five antihistamines per day and she has to use an asthma pump. Due to my intervention the patient started showing improvement after three months and has recovered nearly fully after one year.

30. When I consulted with the patient, it was clear that she was previously healthy and had no previous, current or underlying conditions capable of causing the conditions described above. Her family medical history included heart disease and hypertension – but that, too, is not causally linked to the conditions with which she presented. I attach her patient files as "**AJ8**". I concluded, due to the close temporal association of her conditions and symptoms to both vaccine doses that this patient was injured by the Pfizer vaccine.

Patient six

31. This patient was 60 year old healthy female. She had received one dose of the Pfizer Comirnaty vaccine on 10 June 2021. Within five days of having received the vaccine, the patient presented with upper-respiratory tract infection and tested positive for Covid-19 within five (5) days of receiving the Pfizer vaccination. Fourteen (14) days after vaccination, the patient was hospitalised with low oxygen saturation, low platelets, and arrhythmia.

32. At time of her visit to my practice on 7 September 2021, she was still short of breath, despite prescribed medication. She has to sleep with supplemental oxygen via nasal cannula. She also presented with low platelets which ties into a very well described side effect of the Pfizer vaccines.

33. There was no personal or family medical history that were relevant to the conditions with which she presented. She was healthy and had stopped smoking over ten years ago. It took more than a year for the patient to fully recover. I diagnosed this patient too, with Pfizer vaccine injury.

J.S

Conclusion

34. It is my opinion, based on the facts in this affidavit and on the facts in Dr Edeling's affidavit, that the Pfizer vaccine is unsafe.

ANTON JANSE VAN RENSBURG

The deponent has acknowledged that he knows and understands the contents of this affidavit, which was signed and sworn before me at Lyttelton SAPS on this the 09 day of February 2023 the regulations contained in Government Notice No. R1258 of 21 July 1972, as amended, and Government Notice No. R1648 of 19 August 1977, as amended, having been complied with.

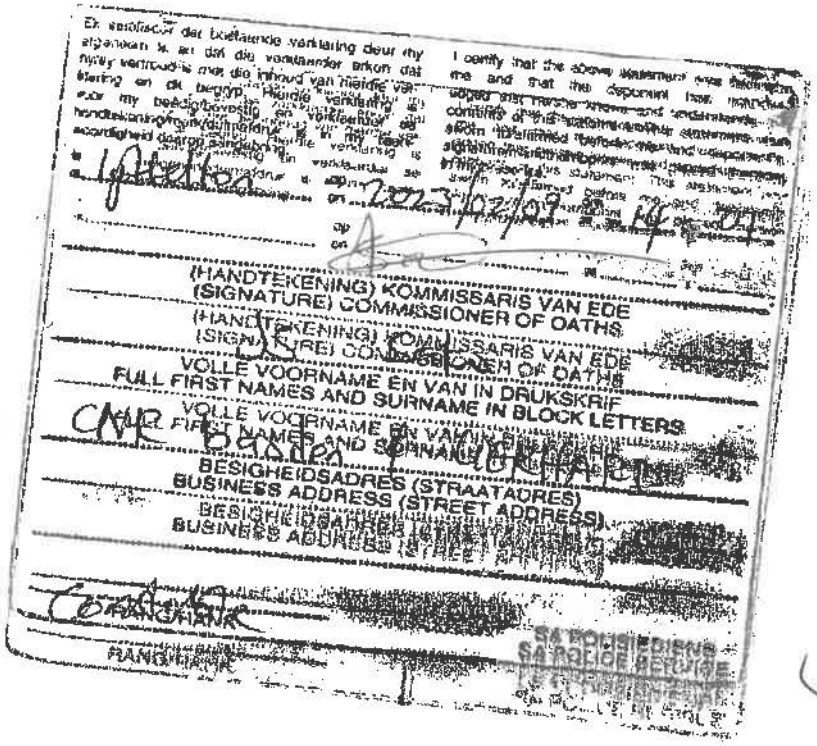
SUID-AFRIKAANSE POLISIEDIENS
SAPS LYTTELTON
2023 -02- 09
COMMUNITY SERVICE CENTRE
SOUTH AFRICAN POLICE SERVICE

COMMISSIONER OF OATHS

Name:

Address:

Position:



Dr. Anton Janse van Rensburg
MBChB (UP), MSc (Nutrition) (UP)
Pr. No: 1582585

7 December 2021

Jacques Rossouw
ICD code for MI: I21.9
Vaccine injury: U12.9
ID: 8206035024087
To come back for consultation: 1 month
39 yrs
Social media
Works for SAPPI

Main: Vaccine injury - heart attack
Now has migraine

Lockdown ZOOM

- 30 Nov 2021 - heart attack - 10 days after 2nd Pfizer
  - Tuesday - no alcohol the day before or on the day
- Had blood clot in his coronary artery
- No major dehydration on the day
- Was hydrating well in the gym
- No pain in legs on the day
- Now has migraines that he has never suffered from
- Stopped smoking 2 years ago
- No major operations in the last 3 years

Tests done to date:
- Angiogram - only showed blood clot not narrowed arteries - Arwyp - Dr Gregorov
- Received stent x1

Family - has brother - healthy
- Heart - nothing - dad is 70
- Stroke - nothing
- DM - none
- Hypertension - Pa

Chronic meds
- None

Supps
- Multivitamin
- Nothing new

Weight
- 101kg
- Height: 1.76

Recent vaccinations?
- Pfizer double
- 14th September
- 6th November

ALLERGIES TO MEDICINE? Paracetamol

Alcohol: Weekends - beer

Sleep:

- Hours: Good
- Slept well the night before

Exam: ZOOM

Diagnoses:

- Vaccine injury

Plan:

1. Script
2. Bloods

New medication

- Ecotrin
- Cardicor
- Aspavor
- Clopiwin

1. Magnesium
   High dose is needed
   1 cap taken 3x dly (preferably chelate)
2. N-Acetyl cysteine
   600mg taken twice daily
3. Vitamin C
   1000mg taken twice daily
4. Co Enzyme Q10
   150mg daily
5. Acetyl L-Carnitine
   1000 - 2000mg per day
6. Selenium
   300 - 600mcg per day

- aspirin
- levocarnitine
  - carnitine
- coenzyme Q10
- atorvastatin
- clopidogrel
- bisoprolol
- magnesium chloride
- acetylcysteine
  - N-acetylcysteine

Monitor Closely

- aspirin + bisoprolol

  aspirin decreases effects of bisoprolol by pharmacodynamic antagonism. Use Caution/Monitor. Long term (>1 wk) NSAID use. NSAIDs decrease prostaglandin synthesis.

- aspirin + clopidogrel

  aspirin, clopidogrel. Either increases toxicity of the other by pharmacodynamic synergism. Use Caution/Monitor. The need for simultaneous use of low-dose aspirin and anticoagulant or antiplatelet agents are common for patients with cardiovascular disease; monitor closely.

- bisoprolol + aspirin

  bisoprolol and aspirin both increase serum potassium. Use Caution/Monitor.

Minor

- atorvastatin + coenzyme Q10

  atorvastatin decreases levels of coenzyme Q10 by unspecified interaction mechanism. Minor/Significance Unknown.

7 December 2021

- Migraines getting better

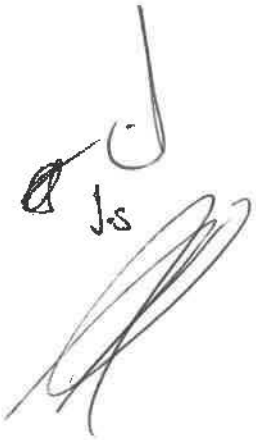
Exam:

- **Weight:** 100.2kg
- Waist:
- BP: Sitting: 110/75
- Lying: 105/70
- Oedema: No signs
- Respiratory: Rate is 21
- Clear lung fields
- Cardiovascular; Peripheral pulses palpable (radial, both feet pulses)
- Abd: Central hernia visible just superior to umbilicus

Plan

- Refer to lawyer
- Refer to Dr van Tonder

- Antiphospholipid syndrome
- Arteriosclerosis / atherosclerosis
- Certain medications, such as oral contraceptives and hormone therapy drugs
- Coronavirus disease 2019 (COVID-19)
- Deep vein thrombosis (DVT) (DVT)
- Factor V Leiden
- Family history of blood clots
- Heart arrhythmia (heart rhythm problems)
- Heart attack
- Heart failure
- Obesity
- Peripheral artery disease (PAD)
- Polycythemia vera
- Pregnancy
- Prolonged sitting or bed rest
- Pulmonary embolism (blood clot in an artery in the lung)
- Smoking
- Stroke
- Surgery



Feedback from Dr Reinier van Tonder

Hi, Jaques Rossouw het n akute koronere sindroom gehad gepresipiteer met Phizer vaksiene en sessie in gym, risikoprofiel onderliggend gemengde dislipidemie en verhoogde uriensuur maar uit verhouding tot sy kliniese presentasie...eerste event op 39 is baie jonk...endoteel disfunksie dus akuut op chronies...sou waarskynlik heelwat later gebeur het as hy Phizer vaksiene gemis het....Fokus nou op sekondere voorkoming en Veral oefenprogram...ek het hom verwys na Biokinetika tweeling by TUKS.Sal verslag en voorskrif stuur, dankie!

Note: Patient never had Covid

Dr. R.J.N. van Tonder

MBChB,MMed(Int)(Pret)
Pr No 0180000190527
INTERNIS PHYSICIAN
- With special interest in Cardiology -
MONTANA HOSPITAAL SUITE 27

Posbus 11925,
Queenswood.
0121

Tel: (012) 742-6450
Faks: (086 292 4489)
Radiotel: (012) 333 6000

14 February 2022

Patient: Mr J. Rossouw
ID No: 820603 5024 087

Ref Dr: A. Janse van Rensburg
Email: antonvanren@gmail.com

Our Reference File: T5058

Dear dr Janse van Rensburg

Thank you for the referral.

CLINICAL PROBLEM:

ISCHEMIC HEART DISEASE

- **ETIOLOGY:**
  Acute coronary syndrome as recently documented angiographically by a colleague (Dr. Grigorov, "plaque rupture").

- **PRECIPITANTS:**
  - Post mRNA Covid vaccines.
  - Exercise session (symptoms starts during gymnasium session).

- **COMPLICATIONS:**

1. Symptomatology: Typical chest pain starts approximately 21 days post Covid vaccination and during workout.

2. Anatomically: Echocardiography: Anatomically normal cardiac substrate. Functionally normal global biventricular systolic and diastolic function. No pulmonary hypertension. Myocardial deformity indices indicate residual peak systolic deformation shortening towards the basal to mid anteroseptal wall but probably in recovery phase.

3. Electrophysiology:
   a. R-CKG: Sinus rhythm @ 61/ min / PR 154 ms / QTc 399 ms.
      Baseline T-wave reversal in anterior-lateral / inferior leads and a non-specific intraventricular conduction defect with pathological q-waves in the inferior leads.
   b. I-ECG: Optimal cardiac conditioning (14.2 METS) associated with a neutral SBP response but appropriate heart rate recovery. Baseline repolarisation disorders improve with exercise and the patient is asymptomatic throughout the examination.

4. Radiology: CXR: Normal.
5. Biochemistry: Bloodwork (Ampath and Lancet) marked for your attention.
   - Trop T 13
   - ProBNP 224
   - HbA1c 5.4%
   - Urine albumin creatinine ratio normal
   - Lipogram: Total Chol 6 / LDL 3.8 / HDL 0.9 / Triglyceride 2.8
   - TSH normal
   - Uric acid 9
   - Antinuclear factor negative

MANAGEMENT

- In summary thus a patient with an acute coronary syndrome associated with risk factors as listed likely precipitated with Covid vaccines (endothelial inflammatory response recently described: article attached) and gymnasium workout.
- For now, focus on secondary cardiovascular prevention with optimal pharmacotherapy as listed as well as appropriate focused cardiac rehabilitation (exercise program).
- Primary genetic hypercoagulability disorders are not currently considered (no significant family history) and therefore not further worked up.
- He will follow up with you and annually with me regarding cardiovascular review as necessary.

- **Current Medication:**
  1. Clopiwin Plus I/d
  2. Cardicor 2.5mg/d
  3. Aspavor 40mg/d

Regards

Dr R.J.N. van Tonder
MBChB, MMed(Int)(Pret)

Circulation

FRAME OF REFERENCE

ORIGINAL RESEARCH ARTICLES

ORIGINAL RESEARCH ARTICLES

CORRESPONDENCE

uitgave .. 16. 11. 2021

Supplement I

American Heart Association

Volume 145, Number 6, February 8, 2022 ISSN 0009-7322 www.ahajournals.org/journal/circ

February 8, 2022
Vol 145, Issue 6

Related Collections

Arrhythmia and Electrophysiology

Dr. Anton Janse van Rensburg
MBChB (UP), MSc (Nutrition) (UP)
Pr. No: 1582585

13 October 2022

Patient two
Weight: 74kg
Cell number:
ICD code: U12.9
53 yrs
Works own business at home
CC referral

Main: Vaccine injury

VIRTUAL CONSULTATION

Official diagnosis?

- Sept 2021 had Pfizer
- Didn't want the vaccination - her psychiatrist told her 'to do it for her fellow humans'
- Within 3 days had side effects - extreme dizziness, vomiting, diarrhoea, stomach pain, vertigo and severe ear pain
- At Constantia park Medicross
- For months had problems
- In April 2022 sick again and this time developed tinnitus (vestibulo-cochlear nerve)
- ENT (Dr Louis Swart - Wilgers consortium) agreed that it could be vaccination - he noted that he is seeing it
- Sent her for MRI - saw nothing
- Medication did not work
- Has received TMJ physio - small reduction
- Reported to SAHPRA last year - has incident report number and no one contacted her

Current

- Tinnitus
- Neuropathic pain
- Muscle aches generally in her body - back particularly affected

List ALL medications that patient has unsuccessfully tried to treat this condition (current and past)?
Current:

- Numerous

List ALL other therapies tried (surgery, physiotherapy, specialists).

- Physiotherapy

Concomitant conditions?

- Hypothyroidism

Medication for concomitant conditions?

- Trustan 40
- Venlor 75
- Euthyrox 50

Supps

- The real thing Omega-3

ALLERGIES TO MEDICINE? Aspirin
Eglonyl

Diagnoses:

- Pain

Plan:

1. **Intermittent daily fasting or periodic daily fasts.**
   Fasting has a profound effect on promoting immune system homeostasis, partly by stimulating autophagy and clearing misfolded and foreign proteins, promoting mitophagy and improving mitochondrial health, as well as increasing stem cell production. Intermittent fasting likely has an important role in promoting the breakdown and elimination of the spike protein.
   Mechanisms activated in the body by fasting
   - Apoptosis
   - Autophagy
   - Stem cells are produced. They can repair any type of cell (with longer fasts - 3 days and more)

2. **Higher fat and low carbohydrate diet is essential**

3. **Ivermectin:**
   22mg taken daily with food
   Ivermectin has potent anti-inflammatory properties. It also binds to the spike protein, aiding in the elimination by the host. It is likely that ivermectin and intermittent fasting act synergistically to rid the body of the spike protein. A trial of ivermectin should be considered as first line therapy. It appears that patients can be grouped into two categories: i) ivermectin responders and ii) ivermectin non-responders. This distinction is important, as the latter group are more difficult to treat and require more aggressive therapy.

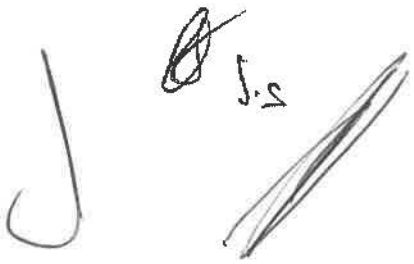
4. **Mibiotix 'Premium Plus' sporebiotic (Dischem)**
   www.mibiotix.co.za
   Dosing instructions:
   Week 1: Take 1 cap every 2nd day with food
   Week 2: Take 1 cap daily with food
   Week 3 to 8: Take 2 caps with food daily

   Maintenance: After completion of the first course of 'Premium Plus' you will use two probiotics going forward. Health Matrix Flora and MiBiotix Daily. Use each for a month at a time and keep switching between the two.
   Annual booster sporebiotic dose: Continue this switch between the 'Flora' and 'Daily' until you reach the annual repeat of the sporebiotics in MiBiotix Premium Plus. Then use the MiBiotix Premium plus again for 2 months.

   Possible symptoms associated with the use of sporebiotics in the first month:
   Abdominal cramping, loose stools and changes in bowel movements. This is completely normal and symptoms should subside within 2-3 days. If symptoms persist, simply discontinue for a few days and start again at a smaller dose. If 1 capsule every other day is too strong, try starting with 1/2 capsule or even 1/4 of a capsule.

5. **Health Matrix Magnesium Chelate**
   500mg per day

6. **Vitamin D3 ('Mega D3' from Integrow.co.za)**
   40 000iu three times per week for one month
   Then one cap per week for 3 months
   Retest blood levels in 4 months' time

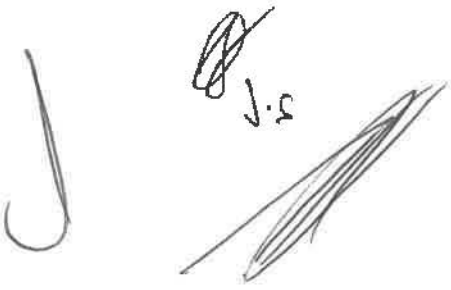


7. **Quercetin:**
   Flavonoids have broad spectrum anti-inflammatory properties, inhibit mast cells, and have been demonstrated to reduce neuroinflammation. Due to a possible drug interaction between quercetin and ivermectin, these drugs should not be taken simultaneously (Ivermectin taken at lunch time and Quercetin taken morning and evening).
   Health Matrix Immune Matrix (www.healthmatrix.co.za) - Contains quercetin, vitamin C & D, zinc, selenium and B vitamins.
   Week 1-4: 2 caps taken twice daily with food
   Medium term: 1 cap twice daily

8. **Vitamin C – use buffered:**
   Week 1: 500mg taken twice daily with food
   Week 2: 1000mg taken twice daily with food
   Week 3: 1000mg taken three times

Other anti-inflammatory strategies

9. **Epsom salt baths**
   Placing Epsom salts (1 cup) in your bath can be done daily or 3-5 times per week
10. **Fresh grated ginger**
    Add this to 2-3 cups of tea per day



Dr. Anton Janse van Rensburg
MBChB (UP), MSc (Nutrition) (UP)
Pr. No: 1582585

Main instruction after last session:
Come back after blood tests

24 October 2022

Patient three
ICD code: U12.9
55 yrs
Cape Town

Main: Vaccine injury MND

ZOOM

- Sept last year - stiffness of L thumb and forefinger - atrophy
- December: Lameness developed in left side calf into foot
- Neurologist made first diagnosis of motor neurone disease in March 2022
- June 2022: Neurologist offered two pharmaceuticals - very expensive
- Patient decided not to pursue this
- Left foot is swollen
- Had Beta Covid Dec 2020
- June 2021 - Pfizer
- Aug 2021 - Pfizer
    - In Sept had movement issues with his left thumb

Body weight
88kg

Current medication and treatments
- RIFE twice per week
- Re-apten 10-10 (Since Feb - Hypertension)

Family
- Father's siblings: ALS (Paternal Grandfather)

ALLERGIES TO MEDICINE? None

Diagnoses:
- Vaccine injury

Plan:
1. Script
2. Bloods - vitamin D

Full vaccine injury protocol

1. **Methylcobalamine**
   Take one sublingual tablet 2x dly
2. **Health Matrix Immune Matrix**
   Contains quercetin, vitamin C & D, zinc, selenium and B vitamins.
   1 cap twice daily
   If symptoms of viral illness are present increase dose to:
   2 caps twice daily
3. **Health Matrix Multinutrient for men (www.healthmatrix.co.za)**
   Contains Resveratrol and Green tea which helps nerve tissue.
   2 capsules with breakfast
   1 capsule with supper
4. **Health Matrix Magnesium chelate caps**

Take 1 cap 2x dly

5. **Health Matrix Omega-3 fish oil or The Real Thing from Dischem**
   2 capsules with breakfast and 2 capsules with supper
6. **Co-Enzyme Q10 150mg**
   Take 1 capsule daily
7. **Alpha Lipoic acid (Dischem or Integrow.co.za)**
   250mg taken twice daily
8. **ACC 200**
   Take 1 fizzy tab three times daily
9. **Ivermectin:**
   18mg taken daily with food
   Ivermectin has potent anti-inflammatory properties. It also binds to the spike protein, aiding in the elimination by the host. It is likely that ivermectin and intermittent fasting act synergistically to rid the body of the spike protein. A trial of ivermectin should be considered as first line therapy.
10. **Mibiotix 'Premium Plus' sporebiotic (Dischem)**
    www.mibiotix.co.za
    Dosing instructions:
    Week 1: Take 1 cap every 2nd day with food
    Week 2: Take 1 cap daily with food
    Week 3 to 8: Take 2 caps with food daily

    Maintenance: After completion of the first course of 'Premium Plus' you will use two probiotics going forward. Health Matrix Flora and MiBiotix Daily. Use each for a month at a time and keep switching between the two.
    Annual booster sporebiotic dose: Continue this switch between the 'Flora' and 'Daily' until you reach the annual repeat of the sporebiotics in MiBiotix Premium Plus. Then use the MiBiotix Premium plus again for 2 months.

    Possible symptoms associated with the use of sporebiotics in the first month:
    Abdominal cramping, loose stools and changes in bowel movements. This is completely normal and symptoms should subside within 2-3 days. If symptoms persist, simply discontinue for a few days and start again at a smaller dose. If 1 capsule every other day is too strong, try starting with 1/2 capsule or even 1/4 of a capsule.
11. **CBD dominant oil**
    Follow titration that will be emailed to you
    Settle on a dosage of 50mg CBD total per day

29 November 2022
Feedback
There are a few days to for 1 month of the cocktail of prescription started 1 November 2022.

I include a chart I created to easily see what I have taken and when.
The Ivermectin I only received after the 1st week, hence the blank dates there.

We need to assess in the next month to decide what else to do

Plan:

- Add GG at 2 caps per day and re-assess in two months time

Dr. Anton Janse van Rensburg
MBChB (UP), MSc (Nutrition) (UP)
Pr. No: 1582585

Main instruction after last session:
Come back after blood tests

19 September 2022

Patient four
ICD code: U12.9
73 yrs

Main: **Vaccine injury**
Parkinson's
Back pathology

- Knee replacement 2018 and 2019
- Aug 2020 neck operated
- Feb 2021 Lumbar fusion
  - Contracted hospital bug
- March 2021 - revision of back operation
- April 2021 - pain control

Then 31 May 2021 - Pfizer
- 5 of June - in bed sick
- 25 June admitted to Kloof hospital
  - Obstructive jaundice
  - Gallbladder removed
  - Blood clots developed as well
  - Parkinson's became worse - more tremors in whole body - all limbs affected
  - Received Lasix and Bilicor
  - Developed abscesses all over body
  - Sept 2021 - rehabilitation
  - Weight: 80kg

Tests done to date:
- Is with Dr Erasmus the physician at Kloof
- Patient struggling to get appointment

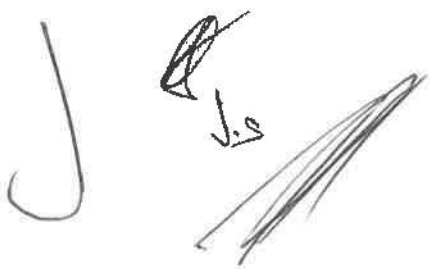
Current medication
- Bilicor - post jab
- Lasix - post jab
- Parkinsons
  - Azilec
  - Pexola
  - Symadin
  - Madopar

Family
- None

Recent vaccinations?
- Pfizer

ALLERGIES TO MEDICINE? None

Exam:
General impression: Healthy
Blood pressure: 145/87
GASTHELLD: N
ENT: N



Neurological: N
Abdomen: N
Cardio: N
Skin: N
Lungs: Clear
Musculoskeletal: N

Diagnoses:

- Vaccine injury

Plan:

1. Script
2. Bloods

Clear All
Patient Regimen

- **bisoprolol**
- **furosemide**
- **pramipexole**
- **rasagiline**
- **amantadine**
- **ivermectin**
- **coenzyme Q10**

Monitor Closely

- bisoprolol + furosemide

  bisoprolol increases and furosemide decreases serum potassium. Effect of interaction is not clear, use caution. Use Caution/Monitor.

Back to top

PLAN:

- Treat with ivermectin to bind spike protein
- Try to recover some function
- Prevent future illness

4 October 2022

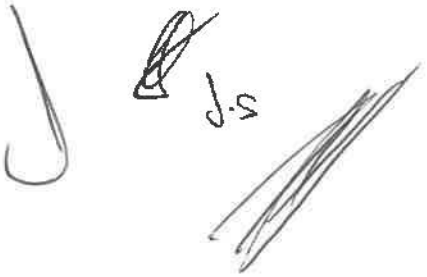
- D-Dimer: 2.22
  - Discussed this finding with specialist physician Stephen Schmidt and he said we cannot use this at this point as it could be indicating acute phase reaction
- Kidney: N
- S-ALKALINE PHOSPHATASE 203 IU/L *H 53 - 128
- S-g-GLUTAMYL TRANSFERASE 60 IU/L 0 - 64
- S-ALANINE TRANSAMINASE 23 IU/L < 50
- S-CRP, Ultra sensitive 11.9 mg/L
- INTERLEUKIN 6 4 pg/mL < 7
- > ERYTHROCYTE COUNT 4.65 x10^12/L 4.5 - 6.5
- > HAEMOGLOBIN 13.3 g/dL L 13.8 - 18.8
- > HAEMATOCRIT 0.41 L/L 0.40 - 0.56
- > MCV 88.8 fL 79 - 100
- > MCH 28.6 pg 27 - 35
- > MCHC 32.2 g/dL 32 - 36
- > RDW 14.5 % 11.0 - 16.0
- > VITAMIN D 25 27 ng/mL
- > S-VITAMIN B12 188 pmol/L > 145

Elevated ALP:

- Diseases or infections of the gallbladder, liver, intestine or bone.
- Medications could cause it which includes oral contraceptives and antibiotics like erythromycin.
- Alcohol consumption can also elevated ALP
- Lack of nutrients like vitamin D, calcium, protein, magnesium and zinc.

Script

1. **Ivermectin: 16mg caps.**
   18mg taken daily with food for 4 weeks
2. **Silver (Strictly use 'Silverlab' 18 ppm ionic silver)**
   Oral protocol:
   15mL taken twice daily for 5 days
   Nebulisation protocol:
   For the first 2 weeks: 5mL nebulised three times per day
   Week 2-4: 5mL nebulised twice per day
   Medium term: 5mL nebulised daily
3. **Melatonin:**
   Week 3: 3mg taken before bedtime
4. **Health Matrix Magnesium Chelate**
   1 cap twice per day
5. **Quercetin:**
   Week 1-4: 2 caps taken twice daily with food
   Medium term: 1 cap twice daily
6. **Mibiotix 'Premium Plus' sporebiotic (Dischem)**
   www.mibiotix.co.za
   Dosing instructions:
   Week 1: Take 1 cap every 2nd day with food
   Week 2: Take 1 cap daily with food
   Week 3 to 8: Take 2 caps with food daily
7. **Eterna (Delta Tocotrienols or T3)**
   Dosage: 1 cap twice daily
8. **Vitamin D3 ('Mega D3' from Integrow.co.za)**
   40 000iu twice per week for 2 months
   Then one cap per week for 2 months
   Retest blood levels in 4 months time
9. **Health Matrix Multinutrient for men (www.healthmatrix.co.za)**
   2 capsules with breakfast
   1 capsule with supper



Dr. Anton Janse van Rensburg
MBChB (UP), MSc (Nutrition) (UP)
Pr. No: 1582585

30 May 2022

Patient five
ICD code: U12.9
55 yrs
Speech therapist

Main: Covid vaccine adverse event
- **Chronic urticaria**
- **Asthma**

- June 2021 - Pfizer
- 24 hours afterwards eyes and throat swollen
- GP injected her
- 6 weeks later went for 2nd Pfizer
- She is now allergic to things that she was not allergic to before - gets hives
- Allergies became progressively worse - chronic urticaria as per dermatologist
- No one has solutions - including specialist physician
- Regular cortisone dosages

Now daily:
- 5 x antihistamines per day
- Asthma pump
- Triggers?
  - Histamine containing foods
  - Dairy

Tests done to date:
- Blood tests by GP
- CRP = 17
- Autoimmune = negative

Family
- Heart
- Hypertension

Menstrual cycle:
- Menopause

Recent vaccinations?
- Pfizer x 2

ALLERGIES TO MEDICINE? Stemitil Maxolon

Exercise: Nil

Sleep:
- Good
- Restless legs

Sunlight per day? Little

****

Issues to focus on:
- Intestine
- I-Recover - vaccine protocol
- Sunlight

****

Diagnoses:

- Vaccine injured

Plan:

1. Script
2. Bloods

Current medication

At 1st visit

Cleogest
Cilift
Lenamet (Cimetidine)
Xyzal – Rupallerg - Allerway
Topraz
Vanair

Current supplements

At 1st visit

Zinc Magnesium at night

1. **Intermittent daily fasting or periodic daily fasts.**
2. **Ivermectin:**
3. **Low dose naltrexone (LDN)**
4. **Melatonin:**
5. **Aspirin**
6. **Vitamin C – use buffered:**
7. **Vitamin K2**
8. **Quercetin:**
9. **Health Matrix Flora probiotic**

22 August 2022

- Patient doing much better
- Could stop the cortisone but is still taking the 6 tablets of anti-histamine per day

Plan

- Add sporebiotics to the protocol

Improvement reported after initiation of sporebiotics

Dr. Anton Janse van Rensburg
MBChB (UP), MSc (Nutrition) (UP)
Pr. No: 1582585

7 September 2021

Patient six
ICD code: U12.9
To come back for consultation: 1 month
60 yrs

Main: Post Pfizer ITP
Long Haul Covid syndrome
Arrhythmia
Rheumatoid Arthritis

- Vaccinated 10th of June 2021 with Pfizer
- Stopped Methotrexate for one week before Pfizer
- 5 days later had Covid
- Day 14 hospitalized
- Arrhythmia picked up – Covid related – Amiodarone
- Struggling with her lungs since then – low saturations
- Had very low platelets in the hospital – 12
- Platelets transfusion
- Stopped smoking 10 years ago – 35 pack years
- CT scan was clear
- Does not feel well after
- Weight: **105kg**

Other doctors seen
- Cardiologist – Amiodarone
  - Spirometry gave 92% result
- Other doctor gave Duolin and nebs – home oxygen
- Physio: Gave exercises – can hardly do it

Family
- Heart
- Stroke

Recent vaccinations?
- Pfizer

ALLERGIES TO MEDICINE? None

Exercise: Nil

Sleep:
- Good – sleep with oxygen

Exam:
General impression: Out of breath walking to my office
Blood pressure: 118/81
GASTHELLD: N
ENT: N
Neurological: N
Abdomen: N
Cardio: N
Skin: N
Lungs: Clear

Diagnoses:

- Post Vaccine Covid
- Secondary organizing Pneumonia (OP)?

Plan:

1. Script
2. Refer to pulmonologist
3. Initiate therapy
4. Consider vitamin C drips later

Current medication
At 1st visit
Monteflo
Arycor - Amiodarone
Beta Blocker
Puricos

General

1. **Ascorbic acid capsules (Any pharmacy)**
   Take 1000mg twice daily
2. **Magnesium chelate caps (Health Matrix or Slow Mag)**
   Take 1 cap 2x dly
3. **Health Matrix Nordic Sea Omega-3 fish oil**
   2 capsules with breakfast and 2 capsules with supper

Further viral infection control measures

4. **Health Matrix Immune Matrix**
   Contains quercetin, vitamin C & D, zinc, selenium and B vitamins.
   1 cap twice daily

Intestine

5. **Health Matrix Flora probiotic (www.healthmatrix.co.za)**

1 cap every day

Other

6. **Ivermectin**
   Take recommended dose with food every day

Dr. Anton Janse van Rensburg

MBChB (UP), MSc (Nutrition) (UP), AMP (MBS)
General Practitioner/Algemene Praktisyn
Pr. No: 1582585

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Fax: +27(0) 866 904520

ABBREVIATED CURRICULUM VITAE 2023

QUALIFICATIONS AND CAREER

Matric	Hoërskool President, Johannesburg	1988
MBChB	University of Pretoria	1997
Internship	Tembisa Hospital, Kempton Park	1998
Community service	Tembisa Hospital, Kempton Park	1999
Medical Director	JC Group Health	2000 - 2004
Director	HarvestPharm Wholesale Pharmacy	2000 - 2004
Director	CoSys Technologies	2001 - 2004
Advanced Management Programme	Manchester Business School	2002
C/CMT	International Board of Clinical Metal Toxicology	2004
MSc Nutrition	University of Pretoria	2012
Chief Medical Officer	Executive Wellness Company	2010 - 2021
Private General Practice	Pretoria and Johannesburg	2000 - current
Managing Director	The Source Nutrition Projects	2004 - current

MEMBERSHIPS / PROFESSIONAL ACTIVITIES

South African "Vaccine" Injury Medico-Legal Study Group (SAVIMS) - Member	2021 - current
Pandemics Data & Analytics (PANDA) - Member	2020 - current
South African Vaccine Adverse Events Reporting System (SAVAERS) - Advisor and advocate	2022 - current

South African Society of Integrative Medicine (SASIM) - Member	2021 - current
Elevate Africa National Pre-school Feeding Programme - Lead formulator	2006 - current
Brainchild Fund Non-profit Organisation (NPO) - Trustee	2019 - 2022
South African Directorate Food Control: HIV/AIDS Advisory Committee member	2004
World Health Organization: Advisory capacity remote primary healthcare facilities.	2002
The Resuscitation Council of Southern Africa: Cardiopulmonary resuscitation instructor.	2001
Graduate Academy of Southern Africa - Governing Board member	2002 - 2003
Head of on-site clinic operations, Mozal Aluminium Smelter Construction phase, Maputo, Mozambique	2000 - 2002
Marketing liaison for community upliftment project (Uzimu Arts) in the Winterveld North of Pretoria	2002
Medical Protection Society (MPS) - member	1998
Registered with the HPSCA	1997

PUBLICATIONS

Peer-reviewed journal publication:
Janse VAN Rensburg A, Wenhold F. Validity and Reliability of Field Resonance Raman Spectroscopy for Assessing Carotenoid Status. J Nutr Sci Vitaminol (Tokyo). 2016;62(5):317-321.

Chapter in book:
Janse van Rensburg A. Finding the Diamond of Health: The Prospector's Guide. In: Holscher F, editor. Diamonds in the dust, crafting your future landscape. Johannesburg. Self-published; 2009. p. 36-50.

Book:
Janse van Rensburg A, The Health Mentoring Programme. Pretoria. Self-published, 2006.

SELECTED ARTICLES / PRESENTATIONS / SUBMISSIONS

SARS-COV-2

Invited guest/speaker:
SARS-COV-2 - SAVIMs live stream presentation - 2022 - Invited speaker - **"Finding solutions for Covid vaccine injuries"**

SARS-COV-2 - Loving Life TV - 2022 - Invited guest - **"Addressing Covid vaccine mandates"**

SARS-COV-2- Flu fighters podcast series with Patrick Holford and Professor Paul Marik - 2020 - Invited guest - "Early treatment options for Covid-19"

SARS-COV-2 - UNISA - 2020 - Invited speaker - "Covid-19 prevention and treatment strategies"

SARS-COV-2 - University of Zululand - 2020 - Invited speaker - "Covid-19 prevention and treatment strategies"

SARS-COV-2- Flu fighters podcast series with Patrick Holford and Professor Paul Marik - 2020 - Invited guest - "Early treatment options for Covid-19"

SARS-COV-2- Interview on the "High Performance Teams" show - 2020 - Invited guest - "How can aircrew protect themselves whilst flying into Covid-19 hot zones?"

Video productions:
SARS-COV-2- Video production - 2021 - Self-published - "Understanding the Omicron variant: Prevention and treatment strategies"

SARS-COV-2- Video production - 2021 - Self-published - "I've had Covid. Am I immune?"

SARS-COV-2- Video production - 2020 - Self-published - "Why I'm not concerned to send my children back to school during the pandemic"

SARS-COV-2- Video production - 2020 - Self-published - "How successful ICU teams are treating Covid-19 and saving lives"

SARS-COV-2- Video production - 2020 - Self-published - "How to protect yourself against Covid-19 and other viral infections when going back to work after lockdown"

SARS-COV-2- Video production - 2020 - Self-published - "Is there a link between electromagnetic frequency signals and viral infections?"

SARS-COV-2- Video production - 2020 - Self-published - "Will the BCG vaccine save us from Covid-19".

SARS-COV-2- Live Q&A video production - 2020 - Self-published - "Answering the most pressing questions about the Covid-19 infection".

SARS-COV-2- Video production - 2020 - Self-published - "Improving sleep patterns as a way to improve your immune response and extend your life"

SARS-COV-2- Video production - 2020 - Self-published - "Intravenous vitamin C. A treatment that saves lives"

SARS-COV-2- Video production - 2020 - Self-published - "How to exploit the weaknesses of coronavirus (Covid-19)"

SARS-COV-2- Video production - 2020 - Self-published - "Understanding which hand sanitisers will actually work"

SARS-COV-2- Video production - 2020 - Self-published - "Correct hand washing technique"

SARS-COV-2- Video production for the hearing impaired - 2020 - "Protect yourself against viral infections (Including Coronavirus)"

SARS-COV-2- Video production - 2020 - Self-published - "Protect yourself against viral infections (including Coronavirus)"

Scientific meetings:
SARS-COV-2 - Regular Scientific Online Meetings - 2021 & 2022

OTHER TOPICS

Presentations / keynotes / conferences / articles:
SA Veterinary & Para-Veterinary Biennial Congress - 2022 - Invited speaker - "The correct legal application process for medicinal cannabis for veterinarians".

Made to thrive podcast - 2022 - Invited guest - "How to incorporate correctly prescribed medicinal cannabis into treatment protocols"

Cannabis Extraction Show - 2022 - Invited guest - "Patient testimonies using correctly prescribed medicinal cannabis"

Bestmed - 2022 - Invited speaker - "Identifying and managing depression in men"

The National Consumer Tribunal - 2021 - Invited speaker - "Cancer awareness in men"

Johannesburg Stock Exchange - 2021 - Invited speaker - "Men's Health in Perspective"

Old Mutual - 2014, 2021 - Invited speaker - "The health habits of highly effective people"; "The human microbiome, a new frontier"

High Performance Teams show - 2020 - Invited guest - "How high performance teams stay healthy"

SAPPI - 2020 - Invited speaker - "Cancer awareness in men"

Liberty - 2020 - Invited speaker - "Nutritional strategies in the management of HIV/AIDS"

Action Coach South Africa - 2020 - Invited keynote speaker - "Taking extreme ownership of your health"

KBC Health & Safety - 2020 - Invited speaker - "Improving resilience"

Family Hope Centre, Philadelphia. South African Child Brain Development Conference - 2019 & 2020 - Invited speaker - "Managing the microbiome of the brain injured child"; "Heavy metal toxicology screening in the brain injured child"

MPC Consulting General Practitioners Conference - 2019 - Invited speaker - "Metabolic Endotoxaemia and Chronic Disease - the Sporebiotic link"

Department of Science and Technology - 2014, 2017 - Invited speaker - "Breast, cervical and prostate cancer"; "Mood management'

Gauteng Gambling Board - 2017 - Invited speaker - "Effective tools to manage mood"

Transnet - 2017 - Invited speaker - "Stress management principles"

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Nedbank - 2017, 2020 - Invited speaker - "Hygiene, not what you expect"; "Cancer"; "The health habits of highly effective people"

Pick and Pay national leader group - 2016 - Invited keynote speaker - "The health habits of highly effective people"

Sector Education and Training Authority (SETA) - 2016 - Invited speaker - "Mastering mental wellness"

Auditor General - 2016 - Invited speaker - "Weight management principles"

Nando's leadership - 2016 - Invited speaker - "Executive wellness principles"

The Council for the Built Environment (CBE) - 2016 - Invited speaker - "Cancer"

The Johannesburg Social Housing Company - 2016 - Invited speaker - "Cancer awareness for men"

SAB Miller - 2015 - Invited speaker - "Stress management principles"

Netsurit Exco - 2015 - Invited keynote speaker - "The health habits of highly effective people"

Department of Treasury - 2015 - Invited speaker - "The health habits of highly effective people"

SABC - 2015 - Invited speaker - "Managing tuberculosis risk"

Department of Planning, Monitoring and Evaluation (DPME) - 2015 - Invited speaker - "Managing disease over 40"; "Reproductive health"; "Fibroids"

SASOL - 2007 - 2015 - Invited Speaker - Several keynote addresses and official co-presenter of Work Life and Beyond Programme

First National Bank Premier Banking - 2015 - Invited speaker - "The health habits of highly effective people"

Transnet National Ports Authority - 2015 - Invited keynote speaker - "The health habits of highly effective people"

Smollan - 2015 - Invited speaker - "The health habits of highly effective people"

Distell - 2012, 2013, 2014 - Invited speaker - "The health habits of highly effective people"

Transnet - 2015 - Invited keynote speaker - "The health habits of highly effective people"

South African Revenue Service (SARS) Exco - 2015 - Invited Keynote Speaker - "The importance of holistic diagnostics for business leadership"

Cooperative Governance and Traditional Affairs - 2014 - Invited speaker - "Nutritional strategies in the management of HIV/AIDS"

Business Network International - 2014 - Invited Keynote Speaker - "Preventing burnout in business owners"

Group 5 Construction - 2014 - Invited speaker - "Prevention and management of burnout"

Bonitas House Call - SABC 2 - 2013 - Invited studio guest - "Nutritional supplement regulation in South Africa"; "Water safety in South Africa"

SANRAL - 2013 - Invited speaker - "Nutritional strategies in the management of HIV/AIDS"

CSIR - 2016 - Invited speaker - "Cancer"

Young Presidents Organisation - 2014 - Invited speaker - "Women's health"

Wits Health Consortium - 2014 - Invited speaker - "Nutritional supplementation in perspective"

ANN7 - Invited speaker - 2013 - Article - "Food-based toxins and how to avoid them"

Action Coach South Africa - 2013 - Invited speaker - "The health habits of highly effective people"

South African Society of Occupational Health Nursing Practitioners - 2012 - Invited keynote speaker - "Cancer in women"

SASOL Group Services - 2012 - Invited speaker - "The Brain Chemistry Optimisation Programme"

SASOL Group Exco - 2012 - Brain chemistry optimisation coach to Sasol group exco

Bankmed - 2012 - Invited keynote speaker - "Weight management principles"

Conference on Health, Wellness and Society - San Francisco, USA - 2011 - Academic presentation - "Reliability and validity of Resonance Raman spectroscopy as a non-invasive assessment tool of carotenoid status"

Ideas magazine - 2009 - Article - "Longevity and the link to food and lifestyle"

South African Directorate Food Control - 2009 - Invited speaker - "Comments on proposed legislation on the reduction of certain trans-fats in foodstuffs intended for sale in South Africa"

Woolworths - 2012 - Invited speaker - "Stress management principles"

Leef magazine - 2009 - Article - "Holistic healthcare in perspective"

Momentum - 2007 - 2009 - Invited speaker - Various presentations over a two-year period regarding wellness

University of Pretoria Occupational Therapy Department - 2005 - 2008 - Invited lecturer - "Nutritional management of attention deficit and hyperactivity disorder"; "Consideration of key wellness principles in patient care"

Radio Pulpit - 2008 and 2009 - Invited guest - Programme series on family wellness

Diabetes Focus Magazine - 2008 - Article - "Unique multi-ingredient food formulations in the management of diabetes"

Zuid Afrikaans Hospital Hand Surgeons - 2007 - Invited speaker - "Nutritional strategies to reduce inflammation in arthritis with varying etiology"

Association for Dietetics in South Africa (ADSA) - 2006 - Invited keynote speaker - "Fats and oils in South Africa"

University of the Witwatersrand Pharmacology Department - 2006 - Invited speaker - "Understanding the integration of nutritional supplementation in patient care"

The Food and Beverage Reporter Magazine - 2006 - Article - "The oil crisis in food production"

Your Family magazine - 2006 - Article - "Nutritional management of attention deficit"

SAFM Radio - 2006 - Invited guest - "The application of fats and oils in human wellness"

Radio Rippel - 2006 - Invited guest - "Core principles of wellness"

Radio 702 - 2005 - Invited guest - "Bottled water in South Africa"

South African Directorate Food Control - International Codex Alimentarius Committee for Food Labelling Health Claims Guideline document - 2004 - Co-author "Disease application of nutritional supplementation"

Channel 7 Radio - Namibia - 2004 - Invited studio guest - Eight broadcast series on nutrition

SABC 2 - 2003 - Invited studio guest - "Different approaches in patient care"

SADEC roundtable on HIV/AIDS in the workplace - 2002 - Invited speaker - "HIV/AIDS and nutrition"

Graduate Academy of South Africa - 2002 - Lecturer - One year course on "Sport Nutrition and Drugging" for final year sports science students

CPD ACCREDITED PRESENTATIONS

Product and dosing selection when treating with medicinal cannabis - Accredited 2021.

Cannabis as medicine - the science of effective and responsible prescription - Accredited 2020.

Metabolic Endotoxaemia and Chronic Disease - the Sporebiotic link. Accredited 2019.

Child Brain Development and Rehabilitation - Accredited 2018.

Probiotics and its application in practice - Accredited 2013.

EXPERIENCE AS WELLNESS COACH TO BUSINESS LEADERS

Consultations and wellness reports of South African business leadership: > 5900

Organisation leadership represented include:
- South African Reserve Bank
- South African Revenue Service
- Transnet

- Department of Science and Technology
- Auditor General
- Nedbank
- Standard Bank
- ABSA
- Ernst & Young
- SASOL
- TOTAL
- DHL
- Multichoice
- Life Hospital Group
- Barloworld
- Adcock
- SAPPI
- Vodacom