Sent: Tuesday, November 13, 2018, 11:23 AM
Subject: RE: Questions re: medical devices from CBC, Radio-Canada, the Star

Health Canada is committed to providing Canadians with timely access to safe, effective and high-quality medical devices. As part of the Department's mission to help Canadians maintain and improve their health, Health Canada evaluates and monitors the quality, effectiveness and safety of medical devices throughout their lifecycle.

Product life cycle refers to all stages in the pre- and post-market "life" of a health product, including:

- Investigational tests;
- Submission of product information to Health Canada for review and evaluation;
- Decision whether to authorize the sale of the product in Canada
- Public access to the product
- Post-market surveillance, inspection and investigation.

The Department's work to minimize the risk of health products falls into three main areas:

- Review and Evaluation process to assess products against safety, quality and effectiveness standards before allowing them onto the market in Canada, and to determine whether products are suitable to use in medical device investigational tests;
- Compliance and Enforcement activities to ensure that products and procedures comply with the Food and Drugs Act and the Medical Devices Regulations; and
- Monitoring and Tracking to identify and address any problems and to assess the effectiveness of products once they are on the market.

Health Canada assesses the risks of all health products and verifies their quality and effectiveness before they are allowed to be used by Canadians. Regulations defining the conditions for activities and materials associated with the testing, manufacture, preparation, preservation, packaging, administration, storage and sale of any health product are set out in the Food and Drugs Act, the Food and Drug Regulations and the Medical Devices Regulations.

If the Department concludes that the benefits of a medical device outweigh the risks of the device when used as intended, and that identified risks associated with the use of the device can be mitigated or managed, we provide the manufacturer with a medical device licence.

Health Canada continues to monitor the safety, effectiveness and quality of medicines and health products such as medical devices after they reach the marketplace. This provides new and up-to-date information that becomes available only after people start using health products under "real life" conditions. Once a product goes onto the market, we watch for signals that there may be a problem.

Signals may come from many sources, including:

- Published studies
- Reports from other levels of governments and international organizations

- Domestic and international complaint and incident reports
- Information received from manufacturers

A “signal” is an early indication that there may be an issue with a device. These signals go through a process of analysis to determine whether there is a safety issue that requires further action.

Some of the actions we may take to address safety issues for biotechnology-based health products on the market include:

- Continuing to monitor the product
- Reassessing the risk-to-benefit profile of the product
- Asking the manufacturer to make changes to the labelling (e.g., changes to directions for use, warnings about side-effects or interactions with other products)
- Issuing advisories or warnings for healthcare professionals, hospitals and consumers
- Removing the product from the marketplace (e.g., recalls).

For more information about the medical device regulatory system lifecycle, please consult: https://www.canada.ca/en/health-canada/services/science-research/emerging-technology/biotechnology/health-products/product-life-cycle-medicines-health-products-biotechnology.html

Q1. From 2008 to present, Health Canada has approved 93.7% of all the licence applications it received for Class III and IV devices. During this time period, FDA approvals of high-risk devices reportedly ranged from 59% to 98%. Why have Health Canada’s approval rates been at times so much higher than those of the U.S. device regulator?

The manufacturing and sale of medical devices is a global industry and Canadian approval rates are similar to those in the United States. In fact, many medical device companies will choose to launch in a large market such as the United States or Europe before coming to Canada, meaning that many of the devices Health Canada approves have already been approved by the FDA or EMA.

Health Canada licensed 92.5% of Class III applications and 95.2% of Class IV applications in 2015, the latest year for which statistics are available from the US FDA for comparison purposes. This compares with a 98% approval rating of applications for pre-market approval by the FDA in 2015.

Please note that the statistics for authorizations in Canada do not take into account applications withdrawn by manufacturers, recommendations made by Health Canada staff to modify the indications for use or undertake additional testing of submitted devices, or the withdrawal of specific models of devices during the review process. Medical device licence applications that are grossly deficient—for example, lacking the required evidence of quality systems—are not accepted for review and do not appear in the Canadian statistics. In

addition, companies applying for licensure of their medical devices work to ensure that they have data to support the granting of a medical device licence before submission of an application. All these factors could contribute to apparent high application approval rates in general.

Q2. Using the number of Health Canada employees involved in the review and approval of medical devices, we found that since 2013, each Health Canada evaluator has been responsible for reviewing applications for anywhere from 52 to 90 high-risk devices each year. This doesn't even consider work involved in reviewing Class I and II applications. How can Health Canada employees confidently evaluate high-risk devices for safety and efficacy if they are in charge of reviewing as many as 90 devices each year?

Not all applications related to Class III and IV devices require an evaluator to perform a scientific review. For example, some applications involve only administrative changes, and these do not require a scientific review.

In 2017, an individual evaluator at Health Canada conducted, on average, 25 scientific reviews for Class III and IV new and amendment applications (63 evaluators reviewing 1578 new and amendment Class III and IV applications requiring scientific review).

The number of reviews of medical devices done each year varies depending on the number of submissions received, and the quality and complexity of the applications.

Q3. There are many implantable devices that were approved with minimal or no clinical testing in humans. Some of these products were later subject to safety warnings and pulled from the market. For example, at the time TVT Secur System was approved in 2006, testing had only been done in animals and cadavers, according to published research. The Sprint Fidelis leads, which were ultimately withdrawn from the market and attributed to several deaths worldwide, was supported by animal and bench testing compared to an earlier predicate when it was approved in several countries in 2004, according to FDA documents. Why did Health Canada approve products that were later subject to safety concerns based on no new evidence from human clinical trials?

All Class III and IV medical device licence applications must be supported by evidence of clinical effectiveness. The Canadian regulatory requirements to demonstrate clinical effectiveness allow evidence in several forms, including clinical trials, clinical reviews, meta-analyses and real-world evidence reviews.

In general, Health Canada requires randomized controlled trials where a proof-of-principle study is used to demonstrate that a therapeutic product is safe and effective. This is true for novel high-risk medical devices. In many cases, however, applications for new medical device licences are based on an earlier generation of a similar device that was previously licensed in Canada. In these cases, evidence of safety and effectiveness can be demonstrated based on a comparison to currently licensed devices with similar designs and

performance characteristics.

With regard to the Sprint Fidelis lead, bench testing and animal studies provided evidence of safety and effectiveness of the device based on the state of knowledge at that time. The testing met internationally accepted standards for safety and effectiveness as outlined by the International Organization for Standardization (ISO). The failures associated with the Sprint Fidelis highlighted that the stresses applied to the leads were more severe than previously assumed.

It wasn't until there was a large number of Sprint Fidelis devices implanted, with follow-up for approximately three years, that an initial signal was observed that the rate of failure was higher than with other licensed devices. Based on this information, Health Canada, along with other global regulators, halted sales of the Sprint Fidelis.

Q4. Roughly how many of the devices approved each year are not supported by clinical testing in humans?

All applications for Class III and IV device licences are supported by evidence of clinical effectiveness. The Canadian regulatory requirements to demonstrate clinical effectiveness allow evidence in several forms, including clinical trials, clinical reviews, meta-analyses and real-world evidence reviews. Health Canada's database does not differentiate products based on the type of evidence submitted, so the department is not in a position to provide percentage estimates of the types of evidence submitted.

Q5. Surgeons and experts have told us that the lack of meaningful clinical testing for devices means that patients getting implanted with approved devices are essentially participating in "one big clinical trial." Do you have any comment?

Health Canada requires applications for all Class III and IV device licences to be supported by evidence of clinical effectiveness, including clinical data. Although these devices provide significant benefits to the health of Canadians, all drugs and medical devices come with some degree of risk. Health Canada licenses only those devices for which a risk-to-benefit profile is favourable. Residual risks are disclosed through labelling information, which is reviewed by Health Canada and is also to be disclosed to patients by their healthcare professionals.

In addition, Health Canada oversees the clinical testing of medical devices through Part 3 of the Medical Devices Regulations, which is referred to as Investigational Testing. These trials involve medical devices that are in earlier phases of development and are not yet licensed in Canada. They will provide additional clinical evidence to support a licence application for the device in Canada. Such clinical trials are authorized only after careful consideration of the risk-to-benefit ratio for patients and when the benefits outweigh the risks.

Q6. Based on Health Canada's own figures, more than 75% of the medical device bureau's budget comes from application fees paid by manufacturers. How can Health Canada make sure it remains independent when approving and monitoring devices if

it heavily relies on the industry financially?

As in many other countries, Health Canada's regulatory activities are funded through both public funds and revenues from user fees paid by industry. The fees support unbiased, independent reviews, and are paid even if a drug or medical device is not approved. Individual reviewers who make the decisions are not involved in collecting fees and have no way of knowing whether fees have been paid or not. Fees paid by industry in no way influence the independence of Health Canada's review.

The overriding principle for all Health Canada activities is the health and safety of Canadians. Health Canada's approval of medical devices is based solely on the evidence of a product's safety, quality and effectiveness, and is subject to public scrutiny.

Health Canada has been charging fees to industry since the mid-1990s to recover a portion of its costs for regulatory activities. Health Canada is in the process of updating its fees, which were last updated in 2011, to reflect current costs of service delivery and to ensure that the industry pays its share.

Q7. Clinical trial data, pre-market approval documents, post-approval studies, post-market surveillance studies, inspection reports and warning letters sent to manufacturers are publicly available in a number of developed countries, including countries in the European Union, Australia, Japan and the United States. Why isn't that data publicly available in Canada?

Health Canada is committed to openness and transparency and does, in fact, make information on medical devices public. Every regulator's practices differ somewhat, and the documents and other information they make available may differ as a result.

Health Canada conducts post-market approval safety reviews for medical devices when a potential safety issue is identified. Once Health Canada completes a safety review, it publishes a summary safety review, which highlights key findings. This summary safety review informs Canadians of what was found and what actions were taken by Health Canada if any. The full safety reviews are available from Health Canada by request. Results of post-approval studies conducted by manufacturers, if available, are included as part of Health Canada's safety reviews, along with other sources of information to help determine risk mitigation measures and other regulatory actions, if required.

Health Canada may inspect anyone who has a medical device establishment licence (MDEL) to ensure that they comply with the Food and Drugs Act (Act) and the Medical Devices Regulations (Regulations). These inspections support Health Canada's national compliance and enforcement program. Health Canada posts an Inspection Report Card on its website as part of its commitment to openness and transparency. The report card summarizes the findings of inspections of MDEL holders. Such report cards have been available on Health Canada's website since 2016. They include inspections dating back to January 2012.

You can see the inspection findings at: https://www.canada.ca/en/health-canada/services/inspecting-monitoring-drug-health-products/drug-health-product-inspections.html

Warning letters are a tool used by other regulators, such as the US FDA, to communicate significant violations of their regulatory requirements found during an inspection. The report card is our main transparency tool and serves as a comprehensive summary for disclosing inspection outcomes to Canadians and notes where compliance action has been taken. In some cases, compliance action has been prompted by Health Canada's compliance letters, which are comparable to the US FDA's warning letters.

At this time, Safety recalls and safety alerts are issued online for individual product licence suspensions that result from a finding that a medical device is unsafe. For product licence suspensions and cancellations that are not the result of a safety alert, patients and healthcare professionals can access Canada's Medical Device Active Licence Listing, which is an online database used to identify medical devices that are authorized for sale in Canada. The database is updated on a daily basis.

Health Canada is striving to increase transparency and is continuously making improvements to inform the public of the outcomes of inspections, including improving web-based searchability tools and access to information for Canadians.

Q8. Medical device incidents (i.e. adverse events) are routinely released through a public, searchable database in a number of developed countries, including Australia and the United States. Why isn't that data publicly available in Canada?

At present, Medical Device Problem Reports cannot be accessed through an online database similar to the Canada Vigilance Adverse Reaction Online Database, although the Department is examining options for online access to medical device reports.

In addition, through its Regulatory Transparency and Openness Framework, Health Canada is pursuing initiatives to increase the regulatory health and safety information that is available to Canadians. Currently, Canadians have access to Health Canada's Recalls and Safety Alerts Database.

Q9. How is Health Canada using its own database to monitor potential trends and risks? How much of that monitoring is done using foreign reports vs. domestic reports? At what frequency is Canadian data analyzed to find possibly problematic devices?

As per the Medical Devices Regulations, manufacturers and importers of medical devices are required to submit to Health Canada reports concerning any incident that comes to their attention whether inside or outside Canada and involving a device that is sold in Canada and that: (a) is related to a failure of the device or a deterioration in its effectiveness, or any inadequacy in its labelling or in the directions for use; and (b) has led to the death, or a serious deterioration in the state of health, of a patient, user or another person, or could do

so, were it to recur. The requirement to report an incident that occurs outside Canada does not apply unless the manufacturer has indicated, to a regulatory agency of the country in which the incident occurred, the manufacturer's intention to take corrective action, or unless the regulatory agency has required the manufacturer to take corrective action.

With respect to frequency, on a daily basis, Health Canada performs the entry and initial assessment of Canadian medical device incident reports in order to triage reports that may require further assessment or immediate regulatory action. When monitoring the risk-to-benefit profile of medical devices sold in Canada, Health Canada analyzes 100% of the Canadian data of activities to identify and analyze potential trends and risks. Information needed to understand the Canadian context is always prioritized, with information from international sources used to supplement as appropriate. In particular, as Canada makes up a small percentage of the global market, analysis related to identifying and assessing rare incidents benefits from the inclusion of international medical device incident data shared with Health Canada by other regulators. Health Canada has a systematic approach in place to identify changes to the risk-to-benefit profile of medical devices sold in Canada. This approach includes the regular review of information housed in the Medical Device System (MDS) database, such as mandatory and voluntary problem reports, as well as recalls.

Foreign information housed outside the MDS database is also included, as appropriate, in Health Canada's overall approach to monitoring potential safety risks.

This information includes:

- Scientific literature from international sources
- Safety communications issued by foreign regulatory agencies
- Foreign reports available through databases of the respective regulators
- Information-sharing reports received through the National Competent Authority Report (NCAR) program or other information-sharing agreements

Q10. Health Canada does not require manufacturers to provide their sales numbers. Data analysts and researchers we've spoken to argue that, this lack of a common denominator makes any statistics about medical device incidents (MDIs) and injuries all but useless. For example, 50 deaths among 100 insulin pump users is completely different from 50 deaths for every 100,000 insulin pump users. How does Health Canada account for that missing data when analyzing its adverse events data?

In fact, Health Canada does make use of sales information in its regulation of medical devices and obtains this information in a number of ways.

In addition to using sales data for post-market activities, Health Canada requires the marketing history of a device for the review of licence applications for Class III and IV medical devices. This includes sales figures in major international jurisdictions, and any reported recalls or other major post-approval events. The Department also receives information on the predicate devices when amendment applications are received. The Department considers that information in the context of the application. If concerns are brought to light related to the post-market experience of the device (whether in Canada or

elsewhere) or if the device is novel without a strong history, Health Canada may request additional information, further studies, and revisions to labelling, or it may refuse to issue a licence.

Health Canada considers information related to the sales of medical devices to be an important element in monitoring the safety and effectiveness profile once a device has been marketed. As part of Health Canada's post-market medical device safety reviews, the Department requests information from manufacturers, including sales numbers. The information is used to estimate Canadian and international incident rates, and to further guide risk mitigation measures and other regulatory decision-making.

Q11. Health Canada has said in the past that the medical device incidents are widely underreported in our country. We have spoken with physicians who say they don't report, don't have a clear sense of what qualifies as an MDI or find the reporting process too complex. We've also spoken to patients who say they were never informed that they could report. What is Health Canada doing to address this underreporting?

Medical device problem reporting is an essential element in Health Canada's assessments of medical devices. Manufacturers and importers are required to report medical device problems, and the Department encourages anyone purchasing, using or maintaining these products to voluntarily report problems, including physicians and other healthcare professionals. Health Canada also encourages consumers to report complaints involving medical devices to the Department, including the sale of unauthorized devices. Healthcare professionals and consumers are encouraged to report whatever information they may have, even if they are uncertain of all the specific details needed. Health Canada takes a risk-based approach in following up on voluntary complaints and will contact individuals who report incidents to gather more information, as needed. An online form is available to facilitate reporting of medical device incidents, or Canadians can call toll-free at 1-800-267-9675.

Underreporting of adverse reactions and medical device incidents is a challenge for all regulators. Health Canada is addressing this issue in a few ways.
First, Health Canada has proposed regulations under the Protecting Canadians from Unsafe Drugs Act (Vanessa's Law) that would amend the Food and Drug Regulations and the Medical Devices Regulations to require hospitals to provide reports of serious adverse drug reactions (ADRs) and medical device incidents (MDIs) directly to the Department. This is to improve the quantity of reports received and the quality of those reports to ensure sufficient information is submitted to inform decision-making. Mandatory reporting of MDIs by Canadian hospitals is expected to increase the volume of incident reports, which would address, in part, issues with underreporting; an increase in reporting would further inform Health Canada on where additional analysis or action is required.

Second, as part of the implementation of mandatory reporting for hospitals, Health Canada recognizes that increasing and improving the reporting of serious ADRs or MDIs will require outreach and education as well as meaningful feedback to address reporting barriers beyond

the reach of regulations. The Department is developing education and tools as well as information flow processes to support hospitals in meeting mandatory reporting requirements. Those tools will be used to raise awareness among healthcare providers not working in hospitals as well as Canadians in general about the benefit of reporting and how and when to submit reports.

Third, Health Canada continues to optimize its partnership with the Canadian Medical Devices Sentinel Network (CMDSNet). CMDSNet relies on a group of dedicated and trained representatives from more than 16 acute or community-based healthcare facilities within Canada to report high-quality data to Health Canada about adverse events associated with medical devices. This successful active surveillance program has been in existence since 2009. CMDSNet provides a complementary data source for post‑market evaluations. Having access to more information enables Health Canada to identify emerging safety issues in the area of medical devices and to improve the safe use of medical devices. More comprehensive incident data and earlier regulatory interventions also help to provide Canadians with timely new safety information to make informed decisions on the appropriate use of medical devices.

Q12. The number of medical device incidents reported as a death or an injury quadrupled in the past decade - rising from roughly 400 incidents in 2006 to roughly 1,660 incidents reported in 2017. Those figures include 1,358 reports of domestic deaths. How does Health Canada explain that rise?

In fact, while overall reporting of medical device incidents has increased, the proportion of those reports indicating death or injury has remained relatively constant.

Specifically, while the total number of reports to Health Canada has increased approximately fourfold between 2006 and 2017, the percentage of medical device incidents reported as a death has remained at approximately 1% between 2006 and 2017 (1.14% in 2017 and 1.11% in 2006). Similarly, the percentage of medical device incidents reported as an injury has also remained relatively stable (12.43% in 2017 vs. 11.33% in 2006). Year-to-year variations during this time period may be due to changes in methodology including data collection.

Percentage out of total cases received, by year			
Year	**DEATH**	**INJURY**	**TOTAL**
2006	1.11%	11.33%	12.44%
2007	1.00%	7.56%	8.56%
2008	1.31%	8.81%	10.12%
2009	1.86%	11.16%	13.02%
2010	1.31%	8.21%	9.52%
2011	1.16%	6.90%	8.06%
2012	1.46%	8.31%	9.77%

2013	1.37%	13.17%	14.54%
2014	1.27%	17.07%	18.34%
2015	1.11%	14.44%	15.55%
2016	1.19%	15.13%	16.31%
2017	1.14%	12.43%	13.57%

Per the Medical Device Regulations, manufacturers and importers must submit a report within 10 days of an incident leading to the death or serious deterioration in the state of health of a patient, user or another person, and within 30 days of an incident that has not led to the death or serious deterioration in the state of health of a patient, user or other person but could do so were it to recur. All 10-day reports (death and injury reports) are data entered, assessed and coded as a high priority, and are also flagged for review by Health Canada evaluators to determine their potential contribution to signal detection activities.

Health Canada considers the reporting of medical device incidents to be an important part of our surveillance program, with reports coming from manufacturers, healthcare professionals and patients. The increase in the number of medical device incidents received by Health Canada since 2006 may be due to a number of factors, including the enhancement of Health Canada's post-market surveillance and assessment program for medical devices; the continuing commitment to greater transparency and openness to further strengthening trust in our regulatory decisions by the public; the continuing efforts in outreach and engagement of some key stakeholders such as healthcare professional associations; and the establishment of the Canadian Medical Device Sentinel Network. The upcoming regulations on the mandatory reporting of medical device incidents by Canadian hospitals as part of Vanessa's Law are likely to further increase the number of incident reports for medical devices in Canada.

Q13. In Canada, reporting of adverse events is only required by industry. Our analysis of HC's MDI database shows manufacturers repeatedly flout mandatory 10- and 30-day timelines for those reports. Has Health Canada penalized manufacturers for those breaches? If so, please provide details on the numbers and natures of those actions. If not, why? Further, why would Canada not establish mandatory reporting of medical device adverse health incidents for physicians and other healthcare professionals whose observations could help inform the regulator, manufacturers, physicians and the public? In other words, why limit the available body of knowledge about potential medical device-related health risks?

Health Canada has been working on a robust Quality Control Framework to identify late final reports to industry's mandatory 10- and 30-day reports. There is also an initiative underway to replace the current database for medical device incidents. The updated database will include increased quality checkpoints. This will assist in the enforcement of sections 59 and 61 of the Medical Devices Regulations.

The proposed regulations under Vanessa's Law would amend the Food and Drug Regulations and the Medical Devices Regulations to require hospitals to provide reports of

serious adverse drug reactions and medical device incidents directly to Health Canada.

The mandatory reporting requirement would apply to the facility rather than individual healthcare professionals working in the hospital. It is the hospital that is responsible for determining clear internal roles and responsibilities for staff and the best operational approaches to meet the mandatory reporting obligations.

Mandatory reporting by manufacturers and importers is one aspect that Health Canada considers during an inspection of an MDEL holder. During the inspection, the inspector will review the reports of the company to determine whether the process for identifying and reporting problems is effective and whether the reports meet mandatory reporting criteria as required in the Medical Devices Regulations (MDR).
During an inspection, should the inspector determine that a company is not following the mandatory reporting requirements of the MDR, a deficiency observation would be assigned, and the company would be required to submit a corrective action plan to address this deficiency. This deficiency observation would be included in the company's Inspection Report Card posted on Health Canada's website. Should Health Canada be made aware of or suspect underreporting, it would follow up with the company and take compliance actions, as appropriate.

Q14. In 2010, Health Canada closed its Medical Devices Laboratory facility. At the time, former scientists who work in the labs warned the Health minister that the closure undermined the agency's capacity to monitor medical devices for defects or other problems. Today, those in charge of testing devices suspected to have caused health problems are the device makers themselves. Why does Health Canada rely on industry to exclusively test products suspect of having problems? Is there a concern that these companies have a conflict of interest?

The Food and Drugs Act and the Medical Devices Regulations place the onus on industry to provide safe and effective products, with Health Canada stepping in, if necessary, to have manufacturers correct problems as they arise.

Health Canada has never conducted independent testing of devices before their sale in Canada. If Health Canada becomes aware of problems with a device through concerns raised by practitioners, patients, researchers, etc., it investigates the problems, taking appropriate actions, including laboratory testing, as necessary.

A review of Health Canada's laboratory facilities determined that any necessary work could be more efficiently secured by contracting independent laboratory capacity. Today, Health Canada can and does seek independent laboratory insight to ensure public safety. This is more cost-effective and allows the Department to access state-of-the-art facilities across all areas, rather than maintain lab capacity related only to specific scientific domains.

Q15. Expert physicians in implants that we spoke to say a patient device registry for all types of implantable devices could better protect patients than the status quo, which leaves the onus on companies to contact patients via hospitals if there's a

problem. Why does Health Canada continue to oppose a registry (as it did at Senate hearing 27Mar/13 and in April 2018 in response to a petition about surgical mesh oversight)? Many experts told us the current alert system and post-market monitoring is ineffective, and a registry would be better. Do you have a comment?

Health Canada supports the development of patient registries for medical devices by key stakeholders, such as professional associations and manufacturers, or through provincial or territorial initiatives. In general, registries may help further epidemiological research and provide advances in areas of scientific knowledge related to medical device complications. However, the costs associated with the establishment and maintenance of registries are considerable. Registries may also have quality or methodological limitations with regard to the provision of valid and reliable safety and effectiveness information.

Health Canada consults with associations to obtain detailed information on adverse events. The Department uses additional strategies, including leveraging international registries, such as the International Collaboration of Breast Implant Registries (ICOBRA), to identify clinical outcomes and complications. Health Canada is committed to exploring additional post-market surveillance strategies and identifying additional approaches to filling gaps in evidence.

Q16. We spoke to Toronto Dr. Jagmish Butany, who said he tried to raise concerns about problems he was seeing with St. Jude's Silzone heart valves in the late 1990s. He said Health Canada was unresponsive to his concerns. The valves continued to be implanted in Canadians until a worldwide recall in January 2000. Do you have any comment on Dr. Butany's characterization that Health Canada was unresponsive and dismissive of his safety concerns?

Health Canada appreciates receiving information on any concerns or problems related to the use of medical devices in Canada. We receive, and respond to, hundreds of pieces of correspondence yearly and investigate information received as required. The Department cannot comment on discussions held between Dr. Butany and Health Canada back in the late 1990s.

Q17. Our reporting has found several cases where safety warnings or recalls have been issued in other countries but it takes days, weeks, months and even years for similar warnings to be made in Canada. For example, the FDA first issued a safety advisory on a transvaginal mesh in October 2008, warning of rare but serious complications. Health Canada's first warning, spurred in part by international reports, came in February 2010. On IVC filters, the FDA issued a warning in January 2010 about serious complications associated with these products. It followed that up in 2013 advising the filters be removed as soon as protection from a pulmonary embolism is no longer needed. Health Canada's first apparent safety notice about these same products came in July 2016. Why does Health Canada lag behind other regulators in notifying patients about potential problems?

Q18. More serious regulatory actions — such as suspending or removing products

from the market — have also been more swiftly and vigorously taken in other countries. For example, Zimmer's Durom Cup hip implants were suspended and ultimately discontinued in the US, but continued to be implanted here. Transvaginal meshes are the subject of suspensions or pauses in Australia and the UK but Health Canada has said the mesh's benefits continue to outweigh the risks. Why is it acceptable for Canadians to be getting devices that are not available in other countries because they've been deemed too risky?

Q19. We have found voluntary recalls or safety warnings initiated by a manufacturer are sometimes disseminated in the United States days or weeks before they're distributed here. There are several examples of this with Medtronic insulin pump warnings from 2009 to 2014. There is one case of a Canadian woman who received a pump a day after the US recall but the Canadian recall had not yet been announced. She alleges she was never told about the recall, which concerned a serious defect she alleges later led to her having a hypoglycemic event. Why are companies' recalls announced in Canada days or weeks after they're announced in the United States? Is it acceptable that Canadians are potentially being left in the dark?

Q20. We have spoken to patients who have different types of products that have been subject to recalls and market withdrawals -- including meshes, metal-on-metal hips and Essure -- who say they were not notified the products were off the market until months or even years later. Why aren't patients immediately notified if an implantable device they have has been subject to a recall or safety notice? Is Health Canada doing anything to fix this?

Medical devices available in Canada have to comply with the regulatory requirements of the Medical Devices Regulations. Health Canada takes very seriously the need to understand what impact product suspension or removal could have on impacted patients. The Department plays an active role in ensuring that Canadians have access to safe and effective drugs and medical devices. It is important to understand the medical needs and therapeutic options of current and future patients before taking regulatory action. The Department does not make decisions on a product lightly, as some products that may not be beneficial to some individuals are beneficial to others. The Department makes every effort to ensure that it makes a decision appropriate to the Canadian context based on all available sources of information, including Canadian incident reports received, the scientific literature, and input from healthcare practitioners.

During the lifecycle of a medical device, as it moves from its testing phase through to approval for market use, the manufacturer is required to maintain oversight of the device's performance in order to ensure it performs as expected and to maintain the safe use of the device. In addition, Health Canada has established regulations and operational processes for monitoring a device's ongoing performance during its lifecycle in order to further gather real-world evidence, strengthen the post-market safety of a medical device and ensure healthcare professionals and consumers are informed of safety concerns or changes to instructions for use related to the device.

Once Health Canada identifies a potential health or safety risk, it performs an assessment to understand the risk associated with the use of affected devices within the Canadian context. The availability, the use of the medical device and the potential impact may differ in Canada compared to those in other countries. The Department makes every effort to ensure that the appropriate decision is made relative to the Canadian context based on all available sources of information, including Canadian incident reports received, the scientific literature, and input from healthcare practitioners and patients. Health Canada strives to provide information on health product risks to Canadians and to healthcare providers as soon as possible, once a health or safety risk has been identified and examined.

The risks of a health product should never be considered in isolation. Instead, the balance between possible risks and potential benefits needs to be taken into account. When Health Canada determines that the risks associated with a medical device under its current conditions of use are no longer acceptable, the Department takes regulatory actions, which can include, but are not limited to, disseminating a risk communication, updating device labelling, adding conditions to device licences, ensuring effective product recall strategies, conducting product safety reviews, or suspending a product licence. Through increased collaborations and better use of information related to medical devices in Canada, Health Canada strives to develop strategies to increase the efficiency with which health and safety risks are identified, assessed and communicated in Canada.

Recalls exist in regulation as one of the means to manage a product's risk once on the market. A recall is any action taken by a manufacturer, importer or distributor of a medical device to recall or correct the device, or to notify its owners and users of its defectiveness or potential defectiveness, after becoming aware that the device:

a) may be hazardous to health;

b) may fail to conform to any claim made by the manufacturer or importer relating to its effectiveness, benefits, performance characteristics or safety; or

c) may not meet the requirements of the Act or these Regulations.

A recall may include:

1. The removal of the medical device from the market and its consignees;
2. An on-site correction of the medical device;
3. An advisory concerning a problem or potential problem with instructions to work around the problem until an on-site correction can be implemented;
4. The supply of revised labelling related to corrective action;
5. A change or clarification in the Instructions for Use;
6. The supply of instructions to stop using the medical device and to destroy remaining units in stock.

The recalling company has primary responsibility for notifying the public in the interest of protecting the health and safety of Canadians and are required to report recall actions to Health Canada. Health Canada monitors a company's recall compliance and will follow up with companies to monitor the effectiveness of higher-risk recalls. Health Canada takes appropriate regulatory actions when there is a suspected non-compliance in recall reporting.

In addition, some situations could result in Health Canada's issuing a public notification in a further attempt to reach patients and consumers.

More information on medical device recalls can be found here: https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/problem-reporting/medical-devices-recall-guide-0054.html#a9

Foreign regulatory jurisdictions, such as the US FDA, approach medical device recalls in a similar way. However, there are differences between the US FDA and Health Canada recall requirements. It is the responsibility of every company, in the markets they serve, to understand and tailor their recall strategy according to the requirements of each jurisdiction, which vary and may contribute to the difference in the timeline for the notification of a recall or the proposed mitigation strategy. Factors that could lead to variances in the need for and timing of a recall could include:

- Whether recalls in another jurisdiction, such as in the US, apply in the Canadian market as there may be different conditions of use of the device within the healthcare system
- Variability of distribution channels for the devices
- Impact of a recall on the healthcare system, including potential shortages
- Whether recalls in another jurisdiction, such as in the US, apply in the Canadian market as there may be different medical device lots, batches or models affected.

Under the Protecting Canadians from Unsafe Drugs Act (Vanessa's Law), a number of post-market initiatives are being undertaken to strengthen the safe use of medical devices once they are on the market. For example, the Food and Drugs Act has been revised to provide Health Canada with the powers to order a mandatory recall in order to more rapidly address unsafe health products when needed. Furthermore, Health Canada will be strengthening recall reporting by further defining reporting requirements in regulations, including timelines, and requiring manufacturers and importers to submit risk assessments earlier in the notification process. This initiative is targeted for consultations in spring 2019.

More information is available here: https://www.canada.ca/en/health-canada/corporate/about-health-canada/legislation-guidelines/acts-regulations/forward-regulatory-plan/2016-2018/regulatory-initiative-regulations-amending-food-drug-regulations-medical-devices-regulations-recall-therapeutic-products.html

Q21. Your director general in 2013 acknowledged that Health Canada still hadn't assessed the efficacy of your 'risk communications' as called for by auditor in 2011. What improvements if any have been made since then?

Working with outside consultant expertise, Health Canada has developed a standardized methodology to evaluate the effectiveness of health product risk communications and made changes to improve the reach, clarity, impact and timeliness of its communications products. Health Canada has also streamlined its processes, modernized its tools and renewed its focus on using plain language to enhance consumer uptake and increase engagement of

stakeholders (e.g., healthcare professional groups and associations). This helps Health Canada to craft messaging and enhance the dissemination of risk communications.

Health Canada is modernizing information dissemination by expanding its use of social media tools such as Twitter as well as mobile applications (e.g., Government of Canada Recalls and Safety Alerts Mobile Application) to complement traditional communication activities. These technologies allow the Department to reach more Canadians quickly and efficiently and to leverage partner and stakeholder networks to promote important health and safety information. Health Canada continues to explore new and innovative ways to help evaluate and improve the effectiveness of risk communications, such as artificial intelligence, to better understand the level of engagement with healthcare professionals and their information needs and preferences.

Health Canada is also undertaking an external evaluation of its current methods for reaching different target audiences with an eye towards continued improvement in our communications and knowledge translation to stakeholders. The results of that evaluation will inform a work plan for improvement in the coming year.

Health Canada continues to send email notifications directly to 28,500 subscribers through its MedEffect e-Notice system. As a reminder to healthcare professionals, Health Canada also publishes a monthly recap in the Health Product InfoWatch of all recent risk communications.

Q22. Under Health Canada's current inspection system, the regulator only physically inspects facilities that have a device establishment licence -- often the Canadian headquarters for larger device manufacturers. These inspections have been described as administrative in nature. Inspections of the Canadian facilities that manufacture high-risk devices are done by accredited, private companies hired by the manufacturers themselves. The results of these audits are then given to the regulator. Why does Health Canada do the administrative MDEL inspections while leaving the physical inspections of facilities where high-risk devices are made to private companies?

When the Medical Device Regulations were brought into force in 1998, the quality standard, ISO 13485, was a requirement to obtain a medical device licence. At the time, Health Canada did not have a medical device inspection program, and so the Department decided to use a third-party auditor system to meet this requirement. Subsequent to that decision, Health Canada created a medical device inspection program to oversee the post-market aspects of the MDR, in order to oversee importers, distributors and Class I manufacturers, all of whom were not captured under the third-party auditing system.

MDEL inspections are not an administrative process. Health Canada may inspect anyone who has a medical device establishment licence to ensure that they comply with the Food and Drugs Act (Act) and the Medical Devices Regulations (Regulations). These inspections support Health Canada's national compliance and enforcement program. Health Canada inspections of companies in Canada are conducted on location and include manufacturers of

Class I devices and importers and distributors of Class I-IV medical devices. Inspectors check for compliance with regulatory requirements for complaint handling, labelling, recall effectiveness, and device licensing to ensure that products are safe and that appropriate oversight is taken to ensure the integrity of the supply chain in Canada. The Medical Device Program has a comprehensive licensing and inspection program to ensure that each aspect of the product lifecycle and distribution chain is accounted for and strengthens the overall safe use of medical devices by Canadians.

It is important to note that Section 23 of the Act gives inspectors the power to examine and take action against anything that is not compliant with the Act and Regulations. Inspectors decide on the course of action to take based on risks, deviations from the Act and Regulations, deficiencies or failures that could impact health and safety.

This two-system design of medical device establishment inspections, including MDEL inspections by Health Canada inspectors and third-party auditors, provides effective oversight of both manufacturing practices and quality of high-risk products, as well as important controls for establishments conducting complaint handling or recalls.

Note that the third-party auditing system for higher-risk products facilitates market access to medical devices for patients in Canada. The new Medical Device Single Audit Program (coming into force January 1, 2019) is a single audit system that allows medical device manufacturers to rely on a single recognized audit to satisfy the pre-market licensing requirements for multiple countries and facilitates timely access to new and innovative technologies. It is cost-effective for both the regulators and the manufacturers to leverage the existing system and practices of third-party conformity assessment rather than to have regulators independently inspect facilities multiple times, as manufacturing facilities already undergo third-party audits (inspections) on an annual basis for other regulatory jurisdictions (e.g., Europe). Having multiple regulators accepting the same third-party audits under the Medical Device Single Audit Program (MDSAP) will create efficiencies.

The third-party auditors are companies subjected to an accreditation process and recognized by Health Canada under section 32.1 of the MDRs as having sufficient training, experience and technical knowledge in the design and manufacture of medical devices and implementation of quality management systems. For more information, please consult this web link. These registrars are recognized by Health Canada.

Globally, regulators such as Health Canada, the US FDA, Brazil's ANVISA, the Australian TGA and Japan's Ministry of Labour Health and Welfare and Pharmaceutical and Medical Devices Agency are increasingly harmonizing and cooperating on manufacturing inspections through the joint recognition of third-party conformity assessment bodies such as MDSAP for the routine inspection of manufacturing facilities. This approach is beneficial as it produces more frequent and consistent inspections of manufacturing facilities.

Q23. Relying on the inspection results of private companies paid by the manufacturers' they're inspecting raises the concern that the findings included in these reports are favourable to the company footing the bill. What's your response to

these concerns?

The system of third-party conformity assessment used by Health Canada (MDSAP) operates under strict and specific requirements related to impartiality and objectivity, and all conclusions and decisions must be supported by documented objective evidence that is available to regulators.

More specifically, auditing organizations, their personnel and their auditors must meet explicit criteria regarding objectivity and impartiality and are required to adhere to a code of conduct, as well as to disclose any potential or apparent conflicts of interest. The regulators participating in MDSAP verify adherence to these requirements on an annual basis as part of the recognition of these third-party auditing organizations, in accordance with international standards and program requirements.

In addition, auditors are not permitted to offer consulting services or advice to manufacturers they audit (a cooling-off period exists) thus eliminating an additional risk of conflict of interest.

Certification agreements between auditing organizations and manufacturers make no guarantees (implied or explicit) about positive outcomes, and auditing organizations generally include language in their certification agreements that clearly places the responsibility for conformity on the manufacturer, and absolves the audit team and the auditing organization from negative outcomes of the auditing/inspection process.

The system also has built-in safeguards to the effect that all audit results have to be independently reviewed by a second person not involved in the audit to ensure that technical requirements are met and that objective evidence is sufficient to support the conclusions before the results are finalized.

Audit reports and results are also subject to review by regulators.

Although Health Canada routinely relies on private third-party inspections, Health Canada inspectors have the authority to inspect manufacturers under Section 23 of the Food and Drugs Act, including those audited by third parties under the MDSAP program. Should a risk be identified, Health Canada would inspect these manufacturers to ensure compliance and minimize any potential risk to the health and safety of Canadians.

Based on the structural safeguards built into the system, Health Canada is of the view that the advantages of a third-party certification system such as MDSAP outweigh the potential risk introduced by having manufacturers pay for audits/inspections to meet regulatory requirements in any jurisdiction.

Q24. Unlike MDEL inspections, Health Canada does not disclose the results of these inspections done by accredited auditors. Why aren't these online? Do you plan on making them available?

The results of audits performed by registrars recognized by the Health Minister (e.g., MDSAP Auditing Organizations) are not made public because they contain extensive confidential business information. Making such information public would breach Health Canada's obligations to protect such third-party information in its possession.

While manufacturers are required to sign an agreement with their auditing organization allowing the release of the results of audits to regulators, these agreements do not cover any eventual public release of information. We are routinely seeking ways to enhance transparency and to continue to review our practices in the interest of providing more information to Canadians.