EXHIBIT C

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Charles Seife, Professor
ARTHUR L. CARTER JOURNALISM INSTITUTE

Catherine Teti
Deputy Agency Chief FOIA Officer
U.S. Department of Health and Human Services
Office of the Assistant Secretary for Public Affairs
Room 729H
200 Independence Avenue, S.W.
Washington, D.C. 20201

February 6, 2017

RE: Freedom of Information Act Appeal, Reference Number 2016-10322

Dear Ms. Teti:

I am Charles Seife, Professor of Journalism at New York University, and I regularly report on issues concerning math and science, including issues related to public health. I write to appeal the denial of expedited processing of my December 5, 2016 Freedom of Information Act ("FOIA") request for information related to the Food and Drug Administration's ("FDA") approval of the controversial drug eteplirsen, manufactured by Sarepta Therapeutics and marketed as Exondys 51. I also write to appeal the constructive denial of the substance of my FOIA request.

I. Background

By letter dated December 5, 2016, I requested from the Department of Health and Human Services ("HHS") and its component FDA, copies of select records related to the testing and approval of eteplirsen. The FOIA request enumerated six highly delineated and easily searchable categories of records and argued that expedited processing was appropriate under 5 U.S.C. § 552(a)(6)(E). (A true and correct copy is annexed as Exhibit A without the request's several-hundred pages of supporting documentation.)

On December 20, 2016, my attorney contacted the FDA and spoke with the specialist assigned to my case, Ms. Adeyemo, who was unaware that I had requested expedited processing of these records. She also stated that my FOIA request had been placed in the "complex queue" and informed me that an acknowledgment letter had been mailed on December 14, 2015. I did not receive a hard copy until January.

On December 21, 2016, I called the FDA and asked about the status of my request. I was told by Ms. Adeyemo that she would have a supervisor call me back. The supervisor, Ms. Simpson, confirmed that she had received the request some time ago, but had not yet ruled on whether to grant expedited processing. The same day, my attorney and I received by email a form letter denying my request for expedited processing and instructing me to file an appeal within 90 days of

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the receipt of the denial should I wish to contest this determination. (A true and correct copy is annexed as Exhibit B.) Also included in the email was a letter acknowledging my request. (A true and correct copy is annexed as Exhibit C.) To date, I have received none of the documents I have requested, nor have I been told that any of the information is exempt from disclosure under FOIA as required by law. *See* 45 C.F.R. § 5.33; 5 U.S.C. § 552(a)(8)(A).

II. Basis for Appeal

a. Expedited Processing

Pursuant to HHS regulation 45 C.F.R. § 5.61, I appeal the FDA's refusal to grant expedited processing. FOIA provides that expedited processing requests must be granted when a "compelling need" for the information exists. 5 U.S.C. § 552(a)(6)(E). A compelling need is demonstrated when the requestor is "a person primarily engaged in disseminating information" and there is an "urgency" to "inform the public concerning actual or alleged Federal Government activity." *Id.*

For all of the reasons stated in my initial FOIA request, I meet both criteria. I am an established science and math journalist who has written in numerous mainstream and scientific publications about the FDA. (True and correct copies of various articles are annexed as Exhibits D-G.) I intend to publish an article or series of articles about the testing and FDA approval of eteplirsen.

The matter is of urgent concern because it is a "breaking news story" and my request would cast light on potential flaws in the studies on which approval was based and on the improper outside influence during the approval process. Ex. A.[1] The approval of eteplirsen is also a matter of "urgent" concern because the drug costs over $300,000 per year—$500,000 per year for boys over 55 pounds[2]—and has yet to be prescribed broadly. To date, only about 250 individuals out of the thousands of boys affected by the type of Duchenne Muscular Dystrophy ("Duchenne") intended to be treated by the drug have applied for use, according to Sarepta CEO Ed Kaye.[3] Thus, the

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[1] The testing and approval of eteplirsen remains a "breaking news story." Between December 5, 2016, the date of my initial FOIA request, and February 3, 2017, there have been over 150 news articles on the subject. Lexis Advance Research, News Results for: Eteplirsen 12/05/2016-02/03/2017, Lexis Nexis (Feb. 3, 2017). This number excludes medical journals and and legal publications, which have also written extensively on its testing and approval.

[2] Kyle Dennis, *Sarepta May Have More Upside After Sales Data*, Seeking Alpha, Jan. 19, 2017, http://seekingalpha.com/article/4037880-sarepta-may-upside-sales-data (kilograms converted into pounds). (A true and correct copy is annexed as Exhibit H.)

[3] Ben Fidler, *CEO Kaye Details Insurance Battle As Sarepta Launches Duchenne Drug*, Xconomy, Jan. 10, 2017, http://www.xconomy.com/boston/2017/01/10/ceo-kaye-details-insurance-battle-as-sarepta-launches-duchenne-drug/. (A true and correct copy is annexed as Exhibit I.)

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release of the requested information could affect the number of future prescriptions and expenditure of money by patients and insurance companies. Ex. A.

It could also affect the personal and financial wellbeing of patients and their families, who, as the lead scientist of the reviewing committee put it, may opt not to purchase this "elegant placebo" if the drug is less effective than approval would suggest. *Id.* Indeed, patient wellbeing could be greatly affected by the information, as Dr. Kesselheim, a member of the Advisory Committee that voted against approval for eteplirsen, explains in his letter in support of my request for expedited processing. *See* Letter from Dr. Aaron Kesselheim, Assoc. Professor of Medicine at Harvard Medical Sch., to Catherine Teti, Deputy Agency Chief FOIA Officer at the U.S. Dep't of Health & Human Servs. (Jan. 31 2016) [hereinafter "Kesselheim Letter"]. (A true and correct copy is annexed as Exhibit J.) This information could influence whether doctors prescribe the drug, whether insurers cover the drug, and could also inform decisions of families who are mortgaging their homes or making other extreme personal and financial sacrifices to obtain these drugs—a matter of urgent importance to the public. *Id.*

The lowered evidentiary standards of approval for eteplirsen may also pave the way for flawed approval of other drugs. It is imperative that the problems stemming from the process come to light as quickly as possible to influence the interpretation of multiple provisions of the 21st Century Cures Act ("Cures Act"), which went into effect on January 1, 2017,[4] as well as parts of the Prescription User Drug Fee Act, which will be reauthorized in 2017. Ex. A. For example, patient testimonials represent the kind of evidence the FDA took into consideration for its approval of eteplirsen,[5] and are an important aspect of the Cures Act. *See, e.g.*, 21st Century Cures Act, Pub. L 114-255, §§ 3001-04. 130 Stat 1033 (2016). Yet while patient testimonials "can be of value in drug assessment," they do not meet the rigorous standards of blinded studies that account for the placebo effect.[6] Understanding how such evidence influenced key decision-makers within the FDA during the eteplirsen approval process would shed light on the potential abuses of these testimonials for other drugs. In addition, understanding patient testimonials in the context of eteplirsen would illuminate the potential for methodological flaws in subsequent studies and would reinforce the need to reject a broad reading of the Cures Act in forthcoming regulations.

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[4] Juliet Eilperin & Carolyn Y. Johnson, *Obama, Paying Tribute to Biden and Bipartisanship, Signs 21st Century Cures Act Tuesday*, Wash. Post, Dec. 13, 2016, https://www.washingtonpost.com/news/powerpost/wp/2016/12/13/obama-paying-tribute-to-biden-and-bipartisanship-signs-21st-century-cures-act-tuesday/?utm_term=.08cd8784e24d. (A true and correct copy is annexed as Exhibit K.)

[5] *See* David Dittman, *The FDA: Small-Cap Catalyst or Small-Cap Killer*, Wall Street Daily, Dec. 16, 2016, https://www.wallstreetdaily.com/2016/12/16/the-fda-small-cap-catalyst-or-small-cap-killer/. (A true and correct copy is annexed as Exhibit L.)

[6] Aaron Kesselheim & Jerry Avorn, *Approving a Problematic Muscular Dystrophy Drug: Implications for FDA Policy*, 316(22) JAMA Viewpoint 2357 (2016). (A true and correct copy is annexed as Exhibit M.)

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Since my initial request, the need for information related to the approval process for eteplirsen has only become more urgent, and delay in response "would compromise a significant recognized interest." *Bloomberg L.P. v. U.S. Food & Drug Admin.*, 500 F. Supp. 2d 371, 377 (S.D.N.Y. 2007) (quoting *Al-Fayed v. C.I.A.*, 254 F.3d 300, 310 (D.C. Cir. 2001)).

First, the review of eteplirsen more generally has become the prism through which the accelerated approval pathway is viewed, and has been cited by critics and proponents of the FDA as an example of why the process is either too fast and sacrifices sound science or too slow and stymies drug development. For example, members of the pharmaceutical industry complained vociferously that it took years to get eteplirsen approved, and these critics have promised to fight for even faster approval in light of the perceived gravity of Duchenne and similar diseases.[7] In contrast, others argue that the quick deadlines for Phase III trials removed altogether the need to demonstrate efficacy as a prerequisite for approval. Ex. A. Others argue that the FDA is functioning as it should and the approval process at issue here is indicative of that fact.[8] Understanding the standards applied to eteplirsen would provide insight into upcoming proposals propounded by the Trump Administration and regulations and guidance issued by the FDA under its new Commissioner—and this is especially true if the evidence reveals the drug is more effective than believed.[9] In addition, it is necessary to understand how the existing process functions to guarantee that, even absent legislative or regulatory changes, it is free from political meddling by members of Congress, patient groups, or outside advocates.

Second, the FDA has ordered Sarepta to complete a post-market randomized trial by May 2021 to "verify [sic] the clinical benefit of eteplirsen." According Dr. Kesselheim, "[b]arring a major unexpected safety problem, it is unlikely that the new study could provide sufficient evidence leading to removing eteplirsen from the market."[10] If made public, these records may force the FDA to require additional studies or to require methodological alterations to the May 2021 study.

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[7] Tony Corvo, *Insurer Unconvinced By Divided FDA's Approval of Muscular Dystrophy Drug*, The Heartland Inst., Dec. 26, 2017, https://www.heartland.org/news-opinion/news/insurer-unconvinced-by-divided-fdas-approval-of-muscular-dystrophy-drug. (A true and correct copy is annexed as Exhibit N.)

[8] Zachary Brennan, *Politicizing the FDA: What the Trump Win Means for New Pharma Regulations*, Reg. Aff. Prof. Soc'y, Jan. 19 2017, http://raps.org/Regulatory-Focus/News/2017/01/19/26644/Politicizing-the-FDA-What-the-Trump-Win-Means-for-New-Pharma-Regulations/. (A true and correct copy is annexed as Exhibit O.)

[9] *See* Review, *The FDA Empire Strikes Back*, Wall Street J., Dec. 23, 2016, at A14. (A true and correct copy is annexed as Exhibit P.)

[10] Kesselheim & Avorn, *supra* note 6.

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Third, new evidence about eteplirsen could influence the review process conducted by the European Medicines Agency ("EMA") and other international regulatory agencies. The EMA accepted Sarepta's filing on December 21, 2016, and the standard review period is 210 days.[11] Thus, if information pertinent to eteplirsen's FDA approval, safety, or efficacy emerges from my request, it could affect EMA reviewers' decision, *see* Kesselheim Letter, Ex. J, and this is particularly true as the EMA may take patient outcomes into account, not just the clinical trials.[12] As the parents and insurers of European children afflicted with Duchenne prepare to expend vast amounts of money on eteplirsen, anything that would further inform the approval decision is valuable. But if my request for expedited approval were denied, the chance of this influence between regulatory bodies considering the same difficult approval decision would vanish.

Finally, Sarepta's future as a company appears to depend almost entirely on the success of eteplirsen, and Sarepta's financial wellbeing was even a factor considered by Dr. Woodcock during the approval. Ex. A. Since the approval of eteplirsen, financial advisors and investors have picked Sarepta as a stock to watch in 2017,[13] making information concerning the studies upon which approval was based and the approval process of significant continuing news value.[14] For all these reasons, I appeal the denial of expedited processing for my request.

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[11] Richard Staines, *Sarepta Files Controversial Duchenne Drug in EU*, PharmaPhorum, Dec. 21, 2016, http://pharmaphorum.com/news/sarepta-files-controversial-duchenne-drug-eu/. (A true and correct copy is annexed as Exhibit Q.)

[12] Derrick Gingery, *Sarepta Eyes Patient Outcomes To Boost Exondys 51's European Review*, Pink Sheet, Jan. 28, 2017, https://pink.pharmamedtechbi.com/PS119810/Sarepta-Eyes-Patient-Outcomes-To-Boost-Exondys-51s-European-Review. (A true and correct copy is annexed as Exhibit R.)

[13] Adam Feuestein, *Sarepta Opens Up About Duchenne Drug Launch, Allays Investors' Worst Fears*, The Street.com, Jan. 10, 2017, https://www.thestreet.com/story/13948568/2/sarepta-opens-up-about-duchenne-drug-launch-allays-investors-worst-fears.html. (A true and correct copy is annexed as Exhibit S.); Lee Jackson, *Baird Has 4 Red-Hot Biotechs to Buy for 2017 With Huge Upside Potential*, 24/7 Wall Street, Jan. 19, 2017, http://247wallst.com/healthcare-business/2017/01/19/baird-has-4-red-hot-biotechs-to-buy-for-2017-with-huge-upside-potential/. (A true and correct copy is annexed as Exhibit T.)

[14] Indeed, in the wake of news that one of the pivotal trials for eteplirsen was flawed, the stock dropped precipitously and shareholder suits followed. *See, e.g.*, Pl. Br. 44, *Cobran v. Sarepta Therapeutics*, Nos. 15-2135 & 16-1658 (1st Cir. Oct. 14, 2016), E.C.F. No. 37 (asserting that Sarepta defrauded its investors by misrepresenting trial results). (A true and correct copy is annexed as Exhibit U.)

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b. Constructive Denial

I also appeal your agency's constructive denial of my initial request. Under FOIA, a decision to grant or deny a request must be issued within 20 days. *See* 5 U.S.C. § 552(a)(6)(A)(i). In addition, HHS regulations provide that if the agency cannot meet this time limit, it will notify the requestor within twenty days of the "unusual circumstances" preventing it from doing so and when the requester can expect processing to be complete. 45 C.F.R. § 5.24. Under the 2016 FOIA amendments, an agency can withhold information only if "the agency reasonably foresees that disclosure would harm an interest protected by an exemption" or "disclosure is prohibited by law." 5 U.S.C. § 552(a)(8)(A). Any claim of exemption must be supported with "specificity and [in] detail." *Senate of the Commonwealth of Puerto Rico on Behalf of Judiciary Comm. v. U.S. Dep't of Justice*, 823 F.2d 574, 585 (D.C. Cir. 1987) (citing *Parke, Davis & Co. v. Califano,* 623 F.2d 1, 6 (6th Cir.1980) (alteration in original).

To date, FDA has not provided an answer to the substance of my FOIA request or a letter detailing "unusual circusmtances," but only has acknowledged its receipt and stating that the request has been placed in the "complex queue." FDA's failure to produce the requested records or to cite specific exemptions to justify its refusal to disclose the records is improper. FOIA provides that the requestor "shall be deemed to have exhausted his administrative remedies . . . if the agency fails to comply with the applicable time limit provisions." 5 U.S.C. § 552(6)(C)(i). FDA's failure to produce the records or claim any exemption is thus a "constructive denial" of my request. I hereby appeal FDA's constructive denial of my request.

III. Request for Relief

For the foregoing reasons, I am entitled to expedited review. The FDA has failed to meet its legal obligation to disclose the records and information requested. I respectfully request immediate disclosure of the records requested.

This FOIA request seeks information concerning the business of the government agencies responsible for this nation's public health and safety; the information requested concerns the practices behind government analysis and approval of new drugs that may affect millions of Americans; and the disclosure of this information will shed light on important government activity and allow public oversight. The disclosures requested here would therefore further "the basic purpose of the Freedom of Information Act to open agency action to the light of public scrutiny," and no proper basis exists under FOIA to withhold them. *Dep't of Air Force v. Rose*, 425 U.S. 352, 372 (1976) (quotations omitted); *see also id.* at 381 (emphasizing "the policies underlying the Freedom of Information Act, to open public business to public view").

In compliance with 21 C.F.R. § 20.44(d), I certify that the above information pertaining to my request for expedited processing is true and correct to the best of my knowledge and belief. I trust that I will receive your decision within 20 business days as required by 45 C.F.R. § 5.63 and 5 U.S.C § 552(a)(6)(A)(ii). Thank you for your prompt attention to this matter.

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Sincerely,

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