

NOTES

REGULATING RARE DISEASE: SAFELY FACILITATING ACCESS TO ORPHAN DRUGS

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While approximately one in ten Americans suffers from a rare disease, only 5 percent of rare diseases have a U.S. Food and Drug Administration (FDA) approved treatment. Congressional and regulatory efforts to stimulate the development of rare-disease treatments, while laudable, have not resolved the fundamental issues surrounding rare-disease treatment development. Indeed, small patient populations, incomplete scientific understanding of rare diseases, and high development costs continually limit the availability of rare-disease treatments.

To illustrate the struggle of developing and approving safe rare-disease treatments, this Note begins by discussing the approval of Eteplirsen, the first drug approved for treating a rare disease called Duchenne muscular dystrophy. After exploring the current drug regulation system and how this impacts the availability of rare-disease treatments, this Note examines the 21st Century Cures Act's patient experience data provisions and the currently pending Trickett Wendler Right to Try Act. Ultimately, the unmet therapeutic needs of rare-disease patients can be met while protecting patient safety. This Note reasons that, if carefully implemented, the 21st Century Cures Act and the Trickett Wendler Right to Try Act could work in tandem to safely facilitate patient access to rare-disease treatments.

INTRODUCTION.....	1890
I. HOW PATIENTS ACCESS DRUGS: DRUG APPROVAL, DEVELOPING DRUGS THAT MEET PATIENT NEEDS, AND EXPANDED ACCESS TO INVESTIGATIONAL THERAPIES.....	1894
A. <i>The Drug-Approval Process</i>	1894
B. <i>Congressional and Regulatory Efforts to Develop Rare- Disease Treatments</i>	1896

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1. Incentivizing the Development of Rare-Disease Treatments.....	1897
2. The FDA and Patient Engagement.....	1899
C. <i>The FDA's Expanded Access Program: Accessing Investigational Drugs Outside of Clinical Trials</i>	1900
II. UNCONTROLLED PATIENT EXPERIENCE DATA AND UNFETTERED INVESTIGATIONAL DRUG ACCESS: ARE WE HURTING PATIENTS OR HELPING THEM?.....	1904
A. <i>The 21st Century Cures Act and Patient Experience Data</i>	1904
B. <i>The Trickett Wendler Right to Try Act: Accessing Investigational Drugs Without FDA Approval</i>	1909
III. BALANCING PATIENT PARTICIPATION WITH SAFETY: SUGGESTIONS FOR IMPLEMENTING THE 21ST CENTURY CURES ACT AND AMENDING THE TRICKETT WENDLER RIGHT TO TRY ACT.....	1912
A. <i>The FDA Should Control the Solicitation and Submission of Patient Experience Data to Ensure the Process Remains Objective</i>	1913
B. <i>The House of Representatives Should Amend the Trickett Wendler Right to Try Act to Facilitate Access to Investigational Drugs and Maintain Patient Safety</i>	1916
CONCLUSION	1920

INTRODUCTION

“I wish my son had cancer,” Alex Smith admitted following his son’s diagnosis with Duchenne muscular dystrophy (DMD).¹ DMD is a rare,² fatal, and until recently, largely untreatable³ genetic disorder that causes gradual muscular degeneration.⁴ Most DMD sufferers lose the ability to walk by their teens, can no longer eat or use the bathroom independently by their

1. Alex Smith, *‘I Wish My Son Had Cancer’: How Shock Tactics Raised My Charity’s Profile*, GUARDIAN (Aug. 11, 2014, 3:00 AM), <https://www.theguardian.com/voluntary-sector-network/2014/aug/11/wish-my-son-had-cancer-shock-tactics-charity-advertising-campaign> [<https://perma.cc/JTK6-UC75>].

2. In the United States, a rare disease is defined as a disease affecting fewer than 200,000 people nationwide. See 21 U.S.C. § 360bb(a)(2) (2012); see also Benjamin Elgin et al., *When the Patient Is a Gold Mine: The Trouble with Rare-Disease Drugs*, BLOOMBERG (May 24, 2017, 4:00 AM), <https://www.bloomberg.com/news/features/2017-05-24/when-the-patient-is-a-gold-mine-the-trouble-with-rare-disease-drugs> [<https://perma.cc/3PZ4-9MJ8>]. However, calling DMD a rare disease is somewhat of a misnomer, considering that DMD is one of the “biggest genetic killers of boys worldwide.” Marcia Kaye, *The Gene Editors*, U. TORONTO MAG., Summer 2016, at 35. Indeed, there are approximately 15,000 boys living with DMD in the United States and 300,000 worldwide. *What Is Duchenne?*, CUREDUCHENNE, <https://www.cureduchenne.org/about/what-is-duchenne/> [<https://perma.cc/CG2R-E6V3>] (last visited Feb. 14, 2018).

3. See Nick Taussig, *Our Beautiful Sons Could Die Before Us*, GUARDIAN (Aug. 16, 2014, 12:59 AM), <https://www.theguardian.com/lifeandstyle/2014/aug/16/our-beautiful-sons-could-die-before-us> [<https://perma.cc/H248-ES3G>].

4. See *What Is Duchenne?*, *supra* note 2.

twenties, and die by their thirties.⁵ Alex explained, “I felt a cancer diagnosis would have more options . . . a chance to try something—a chance that those with DMD . . . don’t have.”⁶ Nick Taussig felt similarly helpless after learning that his son had DMD and struggled to explain the severity of the diagnosis to friends and family:

“What’s the treatment?” There is no treatment. “What about steroids?” They do little more than postpone the inevitable by a few years. “Might there be a scientific breakthrough?” Possibly, though we cannot count on it. “How are you?” We’re OK, when what we really wanted to say was, we’re drowning.⁷

A DMD breakthrough occurred in September 2016: the U.S. Food and Drug Administration (FDA) approved Eteplirsen, the first drug⁸ for treating DMD.⁹ Using data from an initial clinical study involving just twelve subjects and lacking a placebo control, drug sponsor¹⁰ Sarepta Therapeutics requested that the FDA grant Eteplirsen accelerated approval.¹¹ While this data showed that Eteplirsen only slightly increased dystrophin¹² production,¹³ several trial participants insisted that they had grown stronger since taking Eteplirsen.¹⁴

5. Lisa M. Jarvis, *After Eteplirsen: Duchenne Stakeholders Contemplate What Comes Next*, CHEMICAL & ENGINEERING NEWS (Nov. 14, 2016), <http://cen.acs.org/articles/94/i45/etepirsen-Duchenne-stakeholders-contemplate-comes.html> [<https://perma.cc/7BB2-GZC4>].

6. Smith, *supra* note 1.

7. Taussig, *supra* note 3.

8. This Note uses the term “drug” to refer to prescription medications only and to encompass both drugs and biological products.

9. See Jarvis, *supra* note 5; Sy Mukherjee, *The FDA Just Made Its Most Controversial Drug Approval of the Year*, FORTUNE (Sept. 19, 2016), <http://fortune.com/2016/09/19/fda-drug-approval-exondys-51/> [<https://perma.cc/2PV4-PRJP>].

10. Typically, a drug’s sponsor is its manufacturer or potential marketer. See *Investigational New Drug (IND) Application*, FDA (Oct. 5, 2017), <https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm> [<https://perma.cc/Z4VK-QFP2>].

11. See Jarvis, *supra* note 5. The FDA created the Accelerated Approval Program to hasten approval of drugs designed to treat serious conditions and that fulfill unmet medical needs. *Accelerated Approval Program*, FDA (Mar. 10, 2016), <https://www.fda.gov/Drugs/ResourcesForYou/HealthProfessionals/ucm313768.htm> [<https://perma.cc/6QG7-AWQR>]; see also 21 C.F.R. § 314.500 (2017). A drug must have demonstrated clinical benefit to enter the U.S. market; however, a drug granted accelerated approval can demonstrate clinical benefit using a “surrogate endpoint”—a marker (in the Eteplirsen case, dystrophin levels) that *predicts* clinical benefit—rather than traditionally required functional endpoints (such as life span) which *measure* clinical benefit, thereby shortening the length of clinical trials. See 21 C.F.R. § 314.500; Jarvis, *supra* note 5.

12. Dystrophin is a protein that “keeps muscle cells intact.” *Duchenne Muscular Dystrophy*, MUSCULAR DYSTROPHY ASS’N, <https://www.mda.org/disease/duchenne-muscular-dystrophy> [<https://perma.cc/W8V5-TZBJ>] (last visited Feb. 14, 2018).

13. This data showed that, on average, Eteplirsen increased dystrophin levels by just 0.9 percent of the level seen in someone without DMD. Jarvis, *supra* note 5.

14. See *id.*

An FDA advisory committee reviewed the initial study data and listened to the testimonies of DMD patients, their families, and their doctors.¹⁵ Those testifying included a fifteen-year-old patient who declared that he would “beat this bloody disease,” while pleading with the FDA to not “let [him] die early”; a patient’s mother, who declared that she “[was] not just [a] desperate parent[]” and claimed to “have witnessed the efficacy of [Eteplirsen]”; and a physician who requested the “option to prescribe Eteplirsen,” because “[w]e cannot withhold a safe drug from even one boy who may benefit.”¹⁶ The committee nonetheless concluded that Sarepta had not provided “substantial evidence” from “adequate and well-controlled” studies that Eteplirsen was safe and effective for treating DMD and therefore recommended that the FDA not approve the drug.¹⁷

The FDA, however, disregarded the advice of the advisory committee and conditionally approved Eteplirsen.¹⁸ Announcing Eteplirsen’s approval, Center for Drug Evaluation and Research (CDER) Director Janet Woodcock noted, “In rare diseases, new drug development is especially challenging due to the small numbers of people affected by each disease and the lack of medical understanding of many disorders.”¹⁹ While Eteplirsen’s approval overjoyed the DMD community,²⁰ some critics argued that there was no empirical evidence that Eteplirsen safely and effectively treated DMD, and they pointed to the lobbying campaign undertaken by DMD advocates as having biased the approval decision.²¹

This Note begins with the Eteplirsen story because it illustrates the difficulty of drug regulation in the context of rare diseases. As recognized by the FDA in approving Eteplirsen, rare-disease patients have limited therapeutic options.²² And, as illustrated by the comments of Alex Smith and Nick Taussig, the limited availability of medical treatments causes rare-disease patients and their loved ones much distress.²³ However, with tragedies like thalidomide²⁴ in the not-too-distant past, it is troubling that any

15. See Kyle T. Edwards, *The Role of Patient Participation in Drug Approvals: Lessons from the Accelerated Approval of Eteplirsen*, 72 FOOD & DRUG L.J. 406, 407–08 (2017).

16. *Id.*

17. *Id.* at 408.

18. The approval was conditioned on Sarepta conducting additional clinical testing to demonstrate Eteplirsen’s safety and efficacy in treating DMD. See Mukherjee, *supra* note 9.

19. Press Release, FDA, FDA Grants Accelerated Approval to First Drug for Duchenne Muscular Dystrophy (Sept. 19, 2016), <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm521263.htm> [<https://perma.cc/BTC8-Q2MU>].

20. See Muscular Dystrophy Ass’n, *Eteplirsen Approved in US for Treatment of Duchenne Muscular Dystrophy*, SCIENCE DAILY (Sept. 20, 2016), <https://www.sciencedaily.com/releases/2016/09/160920095640.htm> [<https://perma.cc/Q874-D5T7>].

21. See Mukherjee, *supra* note 9.

22. See Press Release, FDA, *supra* note 19; see also *infra* Part I.B.1.

23. See *supra* notes 1–7 and accompanying text.

24. The United States’ rigorous drug regulations are commonly understood as a reaction to the thalidomide tragedy of the late 1950s and early 1960s. See Margaret Hamburg, *50 Years After Thalidomide: Why Regulation Matters*, FDA VOICE (Feb. 7, 2012), <https://blogs.fda.gov/fdavoices/index.php/2012/02/50-years-after-thalidomide-why-regulation-matters/> [<https://perma.cc/DJ5L-5AP5>]. Outside of the United States, many

new drug could be approved using data from a twelve-person study that did not demonstrate significant clinical benefit,²⁵ as was Eteplirsen.

Two recent items of legislation may benefit rare-disease patients by allowing these patients to play a more active role in the drug regulation process.²⁶ First, section 3001 of the 21st Century Cures Act, passed by Congress in 2016,²⁷ permits the FDA to consider “patient experience data” in approving new drugs.²⁸ Second, in August 2017, the Senate passed the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 (“Trickett Wendler Right to Try Act”),²⁹ which, if made law, would make available—without FDA approval—investigational drugs³⁰ to any person with a “life-threatening disease or condition” who has exhausted available treatments and who cannot participate in any ongoing clinical trials.³¹

This Note considers the value of increased patient participation in the drug regulation process, particularly for those suffering from rare diseases such as DMD. Part I details the current landscape of drug approval and access, principally discussing the Food, Drug, and Cosmetic Act (FDCA), the Orphan Drug Act (ODA), the FDA’s patient engagement initiatives and its

doctors prescribed thalidomide to pregnant women suffering from morning sickness and insomnia, but the drug was later found to cause birth defects. *See id.*; *About Thalidomide: Thalidomide FAQs*, THALIDOMIDE SOC’Y, <http://www.thalidomidesociety.org/what-is-thalidomide/> [<https://perma.cc/52PB-JTZ4>] (last visited Feb. 14, 2018). Ultimately, over 24,000 thalidomide-affected babies were born and an additional 123,000 babies were miscarried or stillborn due to thalidomide consumption in pregnancy. *About Thalidomide: Thalidomide FAQs*, *supra*.

25. A drug demonstrates clinical benefit if it results in the “prolongation of survival or an improvement in symptoms.” FDA, GUIDANCE FOR INDUSTRY: CLINICAL TRIAL ENDPOINTS FOR THE APPROVAL OF CANCER DRUGS AND BIOLOGICS 2 (2007).

26. Patient participation in drug approvals is not a novel concept—in fact, in recent years, the FDA has launched several initiatives to include patients in the drug-approval and development processes. *See* Edwards, *supra* note 15, at 411–23; *see also infra* Part I.B.2.

27. *See* 21st Century Cures Act, Pub. L. No. 114-255, § 3001, 130 Stat. 1033, 1083–84 (2016) (codified at 21 U.S.C. § 360bbb-8c(b)).

28. 21 U.S.C. § 360bbb-8c(b) (Supp. IV 2016). The 21st Century Cures Act defines patient experience data as data intended to provide information about patient experience with a disease or condition, including a disease’s impact on a patient’s life and patient treatment preferences. *Id.*; *see also* 21st Century Cures Act—Provisions to Promote Drug Development, ROPES & GRAY (Dec. 13, 2016), <https://www.ropesgray.com/newsroom/alerts/2016/December/21st-Century-Cures-Act-Provisions-Relating-to-Promoting-Drug-Development.aspx> [<https://perma.cc/J3HA-XMZV>].

29. S. 204, 115th Cong. (2017). In February 2017, Representative Andy Biggs introduced House Bill 878, a companion bill to Senate Bill 204, in the House of Representatives, but the House has not yet passed this bill. *See* H.R. 878, 115th Cong. (2017); Sarah Karlin-Smith & Seung Min Kim, *Senate Approves ‘Right-to-Try’ Drug Bill*, POLITICO (Aug. 3, 2017, 6:45 PM), <http://www.politico.com/story/2017/08/03/senate-right-to-try-drug-bill-241293> [<https://perma.cc/QU8R-3QKX>]. This Note focuses on Senate Bill 204 because it has already passed one chamber of Congress.

30. Investigational drugs are drugs that the FDA has approved for human testing but has not yet approved to be marketed. *See Investigational New Drug (IND) Application*, *supra* note 10.

31. *See* S. 204 § 2(a); James M. Beck, *Federal Right to Try Legislation—Is It Any Better?*, DRUG & DEVICE L. BLOG (Sept. 5, 2017), <https://www.druganddevicelawblog.com/2017/09/federal-right-to-try-legislation-is-it-any-better.html> [<https://perma.cc/3BEJ-ZS9Z>].

“Expanded Access” program. Part II describes section 3001 of the 21st Century Cures Act, as well as the Trickett Wendler Right to Try Act, and analyzes how these laws diverge from traditional safety requirements of drug approval and access. Finally, Part III provides suggestions for implementing section 3001 of the 21st Century Cures Act and amending the Trickett Wendler Right to Try Act to help rare-disease patients access safe and effective medical treatments.

Specifically, this Note argues that in implementing section 3001 of the 21st Century Cures Act, the FDA should establish a review system that scrutinizes both the source and substance of patient experience data submissions. This will ensure that subjective data does not unfairly bias the otherwise objective drug-approval process. Additionally, this Note proposes that the House of Representatives pass the Trickett Wendler Right to Try Act after making amendments to minimize the legal, regulatory, and financial risks for drug sponsors of supplying patients with investigational drugs. In so doing, however, the House must address the safety risks of facilitating access to unapproved drugs by mandating patient counseling, requiring that patients request investigational drugs anonymously, and encouraging patient participation in clinical trials.

I. HOW PATIENTS ACCESS DRUGS: DRUG APPROVAL, DEVELOPING DRUGS THAT MEET PATIENT NEEDS, AND EXPANDED ACCESS TO INVESTIGATIONAL THERAPIES

To appreciate the potential impact of the 21st Century Cures Act and the Trickett Wendler Right to Try Act on rare-disease patients’ ability to access medical treatments, it is necessary to review the current legal and regulatory landscape of drug development, approval, and access. Part I.A details the drug-approval process as governed by the FDCA. Part I.B considers how the drug-approval process frustrates the development of rare-disease treatments and discusses congressional and regulatory attempts to overcome these difficulties through efforts such as the ODA and the FDA’s various patient engagement initiatives. Finally, Part I.C examines how patients can currently access unapproved drugs through the FDA’s Expanded Access program.

A. *The Drug-Approval Process*

Pursuant to the FDCA, new drugs, and new indications³² for already approved drugs, must receive FDA approval to be marketed in the United States.³³ Securing marketing approval is a multistep process during which a

32. An indication is defined as “a particular use of a drug, such as treating asthma.” *See Approved Drug Uses*, PUBMED HEALTH (Aug. 20, 2015), <https://www.ncbi.nlm.nih.gov/pubmedhealth/approved-drug-uses/> [<https://perma.cc/8VC9-3Y4Y>].

33. *See* 21 U.S.C. § 355(a) (2012). This requirement comes from the 1962 amendments to the FDCA (also known as the Kefauver-Harris Amendments), which were passed in reaction to the thalidomide tragedy that swept Europe in the late 1950s and early 1960s. *See* Drug Amendments of 1962, Pub. L. No. 87-781, § 104, 76 Stat. 784 (codified as amended at 21 U.S.C. § 355(a)); *Kefauver-Harris Amendments Revolutionized Drug Development*, FDA

drug's sponsor submits to the FDA "everything about a drug"³⁴ to establish that it is "safe and effective for its intended use."³⁵

The specific requirements of drug approval are as follows. Before commencing clinical testing, a drug sponsor must submit an investigational new drug application (IND) to the FDA.³⁶ The IND must contain preclinical data demonstrating that the drug is safe enough for human testing.³⁷ If the FDA deems it sufficiently safe, the drug then undergoes a series of clinical trials, beginning with small Phase I tests to ensure safety and ending with longer, larger Phase III studies to test efficacy and to monitor adverse reactions.³⁸ After completing at least two "large, controlled clinical trials,"³⁹ the drug's sponsor must file a new drug application (NDA) for the drug to be approved.⁴⁰ The NDA must contain all data accumulated in preclinical and clinical trials, as well as proposed product labeling, usage directions, safety and abuse information, and other relevant details.⁴¹ CDER then decides whether to approve the drug for marketing in the United States.⁴²

(Dec. 5, 2017), <https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm322856.htm> [<https://perma.cc/2GME-PB9K>]; *see also supra* note 24.

34. *Step 4: FDA Review*, FDA (Jan. 4, 2018), <https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405570.htm> [<https://perma.cc/6E9F-BA7K>].

35. *See id.*; *see also* 21 U.S.C. § 355(b)(1)(A). The FDA may refuse to approve a new drug on multiple grounds: if it determines that the drug sponsor did not adequately test the drug for safety and efficacy; if the data provided by the sponsor does not demonstrate that the drug is safe; if the drug's manufacturing, processing, or packing methods are inadequate to preserve the drug; if there is insufficient information to determine whether a drug is safe; or if there is a "lack of substantial evidence" that the drug will have the effect it purports to have. *See id.* § 355(d).

36. *See Step 3: Clinical Research*, FDA (Jan. 4, 2018), <https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405622.htm> [<https://perma.cc/3EVN-FBB5>].

37. *See Development & Approval Process (Drugs)*, FDA (Jan. 16, 2018), <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/> [<https://perma.cc/B3M9-V7V3>].

38. *Step 3: Clinical Research*, *supra* note 36.

39. *See id.*

40. *Step 4: FDA Review*, *supra* note 34. The approval process for biological products (a type of drug that is derived from "living material," such as some vaccines) differs slightly from nonbiologic drugs. *See Frequently Asked Questions About Therapeutic Biological Products*, FDA (July 7, 2015), <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/ucm113522.htm> [<https://perma.cc/22AX-PGMH>]. If initial clinical trials show that a biologic is safe and effective for its intended use, a biologic sponsor must submit a biologics license application (BLA), as opposed to an NDA, to the FDA. *See id.* A BLA, like an NDA, must contain all preclinical and clinical data and relevant product information, like a drug's proposed labeling. *Biologics License Applications (BLA) Process (CBER)*, FDA (Jan. 5, 2018), <https://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicsLicenseApplicationsBLAProcess/default.htm> [<https://perma.cc/W45D-X29P>]. To grant a license, the FDA must determine "that the product, the manufacturing process, and the manufacturing facilities meet applicable requirements to ensure the continued safety, purity[,] and potency of the product." *Frequently Asked Questions About Therapeutic Biological Products*, *supra*.

41. *Step 4: FDA Review*, *supra* note 34.

42. *Id.* This process typically exceeds one year. Alexander Gaffney et al., *Regulatory Explainer: Everything You Need to Know About FDA's Priority Review Vouchers*, REG. AFF. PROFESSIONALS SOC'Y (Dec. 19, 2017), <http://www.raps.org/Regulatory-Focus/News/2015/07/02/21722/Regulatory-Explainer-Everything-You-Need-to-Know-About-FDA's-Priority-Review-Vouchers> [<https://perma.cc/CF9G-ABNF>]. Priority review is available for "promising therapies that treat a serious or life-threatening condition and provide therapeutic

To approve a drug, CDER must determine that the drug's benefits outweigh its risks to the population it is intended to treat.⁴³ To make this determination, CDER reviews the drug's NDA using a structured analytical framework.⁴⁴ First, CDER analyzes the disease or condition that the drug is intended to treat and takes stock of already available treatments.⁴⁵ CDER then determines the drug's benefits and risks by looking to clinical data submitted by the drug sponsor and accounting for uncertainties that may come from "imperfect or incomplete data."⁴⁶ Finally, CDER considers whether any of the drug's risks can be mitigated through the use of risk management strategies, such as labeling that "clearly describes the drug's benefits and risks."⁴⁷ Despite this rigorous analysis, CDER approves most drugs: for example, in 2015, CDER approved 96 percent of NDAs.⁴⁸

B. Congressional and Regulatory Efforts to Develop Rare-Disease Treatments

The rigorous drug-approval process costs drug manufacturers much time and money.⁴⁹ These costs have historically encouraged drug manufacturers to concentrate their development efforts on drugs whose profits exceed the massive costs of approval—typically "blockbuster" drugs that treat common health conditions, like hypertension.⁵⁰ Consequently, most rare diseases—also known as orphan diseases—lack an FDA-approved treatment.⁵¹ Part I.B.1 considers how Congress and the FDA have tried to stimulate rare-disease drug development. It focuses on Congress's passage of the ODA and the establishment the "Priority Review Voucher" program for rare pediatric diseases. Part I.B.2 reviews the FDA's more general efforts to solicit patient

benefit over available therapies." *Development & Approval Process (Drugs)*, *supra* note 37. Priority review is helpful "when the drug is meant to treat a disease whose course is long, and an extended period of time is needed to measure its effect." *Id.* After approval, however, the drug sponsor must conduct additional clinical trials to confirm the drug's safety and efficacy. *See id.*

43. *Development & Approval Process (Drugs)*, *supra* note 37.

44. *Id.*

45. *See id.*

46. *See id.*

47. *See id.*

48. Matthew Herper, *The FDA Is Basically Approving Everything. Here's The Data to Prove It*, FORBES (Aug. 20, 2015, 8:53 AM), <https://www.forbes.com/sites/matthewherper/2015/08/20/the-fda-is-basically-approving-everything-heres-the-data-to-prove-it/#18de3b005e0a> [https://perma.cc/X4KC-PCWV].

49. Indeed, a 2014 study concluded that the average cost of getting a prescription drug on the market was \$2.6 billion and took at least ten years. Rick Mullin, *Cost to Develop New Pharmaceutical Drug Now Exceeds \$2.5 B*, SCI. AM. (Nov. 24, 2014), <https://www.scientificamerican.com/article/cost-to-develop-new-pharmaceutical-drug-now-exceeds-2-5b/> [https://perma.cc/GCK6-MR9U].

50. *See* Peter Ubel, *Is The Golden Era Of Pharmaceutical Profits Over?*, FORBES (July 29, 2016, 11:59 AM), <https://www.forbes.com/sites/peterubel/2016/07/29/is-the-golden-era-of-pharmaceutical-profits-over/#27974f737207> [https://perma.cc/Y2PQ-ECHV].

51. Jan Ascher et al., *How to Successfully Launch a Rare Disease Drug in a Patient-Centric World*, MCKINSEY & CO. (Jan. 2017), <https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/how-to-successfully-launch-a-rare-disease-drug-in-a-patient-centric-world> [https://perma.cc/4X8K-3Z4M].

feedback in drug development and approvals, including “Patient-Focused Drug Development” meetings, the “Patient Representative Program,” and the possible launch of an office of patient affairs.

1. Incentivizing the Development of Rare-Disease Treatments

Considered collectively, rare diseases are not as rare as their name suggests.⁵² Indeed, it is estimated that one in ten Americans has a rare disease.⁵³ However, approximately 95 percent of rare diseases lack an FDA-approved treatment—hence the term orphan diseases.⁵⁴

Prior to the ODA’s passage, pharmaceutical companies hesitated to develop rare-disease drugs because, “[d]ue to the rarity of the conditions and limited demand for treatments,”⁵⁵ there was “no reasonable expectation [that] the sales of the drug[s] would] recover the costs.”⁵⁶ Under pressure from advocacy groups like the National Organization for Rare Disorders (NORD),⁵⁷ Congress passed the ODA in 1983 to encourage drug manufacturers to develop rare-disease, or orphan, drugs.⁵⁸

The ODA financially incentivizes rare-disease⁵⁹ drug development by providing orphan-drug developers⁶⁰ with tax credits⁶¹ and grants to fund drug development.⁶² The ODA also permits new orphan drugs seven years of

52. See Elgin et al., *supra* note 2.

53. *Rare Disease Facts*, NAT’L ORG. RARE DISORDERS 1 (2016), http://cdn.rarediseases.org/wordpresscontent/wp-content/uploads/2014/11/NRD-1008-FactSheet_5.pdf [<https://perma.cc/5XBX-26Y2>].

54. See Ascher et al., *supra* note 51.

55. Taeho Greg Rhee, *Policymaking for Orphan Drugs and Its Challenges*, 17 AM. MED. ASS’N J. ETHICS 776, 776 (2015).

56. *Id.* (quoting RARE DISEASES AND ORPHAN PRODUCTS: ACCELERATING RESEARCH AND DEVELOPMENT (T.F. Boat & M.L. Field eds., 2010)).

57. *Id.*

58. See Orphan Drug Act, Pub. L. No. 97-414, 96 Stat. 2049 (1983) (codified as amended in scattered sections of 15, 21, 26, 35, and 42 U.S.C.); see also Gayatri Rao, *The Rise of Orphan Drug Designations: Meeting the Growing Demand*, FDA VOICE (July 18, 2016), <https://blogs.fda.gov/fdavoices/index.php/tag/orphan-drug-act/> [<https://perma.cc/3ZET-ZQC8>]. Additionally, in 2002, Congress authorized the creation of the Office of Rare Diseases Research (ORDR) at the National Institutes of Health (NIH) by passing the Rare Diseases Act. See Rare Diseases Act of 2002, Pub. L. No. 107-280, § 3, 116 Stat. 1988, 1989–90 (codified at 42 U.S.C. § 287a-1 (2012)). The Rare Diseases Act did not specifically incentivize orphan-drug development but rather encouraged rare disease research by mandating that the ORDR conduct, and provide funding for, research into rare diseases. See 42 U.S.C. §§ 287a to 287a-2 (2012).

59. The ODA, as originally enacted, provided that a rare disease or condition occurs with such infrequency that a drug for treating such a disease cannot not be reasonably expected to recoup the costs of production. See Orphan Drug Act § 2(a). Today, however, a rare disease is also defined as a disease that affects fewer than 200,000 people in the United States. See 21 U.S.C. § 360bb(a)(2) (2012).

60. The FDA must grant a drug “orphan designation” before its sponsor can take advantage of the ODA’s incentives. *Designating an Orphan Product: Drugs and Biological Products*, FDA (Dec. 28, 2017), <https://www.fda.gov/ForIndustry/DevelopingProductsForRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/default.htm> [<https://perma.cc/Q9XF-LPXV>].

61. See I.R.C. § 45C (2012); Rhee, *supra* note 56.

62. See 21 U.S.C. § 360ee; Rhee, *supra* note 56.

market exclusivity in the United States.⁶³ Furthermore, the ODA provides that orphan-drug sponsors can request, and the FDA can provide, written recommendations regarding “non-clinical and clinical investigations” that “would be necessary for [the drug’s] approval.”⁶⁴ These incentives have proven effective: since the ODA’s passage, the FDA has approved more than 600 orphan drugs, compared to ten approvals in the decade before the ODA became law.⁶⁵

In 2012, the FDA launched the Priority Review Voucher program for rare pediatric diseases.⁶⁶ These vouchers are designed to incentivize drug makers to develop treatments for rare pediatric diseases by shortening the approval review period.⁶⁷ After successfully requesting a priority review voucher from the FDA,⁶⁸ the drug sponsor must inform the FDA of its intent to use the voucher for an upcoming NDA submission.⁶⁹ If the FDA accepts the voucher, it agrees to review the drug for marketing approval within six months.⁷⁰ As of December 2017, the FDA has awarded thirteen priority review vouchers for rare pediatric disease treatments.⁷¹

Despite the progress made by the ODA and the Priority Review Voucher program, the fact remains that most rare diseases lack an FDA-approved therapy.⁷² Multiple factors continue to hinder orphan-drug development. For one, small patient populations make it hard to find enough patients on whom to test orphan drugs in a statistically significant manner.⁷³ Particularly desperate patients may resist participating in clinical trials for fear of receiving a placebo and thus not experiencing relief.⁷⁴ Furthermore, drug

63. See 21 U.S.C. § 360cc; Elgin et al., *supra* note 2. New non-orphan drugs, once approved, have three to five years of market exclusivity. Elgin et al., *supra* note 2.

64. 21 U.S.C. § 360aa.

65. Elgin et al., *supra* note 2. In fact, 41 percent of all drugs brought to market in 2014 were orphan drugs. *Id.* In June 2017, the FDA announced its “Orphan Drug Modernization Plan” under which it eliminated a backlog of 200 orphan drug applications and “pledged to never allow such a backlog to accumulate again.” Scott Gottlieb, *FDA Is Advancing the Goals of the Orphan Drug Act*, FDA VOICE (Sept. 12, 2017), <https://blogs.fda.gov/fdavoices/index.php/2017/09/fda-is-advancing-the-goals-of-the-orphan-drug-act/> [<https://perma.cc/88W6-GK5R>].

66. See Gaffney et al., *supra* note 42. A rare pediatric disease affects less than 200,000 people under the age of eighteen in the United States. See *id.*; see also 21 U.S.C. § 360ff(a)(3).

67. See 21 U.S.C. § 360ff(a)(1); Gaffney et al., *supra* note 42.

68. See 21 U.S.C. § 360ff(b)(1); *Rare Pediatric Disease Priority Review Vouchers Draft Guidance*, FDA 13–15 (2014), <https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM423325.pdf> [<https://perma.cc/PY99-CAN5>] (detailing the process that drug sponsors must follow to request a Priority Review Voucher from the FDA). Interestingly, Priority Review Voucher recipients may transfer a voucher to another drug sponsor, even by sale. 21 U.S.C. § 360ff(b)(2).

69. See 21 U.S.C. § 360ff(b)(4); Gaffney et al., *supra* note 42.

70. Gaffney et al., *supra* note 42; see 21 U.S.C. § 360ff(a)(1).

71. Gaffney et al., *supra* note 42.

72. Ascher et al., *supra* note 51.

73. See *Rare Diseases and Expanded Access Policies*, MAPI, <http://mapigroup.com/services/real-world-evidence/rare-diseases-expanded-access-programs/> [<https://perma.cc/G7PQ-GPYD>] (last visited Feb. 14, 2018).

74. See, e.g., *Design Dilemma: The Debate over Using Placebos in Cancer Clinical Trials*, NAT’L CANCER INST. (May 3, 2011), <https://www.cancer.gov/about->

makers prefer to develop drugs that treat “more common” rare diseases because they are more profitable, leaving many “truly rare diseases” without treatments.⁷⁵ With an appreciation of the factors that limit orphan-drug development, it is perhaps easier to understand why the FDA conditionally approved Eteplirsen for treating DMD on such limited data.⁷⁶

2. The FDA and Patient Engagement

Historically, drug approval was a paternalistic endeavor, with the FDA alone determining whether a drug could enter the U.S. market.⁷⁷ Recently, however, the FDA has solicited feedback directly from patients to develop and approve treatments that better fulfill patient needs, as defined by patients themselves.⁷⁸ While this push for patient engagement does not explicitly target the needs of rare-disease patients, it does so incidentally because so many rare-disease patients have unmet therapeutic needs.⁷⁹

In 2012, the FDA began holding “Patient-Focused Drug Development” meetings.⁸⁰ In these public, disease-specific meetings, the FDA consults seriously ill patients who lack adequate treatment options to understand what these patients want and need out of the drug development process.⁸¹ Additionally, the FDA’s Office of Health and Constituent Affairs manages

cancer/treatment/research/placebo-clinical-trials [https://perma.cc/7NT9-J7KV]. For example, Mary Schwartz’s rare cancer was cured by experimental chemotherapy she received in a Phase II clinical trial, but she claims that she would not have enrolled in the trial had it been placebo controlled: “Because of the rarity of my cancer and the almost certainty of fatality, I would not have chosen to participate if there had been a possibility of getting a placebo.” *Id.*

75. See Rhee, *supra* note 56, at 777. Moreover, drug sponsors are free to price their products in a manner that maximizes profit; resultantly, orphan drugs may be prohibitively expensive for patients to access. *Id.*

76. See *supra* notes 17–21 and accompanying text.

77. See Edwards, *supra* note 15, at 413.

78. See Andrew Matthius, *How Patient-Centric Is the Pharma Industry?*, PDD (June 6, 2016) [hereinafter Matthius, *How Patient-Centric Is the Pharma Industry?*], <https://www.pddinnovation.com/blog/2016/06/how-patient-centric-is-the-pharma-industry/> [https://perma.cc/2VUD-Y7WC]. Drug manufacturers have also taken an interest in patient engagement, also referred to in the pharmaceutical industry as patient-centricity. *Id.* Indeed, most major pharmaceutical companies have undertaken patient engagement initiatives in recent years. *Id.* For example, in 2014, Sanofi (a large international pharmaceutical company) appointed Dr. Anne Beal to the role of Chief Patient Officer—a first-of-a-kind role that involves “elevating the patient perspective within Sanofi.” Andrew Matthius, *The Secret to True Patient Centricity from Big Pharma’s First Chief Patient Officer*, PM360 (Mar. 18, 2015), <https://www.pm360online.com/the-secret-to-true-patient-centricity-from-big-pharmas-first-chief-patient-officer/> [https://perma.cc/N5DZ-VANS]. One reason for this push toward patient-centricity may be the perceived impact of patient-centricity on pharmaceutical companies’ bottom lines: one study reported that 85 percent of surveyed pharmaceutical executives believed that patient engagement efforts boost profitability. Matthius, *How Patient-Centric Is the Pharma Industry?*, *supra*.

79. See Ascher et al., *supra* note 51.

80. See Alexander Gaffney, *Patient-Focused Drug Development Tracker*, REG. AFF. PROFESSIONALS SOC’Y (July 1, 2015), <http://www.raps.org/Regulatory-Focus/News/Databases/2015/07/01/19640/Patient-Focused-Drug-Development-Tracker/> [https://perma.cc/D6NE-FQHL].

81. *Id.*

the “Patient Representative” program.⁸² Patient Representatives sit on FDA advisory committees, confer with doctors and scientists engaged in the approval of medical products, and participate in FDA meetings concerning specific diseases and policy issues to ensure that patients are represented in the drug-development and approval processes.⁸³ Furthermore, in March 2017, the FDA announced that it was considering creating an “office of patient affairs” to coordinate patient engagement across the pharmaceutical industry.⁸⁴ The office would facilitate patient engagement by hosting and maintaining data management systems to help patient groups communicate with the FDA.⁸⁵

Viewed in the context of these ongoing efforts to involve patients in the drug-approval and access process, the 21st Century Cures Act and the Trickett Wendler Right to Try Act do not seem like drastic departures from longstanding precedent but rather a logical next step in an ongoing journey toward a drug regulation system in which patients are directly involved.

*C. The FDA’s Expanded Access Program:
Accessing Investigational Drugs Outside of Clinical Trials*

Patients who have exhausted approved treatments for a given disease or condition without experiencing clinical benefit can access experimental treatments in two ways. Patients may qualify for a clinical trial, or, if this is impossible,⁸⁶ they can seek to obtain a drug through the FDA’s Expanded

82. See *Office of Health and Constituent Affairs*, FDA (July 21, 2017), <https://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofExternalAffairs/ucm343095.htm> [<https://perma.cc/M3NH-UEGX>].

83. See *About the Patient Representative Program*, FDA (Jan. 31, 2018), <https://www.fda.gov/forpatients/patientengagement/ucm412709.htm#Criteria> [<https://perma.cc/3EG7-D239>].

84. Zachary Brennan, *FDA Considers Creating New ‘Office of Patient Affairs’*, REG. AFF. PROFESSIONALS SOC’Y (Mar. 13, 2017), <http://www.raps.org/Regulatory-Focus/News/2017/03/13/27103/FDA-Considers-Creating-New-Office-of-Patient-Affairs/> [<https://perma.cc/Q8KV-ZZLZ>].

85. *Id.*

86. See *Expanded Access: Information for Patients*, FDA (Jan. 4, 2018), <https://www.fda.gov/ForPatients/Other/ExpandedAccess/ucm20041768.htm#different-types> [<https://perma.cc/X9UK-QWY5>] (noting that, to grant an Expanded Access request, the FDA must determine that the patient cannot participate in an ongoing clinical trial). Logistically, participating in a clinical trial can be difficult: assuming that there is an ongoing trial for a drug that could treat a patient’s disease, clinical trials can last up to four years. *Step 3: Clinical Research*, *supra* note 36. A patient may need to travel to the trial site, which could make it hard to keep a job and tend to one’s family. See *Clinical Trial Financial Assistance*, PATIENT EMPOWERMENT NETWORK, <https://powerfulpatients.org/project/clinical-trial-financial-assistance/> [<https://perma.cc/B8ZT-3MGZ>] (last visited Feb. 14, 2018). While insurance companies and drug sponsors sometimes pay for a patient’s treatment in a clinical trial, other related costs fall on the patient, such as travel, childcare, and follow-up doctor visits. *Id.* Moreover, there is no guarantee that there will be a clinical trial with eligibility criteria (e.g., age, sex, medical history, and current health status) that a given patient will meet. See *What Are Eligibility Criteria, and Why Are They Important?*, ROSWELL PARK, <https://www.roswellpark.org/clinical-trials/eligibility-criteria> [<https://perma.cc/D9ZN-TKM4>] (last visited Feb. 14, 2018). Additionally, the stakes may be so high that patients are unwilling to participate in placebo trials for fear of receiving a placebo and thus being further

Access program.⁸⁷ This program grants seriously ill patients access to experimental drugs outside of clinical trials.⁸⁸ The Expanded Access program therefore performs the important function of helping patients who cannot participate in clinical trials to access experimental drugs and thereby treat, or attempt to treat, their illnesses. Indeed, access to experimental drugs is especially important in the rare-disease context, given the limited availability of approved therapies.⁸⁹

To obtain an investigational drug through the Expanded Access program, a physician must petition the FDA to grant his or her patient access to the drug.⁹⁰ This physician must be willing to oversee the patient's treatment and work with the FDA and the drug sponsor to obtain the investigational drug.⁹¹ Additionally, the physician must ensure that the patient gives informed consent to using the investigational drug and that an Institutional Review Board (IRB) approves the patient's use of the experimental drug.⁹²

To approve an Expanded Access request, the FDA must determine that the patient has a "serious"⁹³ or "immediately life-threatening"⁹⁴ illness for which there is no other available treatment and that the patient cannot otherwise

distanced from relief or cure. *See Design Dilemma: The Debate over Using Placebos in Cancer Clinical Trials*, *supra* note 74.

87. *See Expanded Access: Information for Patients*, *supra* note 86; *see also* Bob Tedeschi, *With Patients Demanding Experimental Drugs, 'Right to Try' Is Becoming the Law of the Land*, STAT (Mar. 23, 2017), <https://www.statnews.com/2017/03/23/right-to-try/> [<https://perma.cc/EJ8E-666C>].

88. *See Expanded Access: Information for Patients*, *supra* note 86.

89. Meg Tirrell, *When Unapproved Drugs Are the Only Hope*, CNBC (Aug. 5, 2014), <https://www.cnbc.com/2014/08/05/a-case-for-compassionate-use-when-unapproved-drugs-are-the-only-hope.html> [<https://perma.cc/F48L-5KW8>].

90. *See Expanded Access: Information for Patients*, *supra* note 86. To utilize the Expanded Access program, a physician must complete an IND application on the patient's behalf. *Id.* Once the FDA approves the IND, the drug maker ships the drug to the physician, who then dispenses it to the patient. *Id.* The FDA recognizes three categories of Expanded Access: Expanded Access for individual patients (which may be for emergency use), mid-sized patient populations, and widespread use. *Id.* Because the most popular category is individual use, this Note details the individual use Expanded Access category. *See* Jonathan J. Darrow et al., *Practical, Legal and Ethical Issues in Expanded Access to Investigational Drugs*, 372 NEW ENG. J. MED. 279, 279 (2015).

91. *Expanded Access: Information for Patients*, *supra* note 86.

92. *See* 21 C.F.R. § 312.305(c)(4) (2017). Historically, a physician also had to seek the approval of an entire institutional review board (IRB) or an ethics committee for an IND before the FDA would approve an Expanded Access request. *Expanded Access: Information for Patients*, *supra* note 86. The IRB reviewed the IND to ensure that (1) the risks of taking the investigational drug are reasonable in light of the potential benefits and (2) the patient has been adequately informed of these risks, such that their consent is valid. *Id.* Recently, however, the FDA announced that it will only require one IRB member to review Expanded Access requests. *See* Scott Gottlieb, *Expanded Access: FDA Describes Efforts to Ease Application Process*, FDA VOICE (Oct. 3, 2017), <https://blogs.fda.gov/fdavoices/index.php/2017/10/expanded-access-fda-describes-efforts-to-ease-application-process/> [<https://perma.cc/53MM-4C4Z>].

93. 21 C.F.R. § 312.300(b) (defining a serious disease or condition as "a disease or condition associated with morbidity that has substantial impact on day-to-day functioning").

94. *Id.* (defining an immediately life-threatening disease or condition as "a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment").

obtain the experimental drug.⁹⁵ Moreover, the FDA must determine that the experimental drug is sufficiently safe for the requesting patient to use.⁹⁶ The FDA must also conclude that providing the drug outside of a clinical trial “will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval.”⁹⁷ While these requirements are extensive, the FDA approves most Expanded Access requests that it receives.⁹⁸

However, FDA approval of an Expanded Access request does not guarantee a patient access to an investigational drug; rather, access hinges on the drug sponsor’s approval of the request and, sometimes, the patient’s ability to afford the drug. Indeed, the drug sponsor must agree to provide the patient with the investigational drug—and it is not uncommon for drug sponsors to refuse to do so.⁹⁹ Furthermore, if the drug sponsor agrees to provide the investigational drug, it must either absorb the drug’s cost or ask the patient to find a way to pay for his or her own treatment.¹⁰⁰ Seeing as the average price of an orphan drug is \$111,820 per year,¹⁰¹ dispensing

95. See *id.* § 312.305(a)(1); *Expanded Access: Information for Patients*, *supra* note 86.

96. See 21 C.F.R. § 312.305(a)(2) (“[The] FDA must determine that . . . [t]he potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated.”). In other words, the risk of taking the investigational drug cannot exceed the risk of leaving the disease untreated. See *Expanded Access: Information for Patients*, *supra* note 86.

97. 21 C.F.R. § 312.305(a)(3).

98. *Expanded Access: Information for Patients*, *supra* note 86.

99. As Dr. Darshak M. Sanghavi explained:

[C]ompanies hesitate to do anything to jeopardize a product too soon. If they give drugs away, a disastrous side effect or other poor outcome could spur bad publicity and extra scrutiny from regulators. Even more important, if doctors simply let people take untested medicines without going through all the clinical trials, drug companies would most likely never get anyone to enroll in them, never get the data on safety and efficacy for F.D.A. approval and never pass the gateway to big sales. “Even if patients . . . are willing buyers,” writes George Annas, a Boston University expert on medical law, “drug manufacturers are not willing sellers.”

Darshak M. Sanghavi, *The Pills of Last Resort: How Dying Patients Get Access to Experimental Drugs*, N.Y. TIMES (Oct. 31, 2013), <http://www.nytimes.com/2013/11/03/magazine/how-dying-patients-get-access-to-experimental-drugs.html?pagewanted=all> [<https://perma.cc/VN73-7LPX>].

100. See *Expanded Access: Information for Patients*, *supra* note 86 (“The drug company may request authorization from FDA to charge [the patient] the . . . costs of making the drug available . . . or it may elect to cover the cost.”). However, the FDA must authorize the investigational drug’s sponsor to charge for the product. See *Charging for Investigational Drugs Under an IND—Questions and Answers*, FDA 6 (June 2016), <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351264.pdf> [<https://perma.cc/S9H3-23CW>]; see also 21 C.F.R. § 312.8(a) (noting that, if certain criteria are met, a drug sponsor may charge for a drug under an IND). The FDA will authorize a drug sponsor to charge the patient for expanded use of its product when the sponsor (1) reasonably assures the FDA that charging for the product will not interfere with drug development and (2) demonstrates that the amount to be charged complies with 21 C.F.R. § 312.8(d). 21 C.F.R. § 312.8(a); see *id.* § 312.8(c)–(d) (describing the criteria for charging for access to an investigational drug and what costs the drug sponsor may recover).

101. Sarah Jane Tribble & Sydney Lupkin, *High Prices for Orphan Drugs Strain Families and Insurers*, NPR (Jan. 17, 2017, 1:36 PM), <https://www.npr.org/sections/health-shots/2017/01/17/509507035/high-prices-for-orphan-drugs-strain-families-and-insurers>

experimental drugs through the Expanded Access program necessarily imposes a considerable financial burden on drug sponsors, patients, and, occasionally, health insurers.

The FDA's Expanded Access program has been increasingly criticized in recent years.¹⁰² Even though the FDA approves virtually all of the Expanded Access requests it receives,¹⁰³ FDA critics argue that the complicated, time-consuming request process deters patients and physicians from utilizing the program to acquire investigational drugs.¹⁰⁴ In response to mounting criticism, the FDA overhauled its Expanded Access program in 2015 to streamline the request process. It published a new "relatively straightforward" IND request form and launched a website designed to make it easier for physicians to find information regarding investigational drugs.¹⁰⁵

Still unsatisfied, FDA critics have been gaining traction with the passage of "right-to-try" laws in at least thirty-eight states.¹⁰⁶ These state laws "seek to remove the FDA from the equation, allowing doctors, patients, and drug makers to strike their own deals for drugs that have cleared the safety phase of FDA testing."¹⁰⁷ By permitting patients to access investigational drugs without FDA approval,¹⁰⁸ the Trickett Wendler Right to Try Act resembles these state laws.

In October 2017, the FDA announced several adjustments to the Expanded Access program that will purportedly hasten the process of requesting investigational drugs.¹⁰⁹ Moreover, in November 2017, the FDA announced an expansion of the "Expanded Access Navigator Tool" to include rare-

[<https://perma.cc/FM7U-LFRB>]. By contrast, the average annual price of a non-orphan drug is \$23,331. *Id.*

102. See Darrow et al., *supra* note 90 (noting that the Expanded Access program "has become increasingly controversial").

103. See *supra* note 98 and accompanying text.

104. See, e.g., Christina Corieri, *Everyone Deserves the Right to Try: Empowering the Terminally Ill to Take Control of Their Treatment*, GOLDWATER INST. (Oct. 7, 2014), <http://goldwaterinstitute.org/article/everyone-deserves-right-try-empowering-terminally/> [<https://perma.cc/5LR5-UQ9Y>].

105. Alexander Gaffney, *From 100 Hours to 1: FDA Dramatically Simplifies Its Compassionate Use Process*, REG. AFF. PROFESSIONALS SOC'Y (Feb. 4, 2015), <http://www.raps.org/Regulatory-Focus/News/2015/02/04/21243/From-100-Hours-to-1-FDA-Dramatically-Simplifies-its-Compassionate-Use-Process/> [<https://perma.cc/V2MW-SHPY>].

106. Kimberly Leonard, *Koch-Backed Group Urges Passage of 'Right to Try' Bill Allowing Experimental Drugs for Terminal Patients*, WASH. EXAMINER (Jan. 8, 2018, 9:31 AM), <http://www.washingtonexaminer.com/koch-backed-group-urges-passage-of-right-to-try-bill-allowing-experimental-drugs-for-terminal-patients/article/2645255> [<https://perma.cc/53W5-43D3>]; see also Trudy Lieberman, *Opinion, Right-To-Try Drug Proposal Is a Solution for a Non-Existent Problem*, J.-ADVOC. (Sept. 12, 2017, 9:44 PM), http://www.journal-advocate.com/sterling-columnists/ci_31296225/right-try-drug-proposal-is-solution-non-existent [<https://perma.cc/3Q3G-FESL>].

107. Tedeschi, *supra* note 87.

108. See S. 204, 115th Cong. § 2(a) (2017).

109. Gottlieb, *supra* note 92. Physicians are no longer required to seek approval of an IND from an entire IRB; instead, physicians can acquire the approval of just one IRB member. *Id.*; see also *supra* note 92. Moreover, drug companies no longer need to submit to the FDA data regarding suspected adverse reactions to the drugs they provide through the Expanded Access program. Gottlieb, *supra* note 92. Instead, they will need to submit such data "only if there is evidence to suggest a causal relationship between the drug and the adverse event." *Id.*

disease patients.¹¹⁰ The tool will help rare-disease patients to find drug sponsors that dispense drugs through the Expanded Access pathway.¹¹¹

It is too early to tell whether these updates to the FDA's Expanded Access program will materially facilitate patient access to investigational drugs. However, should Congress fail to enact the Trickett Wendler Right to Try Act, critics of the program should take some solace in the fact that the FDA seems to hear their complaints, as illustrated by its efforts to improve the Expanded Access program.

II. UNCONTROLLED PATIENT EXPERIENCE DATA AND UNFETTERED INVESTIGATIONAL DRUG ACCESS: ARE WE HURTING PATIENTS OR HELPING THEM?

Having outlined the laws and regulations governing orphan-drug development, approval, and access, this Part explores how the 21st Century Cures Act and the Trickett Wendler Right to Try Act may change the landscape of drug approvals for the benefit of rare-disease patients. Part II.A discusses section 3001 of the 21st Century Cures Act and how patient experience data—which, as defined, may be collected by any person, *outside* of clinical trials—could alter the otherwise objective drug-approval process. Part II.B examines the risks of granting patients access to investigational drugs without FDA approval, as permitted by the Trickett Wendler Right to Try Act.

A. *The 21st Century Cures Act and Patient Experience Data*

Congress passed the 21st Century Cures Act in December 2016.¹¹² The Act—which Senate Majority Leader Mitch McConnell described as “the most important legislation” passed in 2016¹¹³—enjoyed bipartisan support and passed both houses of Congress with overwhelming majorities.¹¹⁴

The rare-disease community has welcomed the passage of the 21st Century Cures Act,¹¹⁵ which purports “[t]o accelerate the discovery, development,

110. Scott Gottlieb, *FDA Widens Scope of Navigator—Information Tool for Expanded Access*, FDA VOICE (Nov. 2, 2017), <https://blogs.fda.gov/fdavoices/index.php/2017/11/fda-widens-scope-of-navigator-information-tool-for-expanded-access/> [https://perma.cc/2UZT-FM54].

111. *See id.* FDA Commissioner Scott Gottlieb reported that this resource will help rare-disease patients access unapproved therapies. *See id.*

112. *See generally* 21st Century Cures Act, Pub. L. No. 114-255, 130 Stat. 1033 (2016) (codified in scattered sections of 21 and 42 U.S.C.); Sydney Lupkin & Steven Findlay, *Winners and Losers with the 21st Century Cures Bill*, NPR (Dec. 2, 2016, 1:18 PM), <https://www.npr.org/sections/health-shots/2016/12/02/504139105/winners-and-losers-if-21st-century-cures-bill-becomes-law> [https://perma.cc/MCY9-74GJ].

113. Lupkin & Findlay, *supra* note 112.

114. *Id.* (noting that the 21st Century Cures Act passed the Senate by 94 to 5 votes); *see also* Sheila Kaplan, *Winners and Losers of the 21st Century Cures Act*, STAT (Dec. 5, 2016), <https://www.statnews.com/2016/12/05/21st-century-cures-act-winners-losers/> [https://perma.cc/6PM3-B3SR] (noting that the 21st Century Cures Act passed the House by 392 to 26 votes).

115. NORD and other rare-disease patient advocacy groups lobbied heavily for the bill's passage. *See* Jennifer Huron, *Senate Passes Landmark 21st Century Cures Act*, NAT'L ORG.

and delivery” of medical treatments.¹¹⁶ The Act contains several provisions that may facilitate the development of orphan drugs. For example, it extends the “Rare Pediatric Disease Priority Review Voucher Program” and streamlines the review process for genetically targeted drugs and protein-variant drugs for rare diseases.¹¹⁷ It also grants \$4.8 billion in funding for various NIH initiatives, which could spur innovation in the rare-disease field.¹¹⁸ Additionally, section 3001 of the Act mandates that the FDA publicly issue a “brief statement” regarding any patient experience data that the Agency considers in approving a drug.¹¹⁹

Pursuant to the 21st Century Cures Act, patient experience data can be collected *outside* of controlled clinical trials by individuals who are not trained scientists.¹²⁰ The Act provides that patient experience data is “intended to provide information about the experience of patients with a disease, or the impact a disease and management of the disease has on the lives of patients or their caregivers.”¹²¹ Accordingly, by permitting the FDA to consider patient experience data when approving drugs, section 3001 departs from the longstanding practice of approving drugs using evidence

RARE DISORDERS (Dec. 7, 2016), <https://rarediseases.org/senate-passes-landmark-21st-century-cures-act/> [https://perma.cc/7UQL-RL66]. The pharmaceutical industry also lobbied heavily for the Act’s approval. See Trudy Lieberman, *With Media Watchdogs on the Sidelines, Pharma-Funded Advocacy Groups Pushed Cures to the Finish Line*, HEALTH NEWS REV. (Dec. 6, 2016), <http://www.healthnewsreview.org/2016/12/with-media-watchdogs-sidelined-pharma-funded-advocacy-groups-pushed-cures-act-to-the-finish-line/> [https://perma.cc/NHS8-WD44].

116. See 21st Century Cures Act, Pub. L. Nopo. 114-255, pmb., 130 Stat. 1033, 1033 (2016); Mike DeBonis, *Congress Passes 21st Century Cures Act, Boosting Research and Easing Drug Approvals*, WASH. POST (Dec. 7, 2016), <https://www.washingtonpost.com/news/powerpost/wp/2016/12/07/congress-passes-21st-century-cures-act-boosting-research-and-easing-drug-approvals> [https://perma.cc/9N6B-YBGJ].

117. See 21 U.S.C. § 360ff(b) (Supp. IV 2016); Huron, *supra* note 115.

118. See Huron, *supra* note 115.

119. 21 U.S.C. § 360bbb-8c(b). Additionally, the Act exempts the FDA from the Paperwork Reduction Act when requesting information from patients, meaning that the FDA will not have to seek Office of Management and Budget approval before requesting patient experience data submissions from the public. *21st Century Cures Act: Key Provisions (Title III—Development)*, COVINGTON 2 (Dec. 22, 2016), https://www.cov.com/-/media/files/corporate/publications/2016/12/21st_century_cures_act_key_provisions_title_iii_development.pdf [https://perma.cc/Z742-9JCA]; see 21 U.S.C. § 360bbb-8c note (Streamlining Patient Input). Furthermore, the Act requires the FDA to report and publish online how it has used patient experience data in regulatory decisions before June 1, 2021, with follow-up reports in 2026 and 2031. See 21 U.S.C. § 355 note (Report on Patient Experience Drug Development). The FDA has begun implementing section 3001 by adding a “Patient Experience Data” subsection to drug and biologic review documents. See *Implementation of the 21st Century Cures Act: Progress and the Path Forward for Medical Innovation*, FDA (Dec. 7, 2017), <https://www.fda.gov/NewsEvents/Testimony/ucm587804.htm> [https://perma.cc/AY62-ZAP7]. Reviewers of new drugs must “include a brief statement regarding patient experience data and related information” included in new product applications. *Id.*

120. See 21 U.S.C. § 360bbb-8c(c) (describing patient experience data as “data . . . collected by any persons”).

121. *Id.*

from controlled clinical trials.¹²² Section 3001 thus raises many questions, such as what controls the FDA will place on patient experience data submissions and how much weight the FDA will give to patient experience data in drug approvals.¹²³

Some critics of the 21st Century Cures Act are concerned that patient experience data may bias the otherwise objective, data-driven drug-approval process.¹²⁴ Others go further and postulate that considering patient experience data in drug approvals is “incompatible” with the FDCA’s substantial-evidence-of-effectiveness approval standard (the “substantial evidence standard”).¹²⁵

To be sure, the 21st Century Cures Act does not stipulate how much weight the FDA should give patient experience data vis-à-vis clinical data in approving drugs;¹²⁶ and, with the Eteplirsen controversy looming fresh,¹²⁷ it is reasonable to be concerned that anecdotal stories could overpower clinical data in the drug-approval process.

However, the 21st Century Cures Act does not provide that patient experience data could *replace* data gathered from controlled clinical studies in drug approvals.¹²⁸ Rather, section 3001 broadly defines patient experience data as information about a patient’s experience with a *disease or condition*, not specifically with the drug being considered for approval.¹²⁹ This

122. *21st Century Cures Act—Provisions to Promote Drug Development*, *supra* note 28; *see supra* notes 34–47 and accompanying text.

123. Indeed, it may be years before these questions are answered because the FDA is not required to issue final guidance on how it shall implement section 3001 of the 21st Century Cures Act until 2020. *See* 21 U.S.C. § 360bbb-8c note (Patient-Focused Drug Development Guidance). In May 2017, the FDA released a plan for issuing this guidance. *Plan for Issuance of Patient-Focused Drug Development Guidance*, FDA 4–7 (May 2017), <https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM563618.pdf> [<https://perma.cc/5E8E-2J8A>]. The guidance drafting process began on December 18, 2017, when the FDA held a public workshop to discuss appropriate methodological approaches for collecting patient experience data for use in regulatory decision-making. *See* Notice of Request for Comments on Patient-Focused Drug Development, 82 Fed. Reg. 207, 49,838–39 (Oct. 27, 2017). The FDA will hold another public workshop on March 19, 2018, to discuss how anyone seeking to submit draft guidance to the FDA regarding patient experience data may do so. Notice of Request for Comments on Patient-Focused Drug Development, 82 Fed. Reg. 239, 58,816 (Dec. 14, 2017).

124. *See, e.g.,* Farrah R. Raja, *Evidentiary Standards for Drug Approvals in the 21st Century Cures Act: A Continued Trend Towards Valuing Access over Safety for Pharmaceutical Drugs*, 18 N.C. J.L. & TECH. 409, 428 (2017) (criticizing the 21st Century Cures Act for endangering patients by reducing the evidentiary standards of drug approval); *see also* Alan Levinovitz, *The FDA Should Approve Drugs Based on Evidence, Not Emotions*, SLATE (Dec. 13, 2016, 9:00 AM), http://www.slate.com/articles/health_and_science/medical_examiner/2016/12/the_21st_century_cures_act_could_be_dangerous_for_everyone.html [<https://perma.cc/J4W9-6J9B>] (describing the 21st Century Cures Act as permitting “medication approval driven by outrage and desperation, rather than evidence and reason”).

125. *See, e.g.,* Edwards, *supra* note 15, at 448–49.

126. *See* 21 U.S.C. § 360bbb-8c(b).

127. *See supra* notes 9–19 and accompanying text.

128. *See* 21 U.S.C. § 360bbb-8c(b).

129. *Id.* § 360bbb-8c(c). To be sure, section 3001 provides that patient experience data include data that concern “the impact of . . . a related therapy[] on patients’ lives” and “patient preferences with respect to treatment of such disease or condition.” *Id.* However, Congress’s use of the word “includes,” as well as its failure to specifically mention patient experience

expansive definition, along with the FDCA requirement that the FDA refuse to approve drugs that lack substantial evidence of safety and efficacy,¹³⁰ suggest that Congress did not intend for patient experience data to replace clinical data in drug approvals.¹³¹

Indeed, “[e]ach time Congress has amended the [FDCA] to provide [the] FDA with new tools to get drugs to patients faster it has also tacked on a ‘rule of construction’ that preserves the substantial evidence standard.”¹³² No such rule, however, accompanies section 3001 of the 21st Century Cures Act.¹³³ The absence of such a rule of construction further indicates that Congress did not intend for patient experience data to replace clinical data in drug approvals, or otherwise jeopardize the substantial evidence standard for drug approval. Accordingly, while the effects of patient experience data on the drug-approval process remain to be seen,¹³⁴ section 3001, as written, does not necessarily threaten patient safety.

In fact, patient experience data could contribute to the drug-approval process by providing what clinical data cannot: the context to understand the potential impact of a new drug on a patient’s life.¹³⁵ Patient experience data could assist the FDA in answering several questions, such as, how burdensome is a given disease on patients’, and their caregivers’, day-to-day lives? What range of symptoms do patients with a given disease typically suffer? How do patients currently manage these symptoms? Armed with answers to these and other questions, the FDA will be better equipped to identify whether new drugs meet patient needs and, in so doing, will advance its general mission of serving the public health.¹³⁶

with the drug being approved, further indicate that Congress did not intend for patient experience data to replace clinical data in drug approvals. *See id.*

130. *See* 21 U.S.C. § 355(d) (2012) (requiring the FDA to refuse an NDA if the NDA “do[es] not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the [intended] conditions,” if there is “insufficient information to determine whether such drug is safe for use,” or if there is “a lack of substantial evidence that the drug will have the effect it purports . . . to have”).

131. *See Step 3: Clinical Research*, *supra* note 36 (noting that not even preclinical research can be substituted for clinical research or “studies of ways the drug will interact with the human body”). That said, anecdotal patient stories played a role in Eteplirsen’s approval. *See supra* notes 9–19 and accompanying text. Indeed, some point to Eteplirsen’s approval to argue that the 21st Century Cures Act could encourage the FDA to rely on patient experience data in drug approvals at the expense of patient safety. *See, e.g.*, Edwards, *supra* note 15, at 448–49. However, this critique overlooks both the value of patient experience data and the complications of developing drugs for rare diseases. *See supra* Part I.B.

132. Edwards, *supra* note 15, at 447.

133. *See* 21 U.S.C. § 360bbb-8c.

134. The FDA has not yet issued guidance implementing this provision. *See 21st Century Cures Act Deliverables*, FDA (Jan. 16, 2018), <https://www.fda.gov/RegulatoryInformation/LawsEnforcedbyFDA/SignificantAmendmentstotheFDCA/21stCenturyCuresAct/ucm562475.htm> [<https://perma.cc/XFH9-8W2M>]. For a discussion of the FDA’s plan for issuing this guidance, *see supra* note 123.

135. *See What Is Patient Experience?*, AGENCY HEALTHCARE RES. & QUALITY (Oct. 2016), <https://www.ahrq.gov/cahps/about-cahps/patient-experience/index.html> [<https://perma.cc/54D8-B4XZ>].

136. *See Regulatory Radar: 21st Century Cures Act, Patient-Focused Drug Development*, NSF (Mar. 15, 2017), <http://www.nsf.org/newsroom/regulatory-radar-21st-century-cures-act-patient-focused-drug-development> [<https://perma.cc/825M-WMYT>].

Moreover, patient experience data may be especially helpful in orphan-drug approvals.¹³⁷ While laws like the ODA have helped to increase the number of orphan drugs on the U.S. market,¹³⁸ the fact that most rare diseases lack an approved therapy¹³⁹ suggests that the drug-regulation system is inadequate for the needs of rare-disease patients.¹⁴⁰ Certainly, there are many difficulties surrounding orphan-drug development;¹⁴¹ however, the difficulty most pertinent to patient experience data is the struggle drug developers face in identifying appropriate clinical endpoints to measure the efficacy of a drug in treating a given disease¹⁴² due to limited research into rare diseases.¹⁴³ Patient experience data could thus help drug developers and the FDA measure the clinical efficacy of rare-disease drugs because patients, who live daily with their diseases, are well situated to identify the most life-altering aspects of their diseases.¹⁴⁴ Additionally, the systematic collection of patient experience data may help future drug developers, doctors, and patients to better understand the natural histories of rare diseases.¹⁴⁵ Equipped with more information regarding the progression of different rare diseases, drug developers will be able to develop more effective therapies,¹⁴⁶ doctors will

137. See Stephen Smith, *Rare Disease Patient Voices Bring Change to the Clinical Trials Process*, FORBES (Sept. 25, 2014, 10:51 AM), <https://www.forbes.com/sites/medidata/2014/09/25/rare-disease-patient-voices-bring-change-to-the-clinical-trials-process/#38edf6994a11> [<https://perma.cc/M98Z-K2HT>].

138. Recall that over 600 orphan drugs have been approved since the passage of the ODA. See Elgin et al., *supra* note 2; see also *supra* text accompanying note 65.

139. See Ascher et al., *supra* note 51.

140. See COMM. ON ACCELERATING RARE DISEASES RESEARCH & ORPHAN PROD. DEV., RARE DISEASES AND ORPHAN PRODUCTS: ACCELERATING RESEARCH AND DEVELOPMENT 105 (Marilyn J. Field & Thomas F. Boat eds., 2010) (“[R]eview of drugs and biologics intended for small populations needs special consideration and expertise related to appropriate . . . analytic methods.”).

141. See *supra* text accompanying notes 73–75 for a discussion of other difficulties surrounding orphan-drug development.

142. See Erika F. Augustine et al., *Clinical Trials in Rare Disease: Challenges and Opportunities*, 28 J. CHILD NEUROLOGY 1142, 1146 (2013).

143. See *id.*; see also *Rare Diseases: Common Issues in Drug Development Draft Guidance*, FDA 3 (2015), <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM458485.pdf> [<https://perma.cc/9ZBC-7XEN>] (“Because of the small numbers of patients affected, and with clinical experience dispersed among a small number of clinical referral centers, the natural history of rare diseases is often poorly described.”).

144. Indeed, in its “Rare Diseases: Common Issues in Drug Development” draft guidance, the FDA underscored “the need for [drug] sponsors to gain greater biological, clinical, and epidemiological knowledge about the specific rare diseases under investigation.” Michael F. Murphy, *Rare Diseases: Meeting the Unique Challenges of Orphan Drug Development*, APPLIED CLINICAL TRIALS (Jan. 21, 2016), <http://www.appliedclinicaltrialsonline.com/rare-diseases-meeting-unique-challenges-orphan-drug-development?pageID=2> [<https://perma.cc/ND43-RNXM>]; see also *Rare Diseases: Common Issues in Drug Development Draft Guidance*, *supra* note 143.

145. A disease’s natural history “refers to the progression of a disease process in an individual over time, in the absence of treatment.” *Section 9: Natural History and Spectrum of Disease*, CDC (May 18, 2012), <https://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section9.html> [<https://perma.cc/6UEW-GMSM>].

146. *Id.* To elaborate:

A natural history study can provide critical information to guide every stage of drug development from drug discovery to determining effectiveness and safety of the

be able to more easily diagnose patients with rare diseases,¹⁴⁷ and, accordingly, patients will be able to start treating their rare diseases earlier.

*B. The Trickett Wendler Right to Try Act:
Accessing Investigational Drugs Without FDA Approval*

The Trickett Wendler Right to Try Act passed the Senate unanimously in August 2017 and is currently pending House approval.¹⁴⁸ If it becomes law, this Act will permit patients with “life-threatening” illnesses to access investigational drugs without FDA approval.¹⁴⁹

Specifically, the Trickett Wendler Right to Try Act amends the FDCA to permit patients with life-threatening illnesses to request investigational drugs from drug sponsors if the drug has already undergone preliminary testing in a Phase I trial, if the patient has exhausted available therapies, and if the patient is unable to join any ongoing clinical trials.¹⁵⁰ Additionally, a physician must approve the patient’s use of the drug and the patient must provide the physician with “written informed consent regarding” the drug.¹⁵¹ The Act further provides that the FDA shall not use “clinical outcomes” associated with the use of an experimental drug accessed through the “Right to Try” pathway “to delay or adversely affect the review or approval” of the

drug in treating a disease. Knowledge about the disease’s natural history can inform important aspects of drug development including:

Defining the disease population, including a description of the full range of disease manifestations and identification of important disease subtypes[;]

Understanding and implementation of critical elements in clinical study design, such as study duration and choice of subpopulations[;]

Developing and selecting outcome measures that are more specific or sensitive to changes in the manifestations of the disease or more quickly demonstrate safety or efficacy than existing measures[;]

Developing new or optimized biomarkers that may provide proof-of-concept (POC) information, guide dose selection, allow early recognition of safety concerns, or provide supportive evidence of efficacy. In some cases, biomarkers can be used for surrogate endpoints.

Rare Diseases: Common Issues in Drug Development Draft Guidance, *supra* note 143; *see also* Greg Breining, *Rare Diseases Difficult to Diagnose, Cures Hard to Come By*, AAMCNEWS (Apr. 11, 2017), <https://news.aamc.org/research/article/rare-diseases-difficult-diagnose-cures-hard-come/> [<https://perma.cc/KX5B-ZYJ6>] (quoting medical student and rare disease patient David Fajgenbaum as claiming that “[t]he number one reason [for the limited availability of rare disease treatments] is that pathogenesis and the underlying biology of many of these rare diseases is very poorly understood” and that “[i]f you don’t understand the biology of a disease, then it’s very difficult to treat it”).

147. *See* Breining, *supra* note 146. Doctors struggle to diagnose patients with rare diseases because they infrequently encounter rare diseases and because the greater medical community has limited knowledge of many rare diseases. *See id.* It thus follows that greater knowledge of rare diseases will facilitate diagnoses.

148. *See* S. 204, 115th Cong. § 2(a) (2017); Karlin-Smith & Kim, *supra* note 29.

149. *See* S. 204 § 2(a).

150. *See id.*; *see also* Karlin-Smith & Kim, *supra* note 29. To be clear, if it becomes law, the Trickett Wendler Right to Try Act would not replace the FDA’s Expanded Access program but would provide an alternative pathway for accessing investigational drugs outside of clinical trials. S. 204 § 3(1)–(4).

151. S. 204 § 2(a).

drug.¹⁵² The Act also requires all drug sponsors to submit an annual report to the FDA detailing when they have provided experimental drugs through the Right to Try pathway.¹⁵³ Moreover, the Act specifies that neither the drug's sponsor, prescriber, nor another "individual entity" shall be liable for properly using the Right to Try pathway.¹⁵⁴ Accordingly, if the Trickett Wendler Right to Try Act becomes law,¹⁵⁵ FDA critics will finally get a system for accessing investigational drugs that bypasses the FDA.¹⁵⁶

The Trickett Wendler Right to Try Act would also permit doctors to play a lesser role in the investigational drug-access process than they do in the Expanded Access program.¹⁵⁷ Indeed, doctors would only be required to certify that a patient had exhausted all FDA-approved therapies for treating his or her illness for that patient to be eligible to receive an experimental therapy.¹⁵⁸ It thus follows that if the time-consuming Expanded Access program requirements are indeed a barrier to patients seeking investigational drugs, the passage of the Trickett Wendler Right to Try Act could result in increased access to and use of investigational drugs.

However, some critics claim that the bill, if passed, would not actually help patients to access investigational therapies.¹⁵⁹ These critics point to the mechanics of the Expanded Access program: specifically, that the FDA already approves 99 percent of the Expanded Access requests it receives (in under four days)¹⁶⁰ and that the bill does not eliminate the need for drug sponsors to consent to providing patients with investigational drugs outside of clinical trials.¹⁶¹

As previously discussed, this consent can be hard come by:¹⁶² drug sponsors are often reluctant to dispense drugs through the Expanded Access program because an adverse outcome could "spur bad publicity and extra

152. *Id.*

153. *See id.*

154. *See id.* § 2(b).

155. President Trump would likely sign off on a federal right-to-try bill given the support he has voiced for the right-to-try movement. *See* Michael Mezher, *Trump Signals Support for 'Right-to-Try' Movement*, REG. AFF. PROFESSIONALS SOC'Y (Feb. 2, 2017), <http://www.raps.org/Regulatory-Focus/News/2017/02/02/26759/Trump-Signals-Support-for-Right-to-Try-Movement/> [<https://perma.cc/3SLE-D8ZK>].

156. *See supra* note 104 and accompanying text.

157. To compare, under the FDA's Expanded Access program, doctors must sponsor a patient's use of an investigational drug by filing an IND application and must seek to have the IND approved by at least one member of an IRB. *See supra* notes 90–91 and accompanying text.

158. *See* S. 204 § 2(a).

159. *See, e.g.,* Lieberman, *supra* note 106 (arguing that FDA involvement in the Expanded Access program protects patients and that drug companies, not the FDA, hinder patient access to investigational drugs).

160. *See id.*; *see also* Alison Bateman-House et al., *'Right to Try' Won't Give Patients Access to Experimental Drugs. Here's What Will.*, HEALTH AFF. (May 3, 2017), <http://www.healthaffairs.org/doi/10.1377/hblog20170503.059926/full/> [<https://perma.cc/4SNG-NRRC>].

161. *See* Lieberman, *supra* note 106 (emphasizing that drug companies must agree to provide patients with access to investigational drugs).

162. *See* Sanghavi, *supra* note 99 ("Even if patients . . . are willing buyers, . . . drug manufacturers are not willing sellers.").

scrutiny from regulators.”¹⁶³ Additionally, if more patients access investigational drugs outside of clinical trials, drug companies would likely struggle to meet enrollment targets for clinical trials and thus struggle to collect the safety and efficacy data required to secure FDA approval.¹⁶⁴ Furthermore, given the expense of drug development, drug sponsors may lack adequate supplies to freely dispense investigational drugs outside of clinical trials.¹⁶⁵ There is also the practical strain of providing drugs outside of those trials: drug sponsors—particularly small businesses—are forced to handle “constant [investigational drug] requests that they lack the time or the resources to evaluate properly.”¹⁶⁶ Thus, providing patients access to investigational drugs through the Expanded Access program burdens drug manufacturers in many different ways.

That said, as passed by the Senate, the Trickett Wendler Right to Try Act provides that the FDA cannot use adverse outcomes from the use of an investigational drug through the Right to Try pathway “to delay or adversely affect the review or approval” of a drug.¹⁶⁷ Accordingly, if this provision is enacted, it may assuage at least some drug sponsor concerns about providing patients with investigational drugs and, therefore, help patients with life-threatening illnesses to access treatments by incentivizing drug sponsors to dispense experimental therapies. However, drug sponsors would still need to devote inventory and personnel resources to manage Right to Try, as well as Expanded Access, requests.

Burdens on the pharmaceutical industry aside, other critics of the Trickett Wendler Right to Try Act fear that the law, if passed, would weaken important regulatory safeguards that protect patients by exposing them to products that have not been proven to be safe, or even effective.¹⁶⁸ For example, John Osborn and David Beier point to solanezumab, an Eli Lilly drug, to argue that allowing patients unregulated access to investigational drugs is risky: in early clinical studies, solanezumab appeared to effectively treat Alzheimer’s disease, but a Phase III trial proved it to be totally ineffective.¹⁶⁹ Certainly, patients with life-threatening diseases would not

163. *Id.*

164. *Id.*

165. Amy Scharf & Elizabeth Dzeng, ‘I’m Willing to Try Anything’: *Compassionate Use Access to Experimental Drugs and the Misguided Mission of Right-to-Try Laws*, HEALTH AFF. (Mar. 27, 2017), <http://www.healthaffairs.org/doi/10.1377/hblog20170327.059378/full/#s33> [<https://perma.cc/78LU-7ABQ>].

166. Lawrence M. Fisher, *The Ethics of Compassionate Care*, BRIEFINGS, Fall 2015, at 57, 59.

167. S. 204, 115th Cong. § 2(a) (2017).

168. See, e.g., *The Cruel Sham That Is “Right-to-Try” Is One Step Closer to Being Federal Law*, RESPECTFUL INSOLENT (Aug. 4, 2017), <https://respectfulinsolence.com/2017/08/04/the-cruel-sham-that-is-right-to-try-is-that-much-closer-to-being-law/> [<https://perma.cc/8VQJ-YZ73>].

169. John Osborn & David Beier, ‘Right to Try’ *Unapproved Medicines: Should Efficacy Be Optional?*, FORBES (Oct. 7, 2017, 9:26 AM), <https://www.forbes.com/sites/johnosborn/2017/10/07/right-to-try-unapproved-medicines-should-efficacy-be-optional/#190e6a36506d> [<https://perma.cc/Z3NZ-CFTR>].

benefit from facilitated access to medications that do not work or, worse, that are unsafe.

Osborn and Beier's argument, however, goes to the philosophic core of the greater right-to-try movement¹⁷⁰: whether patients with life-threatening illnesses who have exhausted all available approved therapies should be able to try investigational drugs without FDA permission.¹⁷¹ Right-to-try proponents argue that patients are well informed about their illnesses and, therefore, that a paternalistic approach to experimental drug access is not required to protect patient welfare.¹⁷² Others argue that right-to-try legislation offers a lifeline to patients with life-threatening illnesses who cannot participate in clinical trials.¹⁷³ However, some argue that right-to-try laws prey on the vulnerabilities of the life-threateningly ill who, desperate to live, do not fully appreciate the risks of taking a drug that has only undergone a Phase I clinical trial and whose health will thus be seriously endangered.¹⁷⁴ This ethical question is difficult to resolve, particularly in light of the D.C. Circuit's controversial 2007 ruling that terminally ill patients have no fundamental right to access investigational drugs.¹⁷⁵

III. BALANCING PATIENT PARTICIPATION WITH SAFETY: SUGGESTIONS FOR IMPLEMENTING THE 21ST CENTURY CURES ACT AND AMENDING THE TRICKETT WENDLER RIGHT TO TRY ACT

This Part suggests how the FDA should implement section 3001 of the 21st Century Cures Act and how the House of Representatives should amend the Trickett Wendler Right to Try Act. Considering the potential for both pieces of legislation to help rare-disease patients access drugs,¹⁷⁶ as well as the risks of allowing patients to participate in the drug-approval and access

170. Recall that, as of January 2018, at least thirty-eight states have passed right-to-try laws. See Leonard, *supra* note 106.

171. See *supra* notes 106–08 and accompanying text.

172. See generally Carrie Feibel, *Patients Demand the Right to Try Experimental Drugs, but Costs Can Be Steep*, NPR (Mar. 3, 2017, 2:17 PM), <http://www.npr.org/sections/health-shots/2017/03/03/517796956/patients-demand-the-right-to-try-experimental-drugs-but-costs-can-be-steep> [https://perma.cc/4V9W-UE3J] (quoting right-to-try advocate Lina Clark as saying, on behalf of the patient community, “[w]e are smart, we’re informed, we feel it is our right to try some of these therapies, because we’re going to die anyway”).

173. See Corieri, *supra* note 104.

174. See Osborn & Beier, *supra* note 169. As they elaborate,

Even leading cancer care advocates are squeamish about loosening the current expanded access standards without adding safeguards. Dr. Ellen [Sigal], Chair of the Friends of Cancer Research, recalled that her late sister, who had exhausted all treatment options at the time, decided to try an experimental bone marrow transplant procedure; tragically, this resulted in her swift death and studies later concluded that the procedure was less efficacious and more risky than previously thought.

Id.

175. *Abigail All. for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 711–12 (D.C. Cir. 2007); see also *D.C. Circuit Court Rules in Abigail Alliance Case; Affirms District Court Ruling That There Is No Fundamental Right of Access to Experimental Drugs for the Terminally Ill*, FDA L. BLOG (Aug. 7, 2007), <http://www.fdalawblog.net/2007/08/dc-circuit-cour/> [https://perma.cc/JQA3-49CR].

176. See *supra* notes 135–47, 172–73.

processes,¹⁷⁷ these suggestions strive to balance patient safety with easier access to medical treatments.

Specifically, Part III.A argues that the FDA must scrutinize the source of patient experience data submissions to ensure that parties who are financially interested in a drug's approval do not bias the drug-approval process. Part III.A then proposes that the FDA create a standardized questionnaire for patient experience data submissions to ensure that the data is as objective as possible. Next, Part III.B contends that if seriously ill patients are to have increased access to experimental therapies, then the House must amend the Trickett Wendler Right to Try Act to incentivize drug sponsors to provide drugs through the Right to Try pathway. Part III.B further asserts that the House must account for the safety risks of increased access to experimental drugs by mandating patient counseling, requiring that Right to Try requests be made anonymously, and encouraging patient participation in clinical trials.

*A. The FDA Should Control the Solicitation
and Submission of Patient Experience Data
to Ensure the Process Remains Objective*

The 21st Century Cures Act's patient experience data provisions could benefit rare-disease patients in several ways. If the FDA frequently considers patient experience data in approving drugs, this will likely incentivize drug manufacturers, patient advocacy organizations (PAO), and other entities to collect patient experience data for FDA use in drug approvals.¹⁷⁸ Moreover, scientific researchers will be able to harness this data to study the natural histories of rare diseases, most of which are poorly understood.¹⁷⁹ Eventually, a better understanding of rare diseases will enable doctors to diagnose patients with rare diseases more easily and enable drug makers to develop products that better target the causes and symptoms of rare diseases.¹⁸⁰ Certainly, these are promising prospects for rare-disease patients. That said, the 21st Century Cures Act grants the FDA broad leeway to implement section 3001.¹⁸¹ Therefore, the FDA must carefully implement this section to avoid compromising patient safety.

First, and most generally, the 21st Century Cures Act broadly defines patient experience data and does not specify how much weight the FDA

177. See *supra* notes 124–27, 174–75.

178. In addition to drug manufacturers and PAOs, the 21st Century Cures Act explicitly permits disease-research foundations, medical researchers, patients, parents, and caregivers to collect patient experience data for submission to the FDA. See 21 U.S.C. § 360bbb-8c(c) (Supp. IV 2016). Most rare diseases lack an approved therapy. See *supra* note 54 and accompanying text. It therefore seems logical that patient advocacy organizations and other entities interested in rare diseases would want to help get new treatments on the market.

179. See *supra* notes 142–47; see also *Rare Diseases: Common Issues in Drug Development Draft Guidance*, *supra* note 143 (“[T]he natural history of rare diseases is often poorly described.”).

180. See *supra* Part I.B.1.

181. See 21 U.S.C. § 360bbb-8c note (Patient-Focused Drug Development Guidance); *supra* note 123 and accompanying text.

should give this data vis-à-vis clinical data.¹⁸² To ensure that the FDA only approves drugs with substantial evidence of safety and effectiveness, and to quell fears of unsafe or ineffective drugs being approved, the FDA should be explicit in its guidance that patient experience data cannot and will not replace clinical data in the drug-approval process.¹⁸³

More specifically, the 21st Century Cures Act does not instruct how to ensure that patient experience data—permissibly collected by any person, outside of a controlled clinical setting—is reliable.¹⁸⁴ To avoid biasing the otherwise objective drug-approval process, the FDA should carefully control the patient experience data submission process by scrutinizing the source of all submissions. Of particular concern is data collected by drug manufacturers, PAOs, disease research foundations, and researchers (“interested parties”) because these entities are inclined to be financially interested in a drug’s approval. Less likely to be financially interested are individual patients, family members, or caregivers (“disinterested parties”). Being in the business of making drugs for sale, drug manufacturers are inherently financially interested in a drug’s approval. Additionally, PAOs are commonly funded by pharmaceutical companies,¹⁸⁵ and some disease research foundations engage in so-called “venture philanthropy” by investing large sums in pharmaceutical companies.¹⁸⁶ Indeed, researchers could also be financially interested in a drug’s approval since the 21st Century Cures Act does not stipulate that researchers must be unaffiliated with a drug sponsor to collect patient experience data for FDA use.¹⁸⁷

Accordingly, the FDA should develop a hierarchical system for reviewing patient experience data submissions, in which the data’s source determines the amount of authority accorded to it in the drug-approval process. The greater the chance that the collector is financially interested in the drug’s approval, the less weight the data should be accorded in deciding whether a drug should be approved. However, the FDA should allow collectors to

182. See 21 U.S.C. § 360bbb-8c; *id.* § 360bbb-8c note (Patient-Focused Drug Development Guidance); see also *supra* notes 129–31 and accompanying text.

183. The FDA must issue final guidance on how it shall implement section 3001 by 2020. See 21 U.S.C. § 360bbb-8c note (Patient-Focused Drug Development Guidance); see also *supra* note 123 and accompanying text.

184. See 21 U.S.C. § 360bbb-8c; *id.* § 360bbb-8c note (Patient-Focused Drug Development Guidance); see also *supra* note 120 and accompanying text. Instead, the FDA must issue guidance concerning, among other topics, appropriate methods of collecting and submitting patient experience data. See 21 U.S.C. § 360bbb-8c note (Patient-Focused Drug Development Guidance).

185. It is estimated that 83 percent of the largest PAOs in the United States accept contributions from the pharmaceutical industry and that one in five of these PAOs has accepted over \$1 million from pharmaceutical company donors. Emily Kopp & Kaiser Health News, *Groups That Represent Patients Are Ranking in Donations from Big Pharma*, TIME (Mar. 2, 2017), <http://time.com/money/4688501/patient-advocacy-groups-donations-from-pharma/> [https://perma.cc/GR42-7JWF].

186. For example, the Cystic Fibrosis Foundation used its funds to invest in Vertex Pharmaceuticals in 2015. Llewellyn Hinkes-Jones, *Stop Subsidizing Big Pharma*, N.Y. TIMES (Jan. 5, 2015), <https://www.nytimes.com/2015/01/06/opinion/stop-subsidizing-big-pharma.html> [https://perma.cc/B6QC-ZE85].

187. See 21 U.S.C. § 360bbb-8c(c).

overcome the presumption of bias through disclosure: if the collector can show that it has no financial interest in the drug's approval and that it has not received funding or payment from the drug's sponsor, its data should be accorded as much weight as data collected by disinterested parties.

Financial interest in a drug's approval is not the only factor that could unduly bias a patient experience data submission. Indeed, if a submission included personal information about a patient—such as his or her physical appearance, age, income, or marital or family status—this information could potentially inspire sympathy in FDA reviewers and thus bias the FDA in favor of approving a drug.¹⁸⁸ The FDA should therefore require data to be submitted anonymously—in other words, without clinically irrelevant information regarding a patient or group of patients. This would allow the FDA to objectively determine how effective a drug is at treating the most life-altering aspects of a given disease or condition.

The FDA must also ensure that all patient experience data submissions are objectively accurate. To do so, the FDA should compare all patient experience data to data collected through its Patient-Focused Drug Development meetings,¹⁸⁹ provided that such data exists for the disease that a given drug is intended to treat.¹⁹⁰ This comparison would function as a check on patient experience data to ensure that the FDA relies on objectively accurate, minimally biased information.

Moreover, the 21st Century Cures Act leaves the FDA to specify *how* to collect patient experience data for consideration in regulatory decision-making.¹⁹¹ If the FDA does not strictly stipulate appropriate collection methods for patient experience data, collectors could manipulate patient experience data to favor drug approval. For example, if a drug being considered for approval treats symptom X of disease Y, a drug manufacturer could solicit targeted feedback from disease Y patients regarding symptom X to support the drug's approval. The drug manufacturer could thus present the FDA with a skewed perspective of disease Y, which might obscure the FDA's understanding of disease Y and, thus, its decision to approve the drug.

The FDA should, therefore, develop a series of approved questions for the interested parties to use in soliciting patient experience data, and for disinterested parties to answer in making individual submissions. Furthermore, the FDA should refuse to accept patient experience data that does not conform to these approved questions. Such questions could include, "In your opinion, what are the most debilitating symptoms of [given

188. For a related discussion on how personal information can bias a drug sponsor's decision to provide a patient with an investigational drug, see *infra* notes 214–15.

189. See Zachary Brennan, *Califf: Patient Preferences Too Often Overlooked in Medical Product Development, Approvals*, REG. AFF. PROFESSIONALS SOC'Y (Nov. 19, 2017), <http://www.raps.org/Regulatory-Focus/News/2015/11/19/23645/Califf-Patient-Preferences-Too-Often-Overlooked-in-Medical-Product-Development-Approvals/> [<https://perma.cc/HU7H-WVTX>].

190. See *id.*

191. See 21 U.S.C. § 360bbb-8c note (Patient-Focused Drug Development Guidance). Rather, the FDA must issue guidance concerning appropriate methods for collecting patient experience data. See *id.*; see also *supra* note 123.

disease]?” and “How burdensome is [given disease’s] current treatment regime on a patient’s [or your] day-to-day life?” Standardizing the format in which patient experience data is submitted to the FDA will help the FDA to minimize opportunities for submitters to manipulate patient experience data and thus reduce the likelihood of unreliable data biasing the drug-approval process. By collecting minimally biased patient experience data, the FDA will help build the natural histories of all diseases, which, as previously discussed, will especially benefit rare-disease patients.¹⁹²

B. The House of Representatives Should Amend the Trickett Wendler Right to Try Act to Facilitate Access to Investigational Drugs and Maintain Patient Safety

The unmet needs of rare-disease patients are profound.¹⁹³ While patient experience data as collected and reviewed in the manner detailed above¹⁹⁴ will benefit rare-disease patients, these benefits will not be immediately realized. Accumulating patient experience data requires time, and drug makers will need even more time to harness this data to develop new drugs. By facilitating access to experimental drugs, however, the Trickett Wendler Right to Try Act could help some rare-disease patients to access treatments in the meantime. Accordingly, the House of Representatives should pass the Trickett Wendler Right to Try Act, amended as described below, to protect the well-beings of patients and drug makers alike.

One shortcoming of the Expanded Access program is that drug makers often resist supplying patients with investigational drugs.¹⁹⁵ However, sections 2(a) and 2(b)(1)(A) of the Trickett Wendler Right to Try Act may incentivize drug makers to dispense drugs through the Right to Try pathway and thus facilitate patient access to investigational medicines.¹⁹⁶ Accordingly, to materially facilitate patient access to investigational drugs, the House of Representatives must preserve these provisions when amending the Act.

Section 2(a) provides that the outcome of a patient’s use of an investigational drug shall not be used by federal agencies in the drug-approval process.¹⁹⁷ Section 2(b)(1)(A) provides that drug makers will not be liable for providing a patient with a drug through the Right to Try pathway (i.e., without FDA approval).¹⁹⁸ If these provisions become law, the FDA will be unable to prosecute, or to unduly scrutinize in the approval process, drug makers for dispensing unapproved drugs through the Right to Try pathway. Minimizing the legal and regulatory risks of using the Right to Try

192. See *supra* text accompanying notes 145–47.

193. See *supra* note 54 and accompanying text.

194. See *supra* Part III.A.

195. See Sanghavi, *supra* note 99.

196. See *infra* notes 197–98 and accompanying text.

197. See S. 204, 115th Cong. § 2(a) (2017). One concern of drug sponsors regarding the Expanded Access program is that adverse outcomes of investigational drug use could be used by the FDA in deciding whether to approve the drug, therefore jeopardizing the chances of the drug’s approval. See Sanghavi, *supra* note 99.

198. See S. 204 § 2(b)(1)(A).

pathway will likely incentivize drug makers to supply patients with investigational drugs.

Another shortcoming of the Expanded Access program is that either drug sponsors or patients must pay for investigational drugs,¹⁹⁹ which are typically expensive.²⁰⁰ As passed by the Senate, the Trickett Wendler Right to Try Act does not address the monetary costs of providing patients with investigational drugs.²⁰¹ Since drug sponsors are generally better positioned to absorb the high costs of drugs than individual patients,²⁰² the House of Representatives should amend the Act to permit drug makers to receive a modest reduction in the cost of the investigational drug's ultimate NDA. This reduction should be proportional to the number of patients provided with the drug over the course of drug development. Reducing the overall cost of drug approval would further incentivize drug companies to provide drugs through the Right to Try pathway, thereby increasing access to potentially life-saving experimental treatments for seriously ill patients.

While incentivizing drug sponsors to provide patients with investigational drugs is key to facilitating access to investigational drugs, these incentives must be balanced with safety precautions. Indeed, most investigational drugs prove either unsafe or ineffective in clinical testing.²⁰³ The Trickett Wendler Right to Try Act overlooks this reality by failing to define what constitutes adequate informed consent in the specific context of accessing investigational therapies without FDA consent.²⁰⁴

To ensure that patients fully understand the risks of taking investigational drugs—specifically, that investigational drugs are unlikely to cure or improve

199. See *Expanded Access: Information for Patients*, *supra* note 86. While some insurers will cover the cost of investigational therapies, this is not always the case. See *id.* (reminding patients that “most insurance companies will not pay for access to an investigational drug”). Accordingly, this Note assumes that if the drug sponsor will not pay for the drug, the patient will have to bear the cost of the investigational therapy.

200. See Tribble & Lupkin, *supra* note 101 (reporting that the average price of an orphan drug is \$111,820 per year).

201. See S. 204.

202. While health insurance companies may also be able to afford the costs of investigational therapies, compelling them to pay for experimental drugs would not incentivize drug makers to develop drugs to the same extent that reducing the cost of a drug's NDA would, and it could even cause insurance premiums to rise, which certainly would not help patients. See Tribble & Lupkin, *supra* note 101.

203. See Transcript of Hearing Before the Subcommittee on Health of the House Committee on Energy and Commerce, Examining Patient Access to Investigational Drugs 127 (Oct. 3, 2017) (unpublished transcript) (statement of Dr. Ellen V. Sigal, Chair & Founder, Friends of Cancer Research); *The Cruel Sham That Is “Right-to-Try” Is One Step Closer to Being Federal Law*, *supra* note 168.

204. See S. 204 § 2(a). Rather, the Act blankly requires that patients give physicians “written informed consent regarding the eligible investigational drug.” *Id.* This contrasts drastically with the requirements of the Expanded Access program, in which the FDA considers whether the risk of a patient taking the investigational drug exceeds the risk of leaving the patient's disease untreated, and at least one member of an IRB decides whether the risks of a patient taking the drug outweigh the potential benefits of taking the drug, and whether the patient's informed consent is reasonable in light of these risks. See *supra* Part I.C. Since Senate Bill 204 does not require FDA or IRB approval for a patient to access an investigational drug, there is currently no guarantee that a patient's informed consent to using an inherently risky investigational drug is reasonable.

disease symptoms, and may seriously harm patients—the House of Representatives should define what constitutes adequate informed consent in the Right to Try context.²⁰⁵ Because most patients are not trained to interpret scientific data, the House should mandate that the patient’s physician counsel the patient (in terms the patient is likely to understand) on the investigational drug’s clinical trial results, the risks and benefits of the drug treatment for that particular patient, as well as the general risks of taking experimental drugs.²⁰⁶ Such counseling will help patients to make informed decisions regarding their treatment options and will thus promote patient safety. Additionally, given the concerns about the time it takes for patients to access investigational drugs,²⁰⁷ lawmakers should require that patient counseling occur within seventy-two hours of a pharmaceutical company agreeing to dispense an investigational drug to a patient.

The informed-consent measures described above will certainly burden doctors. However, this burden must fall somewhere, because ensuring patients are adequately informed is essential to preserving their safety in the wake of facilitated access to investigational drugs.²⁰⁸ As noted previously, most patients are not trained to interpret scientific data and may struggle to properly measure the risks and benefits of taking an experimental therapy.²⁰⁹ Moreover, considering that the Trickett Wendler Right to Try Act applies only to patients with life-threatening illnesses, a patient’s judgment in deciding whether to try an investigational therapy could be clouded by desperation to live.²¹⁰

Furthermore, drug makers make drugs for profit. Having to devote resources to counseling patients, on top of having to manage Right to Try

205. Testifying before the House Committee on Energy and Commerce on right-to-try legislation, Dr. Sigal argued that informed consent is vital to preserve patient safety:

[P]rovisions for informed consent are essential.

A significant majority of early-phase drugs are dangerous and ultimately prove ineffective with upwards of 90 percent never being brought to the market.

....

Patients petitioning for expanded access deserve accurate information about whether the potential benefits outweigh the risks. This is highly personal calculus

....

. . . [W]e must not subject patients to false hope or unacceptable side effects.

Transcript of Hearing Before the Subcommittee on Health of the House Committee on Energy and Commerce, *supra* note 203, at 127–28.

206. Some right-to-try critics argue that, without FDA oversight, doctors could coerce life-threateningly ill patients into taking experimental drugs. *See, e.g.*, Feibel, *supra* note 172 (quoting Dr. R. Adams Dudley as asking, “If we take the FDA out of it, how do we protect people from physicians . . . that . . . will want to prey on their desperation?”). The House of Representatives can minimize the risk of physicians coercing vulnerable patients by making clear exactly what physicians must tell their patients about investigational drugs in the right-to-try context and thus help patients make informed decisions about their treatment options.

207. *See* Corieri, *supra* note 104.

208. *See* Transcript of Hearing Before the Subcommittee on Health of the House Committee on Energy and Commerce, *supra* note 203, at 127–28.

209. *See supra* notes 205–06 and accompanying text.

210. *See* Fisher, *supra* note 166, at 58 (“[G]etting early access to new drugs is no panacea, yet desperate patients continue to ask for it.”).

requests²¹¹ and absorb the costs of investigational drugs—as this Note proposes they should²¹²—seems to be an undue burden that could dissuade drug makers from utilizing the Right to Try pathway or perhaps even from developing drugs at all. This certainly would not help to increase the availability of rare-disease treatments.

This leaves doctors to counsel patients on the risks of taking experimental drugs. And while it is impossible to predict how many patients will seek to use the Right to Try pathway, the relatively low number of annual Expanded Access requests indicates that legislators need not fear imposing an unbearable or overwhelming burden on physicians.²¹³

Moreover, to further protect patients, the House of Representatives should amend the Trickett Wendler Right to Try Act to require that patients request investigational drugs anonymously. Under the Expanded Access program, patients are increasingly using social media to request investigational drugs.²¹⁴ This tactic is unfair, according to bioethics professor Arthur Caplan, because “[p]eople who are photogenic have an advantage. You’re not going to see some 60-year-old alcoholic in one of these [successful investigational drug] appeals.”²¹⁵ The House should thus amend the Act to require that Right to Try requests are made anonymously—in other words, without personal information, like a patient’s name, appearance, income, or marital status. Without a patient’s personal information, drug makers will be less inclined to be swayed by sympathy²¹⁶ and will, instead, be better able to objectively decide whether to provide a patient with an experimental drug.

Lastly, the House of Representatives should add a provision to the Trickett Wendler Right to Try Act to help encourage patient participation in clinical trials. Accessing a drug through a clinical trial, as opposed to the Expanded Access or Right to Try pathways, is better for patients and drug sponsors alike.²¹⁷ However, patients may not be able to access clinical trials due to

211. *See id.* at 59.

212. This Note argues that drug sponsors, as opposed to patients or health insurers, should absorb the costs of providing patients with investigational drugs through the Right to Try pathway and should be incentivized to do so by receiving a reduction off the cost of the investigational drug’s NDA. *See supra* notes 200–01 and accompanying text.

213. For example, the FDA received only 1757 Expanded Access requests in 2016. *See* Michael Mezher, *FDA Approved Nearly All Expanded Access Requests in FY2016*, REG. AFF. PROFESSIONALS SOC’Y (Mar. 20, 2017), <http://www.raps.org/Regulatory-Focus/News/2017/03/20/27157/FDA-Approved-Nearly-All-Expanded-Access-Requests-in-FY2016/> [<https://perma.cc/4YUV-4ZT9>].

214. *Study: Social Media Is Affecting Patients’ Access to Investigational Drugs*, RELIAS (Jan. 1, 2017), <https://www.ahcmedia.com/articles/139817-study-social-media-is-affecting-patients-access-to-investigational-drugs> [<https://perma.cc/Y3YU-6DP2>]; *see also* Fisher, *supra* note 166, at 59 (describing the “onslaught” of experimental drug requests made through social media as “unrelenting”).

215. Fisher, *supra* note 166, at 59.

216. *See id.* at 60. For example, Dr. Amrit Ray, the chief medical officer of pharmaceutical giant Johnson & Johnson, has described experimental drug requests as “heart-wrenching” and claims that deciding whether to grant a patient access to such a drug is “one of the most difficult decisions [he] face[s] as a physician.” *Id.*

217. *Expanded Access FAQ*, NORD 1 (Aug. 2016), https://rarediseases.org/wp-content/uploads/2016/08/NORD-Expanded-Access-FAQ_Aug2016.pdf [<https://perma.cc/W3HX-FNSV>].

factors like location and may be dissuaded from participation due to responsibilities like childcare and work.²¹⁸ The House should therefore establish a fund to help patients offset some of the costs of participating in clinical trials not covered by trial sponsors, such as lost income and childcare.²¹⁹ This would help more patients participate in clinical trials, which would not only give patients increased access to investigational therapies but also help drug makers recruit more racially, geographically, and socioeconomically diverse patient populations on which to study their products.²²⁰ Such a fund could also help drug makers better manage drug supplies. Instead of doling out drugs on an ad hoc basis through the Expanded Access and Right to Try pathways, drug companies would have better control over their drug supplies and thus reduce the expenditures associated with drug development.

CONCLUSION

As the Eteplirsen story illustrates, despite congressional efforts to facilitate orphan-drug development, rare-disease treatments continue to be in great demand. That one in ten Americans suffers from a rare disease and that most rare diseases lack an FDA-approved therapy confirm that rare-disease patients urgently need medical treatments.

If enacted as this Note suggests—by balancing the need for rare-disease treatments with the need for patient safety—the 21st Century Cures Act and the Trickett Wendler Right to Try Act could help meet the unmet therapeutic needs of rare-disease patients. Specifically, if the FDA carefully scrutinizes the source and substance of patient experience data submissions, the 21st Century Cures Act could facilitate the development of rare-disease treatments. The systematic collection of patient experience data may help to build knowledge of rare diseases so that, eventually, doctors can more easily diagnose these diseases and drug makers can develop more precise treatments.

In the short term, the Trickett Wendler Right to Try Act could help fulfill the more immediate needs of seriously ill rare-disease patients by allowing them to at least attempt to treat their illnesses with experimental drugs. However, these short-term needs can only be properly fulfilled if drug makers are incentivized to provide patients with experimental drugs and patients give adequate informed consent to take them.

Certainly, the 21st Century Cures Act and the Trickett Wendler Right to Try Act will not instantly remedy the orphan-drug development, approval, and access processes such that all rare-disease patients will instantly have access to safe, effective treatments. If enacted carefully and in tandem,

218. See Jennifer E. Miller et al., *Characterizing Expanded Access and Compassionate Use Programs for Experimental Drugs*, 10 BMC RES. NOTES, July 2017, at 1, 3; see also *supra* note 86 and accompanying text.

219. See *Clinical Trial Financial Assistance*, *supra* note 86.

220. Miller et al., *supra* note 218, at 3.

however, these laws could facilitate both short- and long-term access to drugs that might benefit patients suffering from rare diseases.