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Jordan Paradise

*Loyola University Chicago, School of Law, jparadise@luc.edu*

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# THREE FRAMINGS OF “FASTER” AT THE FDA AND THE FEDERAL RIGHT TO TRY

JORDAN PARADISE, J.D.†

## I. INTRODUCTION

In May 2018, Congress passed the controversial Right to Try Act (“RTT Act”), creating a process for terminally ill patients to request access to investigational drugs.<sup>1</sup> The federal RTT Act is not the first legal mechanism that fosters quicker access to investigational drugs.<sup>2</sup> This new right to try is distinct from existing pathways created by law, regulation, or federal administrative agency policy. Various mechanisms facilitated by the U.S. Food and Drug Administration (“FDA”) are significantly more substantial and important in the context of “faster” access to therapeutic products.<sup>3</sup> These mechanisms lie along a spectrum of product development spanning investigational new drug status to postmarket studies and surveillance. I categorize these mechanisms into three areas: *expansion*,<sup>4</sup>

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1. This article uses the term “drugs” to refer both to pharmaceutical drugs and biological drugs.

2. *Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers*, U.S. FOOD & DRUG ADMIN., 1, <https://www.fda.gov/media/85675/download> (last updated Oct. 2017).

3. Janet Woodcock and Peter Marks, *Delivering Promising New Medicines Without Sacrificing Safety and Efficacy*, U.S. FOOD & DRUG ADMIN. (Aug. 27, 2019), <https://www.fda.gov/news-events/fda-voices/delivering-promising-new-medicines-without-sacrificing-safety-and-efficacy>.

4. Expansion describes a change from something smaller to something larger; here, both an expansion of access to a larger patient population and an expansion of input from a larger stakeholder population.

*acceleration*,<sup>5</sup> and *extension*.<sup>6</sup> The RTT Act is an expansion mechanism, because it expands patient access to investigational new drugs as an alternative mechanism to the FDA's longstanding expanded access program.<sup>7</sup> As the Senate noted, the RTT Act "does not establish a new entitlement or modify an existing entitlement, or otherwise establish a positive right." Rather, it "is consistent with and will act as an alternative pathway alongside existing expanded access policies of the Food and Drug Administration."<sup>8</sup>

This article positions the new RTT Act in proper context and explores additional FDA mechanisms that serve to speed up patient access. Part I discusses the content and scope of right to try legislation, as well as the reasons in support of and in opposition to the law. The enacted legislation is only four pages long and introduces a concise procedure for requests for access to investigational drugs.<sup>9</sup> The article next examines FDA mechanisms for expansion in Part II, comparing the RTT Act with the current expanded access program at the FDA. Part II explores two mechanisms of expansion at the FDA: (1) expanded access for patients to investigational drugs and devices ("expanded access" program) and (2) expanded input from patients about experiences with drugs and devices under review at the FDA ("patient experience" data). This expansion of patient input was initiated and implemented within the FDA but further directed by provisions within the 21st Century Cures Act.<sup>10</sup>

Part III analyzes several mechanisms of accelerated review and approval at the FDA, including Fast Track status, priority review, accelerated approval, Orphan Drug status, and Breakthrough designation of promising therapeutics. These hastened mecha-

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5. Acceleration describes procedures for rapid review and approval of products showing promise to address life-threatening conditions or unmet medical needs.

6. Extension describes an increase in the time period allotted for something; here, an extension of clinical trial phases into the postmarket timeframe.

7. See *Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers*, *supra* note 2, at 2 (discussing removal of regulations on treatment use and current categories of expanded access).

8. Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, Pub. L. No. 115-176, § 3(4), 132 Stat. 1372, 1374 (2018) (codified as amended at 21 U.S.C. 360bbb-0).

9. See generally SUSAN THAUL, CONGR. RES. SERV., R45414, RIGHT TO TRY: ACCESS TO INVESTIGATIONAL DRUGS, <https://crsreports.congress.gov/product/pdf/R/R45414> (last updated Nov. 27, 2018).

10. 21st Century Cures Act, Pub. L. No. 114-255, §§ 3001–3004, 130 Stat. 1033, 1083–85 (2016) (codified as amended at 21 U.S.C. 360bbb-8c).

nisms of review and approval are poorly understood, leading to confusion and misunderstanding by physicians and patients alike.<sup>11</sup> They also alter the foundational new drug approval framework originally set forth by Congress in the Kefauver-Harris Drug Amendments enacted in 1962, which strengthened the drug approval process to include not only premarket safety review but also a demonstration of substantial evidence of efficacy through “adequate and well-controlled” clinical trials.<sup>12</sup> Recent empirical scholarship informs this Part, revealing that the growing array of statutory mechanisms to speed up clinical trials, review, and approval are cutting away at longstanding protections afforded by robust measures of safety and efficacy. Part IV discusses extension at the FDA, particularly the extension of evidence gathering in postmarket clinical trials to support showings of safety and efficacy. The article concludes with several reflections on the relationship of the federal RTT Act to these FDA mechanisms of “faster access,” as well as potential implications of expansion, acceleration, and extension on patient safety, patent protections, and drug costs.

## II. THE HISTORY AND HYPE OF THE RIGHT TO TRY ACT

The RTT Act, the federal legislation with the empowering and “crowd-pleasing” title,<sup>13</sup> establishes a procedure by which patients suffering from terminal illness can work with their physician to request access to pharmaceuticals in early-stage clinical trials.<sup>14</sup> The title of the RTT Act is in fact a misnomer, as the legislation provides merely a right to ask the drug sponsor for permission to use the drug, rather than a definitive grant of access to it.<sup>15</sup> The concept is not a novel one, as the FDA has a longstanding expanded

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11. See *Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers*, *supra* note 2, at 2 (describing the FDA’s guidance on implementation of the regulation).

12. Drug Amendments Act of 1962, Pub. L. 87-781, 52 Stat. 1049, 1052 (codified at 21 U.S.C. § 301 et seq).

13. Claudia Wallis, *The So-Called Right to Try Law Gives Patients False Hope*, SCI. AM. (Sept. 1, 2018), <https://www.scientificamerican.com/article/the-so-called-right-to-try-law-gives-patients-false-hope>.

14. See *Right To Try*, U.S. FOOD & DRUG ADMIN, <https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try> (last updated Jan. 14, 2020).

15. Roseann B. Termini, *The Latest “Federal Movement” in the Food and Drug Law Arena: The Federal Right-to-Try or Rather Right-to-Know and Thus Request Investigational Therapies for Individuals with A Life-Threatening Disease or Condition*, 16 IND. HEALTH L. REV. 101, 118 (2018).

access policy and process that accomplishes the same end result, though in a more public health and safety-focused manner.<sup>16</sup>

National coverage of the rights of patients to access investigational drugs has been prominent in the last few years due to several factors, including patient advocacy campaigns through social media, its portrayal in the critically acclaimed film *Dallas Buyers Club*, and widespread enactment of state right to try bills.<sup>17</sup> The outcomes of two legal cases have also shaped the debate in this area. Nearly a decade ago, in *Abigail Alliance v. von Eschenbach*, the D.C. Circuit held that terminally ill patients had no fundamental right to experimental therapy that had not yet received approval by the FDA.<sup>18</sup> Abigail Alliance had petitioned the FDA to promulgate new regulations allowing drug sponsors to market investigational new drugs to terminally ill patients once the drugs had completed Phase 1 safety trials.<sup>19</sup> After the FDA denied the petition, Abigail Alliance filed a lawsuit alleging violation of a constitutionally protected right.<sup>20</sup> This outcome followed a previous Supreme Court case, *U.S. v. Rutherford*, where the Court held that there was no special right for terminally ill patients to access a drug that was subject to a pending new drug application where safety and efficacy had not yet been established by the FDA.<sup>21</sup>

The RTT Act, signed into law in May 2018, follows legislation in 41 states that provided a mechanism to request access to investigational drugs.<sup>22</sup> A brainchild of the Goldwater Institute, state right to try legislation emphasized patient autonomy and liberty in making choices about treatment options in the face of life-threatening disease.<sup>23</sup> Supporters of the RTT Act argue that the federal legislation removes unnecessary barriers caused by regulation, ensures timely access, reduces inequalities for individuals not able to travel

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16. *Id.* at 113–16 (discussing FDA action prior to the RTT Act).

17. Sam Adriance, *Fighting for the “Right To Try” Unapproved Drugs: Law as Persuasion*, 124 YALE L. J. FORUM, 148, 148–151 (Dec. 4, 2014), <https://www.yalelawjournal.org/forum/right-to-try-unapproved-drugs>.

18. *Abigail Alliance v. von Eschenbach*, 495 F.3d 695, 697 (D.C. Cir. 2007). The FDA subsequently revised regulations to allow requests for access to investigational drugs following completion of Phase 1 clinical trials in 2009. 21 C.F.R. § 312 (2009).

19. *Abigail Alliance*, 495 F.3d at 699.

20. *Id.* at 700.

21. *U.S. v. Rutherford*, 442 U.S. 544, 553 (1979).

22. Termini, *supra* note 15, at 102–03.

23. Jacqueline Howard, *What You Need to Know About the Right To Try Legislation*, CNN, <https://www.cnn.com/2018/03/22/health/federal-right-to-try-explainer/index.html> (last updated May 29, 2018, 1:50 PM), .

abroad to access the drug in another country, and offers hope to terminally ill patients.<sup>24</sup>

Colorado enacted the first state right to try law in May 2014.<sup>25</sup> While state right to try laws vary, the key requirements are largely consistent: the patient must have a terminal diagnosis; the drug requested must have passed Phase I clinical trial safety testing; the healthcare provider must recommend the drug based on their medical opinion of the patient; and the patient must give informed consent.<sup>26</sup> The federal legislation likely impliedly preempts these state laws despite no express preemption provision within the statute.<sup>27</sup>

The RTT Act is a short piece of legislation consisting of one substantive section that amends the Food, Drug and Cosmetic Act by adding a new Section 561B followed by a “Sense of the Senate” section.<sup>28</sup> The legislation provides “eligible patients” with a “life-threatening disease or condition” who have “exhausted all approved treatment options” and are “unable to participate in a clinical trial involving the investigational drug” with the ability to request access from the drug sponsor.<sup>29</sup> The request must be certified by a physician in good standing and who may not be compensated for that certification.<sup>30</sup> The patient must provide written informed consent, though the process is not subject to FDA informed consent requirements.<sup>31</sup>

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24. D. Carrieri et al., *The Ethical Plausibility of the “Right To Try” Laws*, 122 CLIN. REV. ONCOLOGY 64, 66 (2018). “Hope is a powerful drug.” M.E. Blair Holbein et al., *Right Now, In the Right Way: U.S. Food and Drug Administrations’ Expanded Access Program and Patient Rights*, 2 J. CLIN. & TRANSL. SCI. 115, 117 (2018).

25. D. Carrieri et al., *The Ethical Plausibility of the “Right To Try” Laws*, 122 CLIN. REV. ONCOLOGY 64, 64 (2018).

26. *Id.*

27. Mark Borreliz et al., *Federal “Right to Try”: Don’t Disregard Your State Laws Yet!*, JD SUPRA (June 13, 2018), <https://www.jdsupra.com/legalnews/federal-right-to-try-don-t-disregard-90983>.

28. See Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, Pub. L. No. 115-176, § 3(4), 132 Stat. 1372, 1374 (2018) (codified as amended at 21 U.S.C. 360bbb-0) §§ 2(a), 3. A prior piece of legislation, the 21st Century Cures Act, contained provisions requiring drug manufacturers and distributors to make public their expanded access policies, otherwise termed compassionate use, for investigational drugs undergoing clinical trials. 21st Century Cures Act, Pub. L. No. 114-255, § 3032, 130 Stat. 1033, 1100-01 (2016) (codified as amended at 21 U.S.C. § 360bbb).

29. 21 U.S.C. § 360bbb-0a(a)(1)(A)-(B).

30. 21 U.S.C. § 360bbb-0a(a)(1)(B).

31. 21 U.S.C. § 360bbb-0a(a)(1)(C).

Under the RTT Act, an “eligible investigational drug” is a drug for which Phase 1 clinical trials have been completed, no existing approval or license exists, and an application has been filed or is under investigation in a trial to support a claim of effectiveness. Further, these drugs are subject to an active investigational new drug (“IND”) and must not be discontinued by the manufacturer.<sup>32</sup> Investigational drugs subject to a clinical hold imposed by the FDA are not eligible.<sup>33</sup> These provisions make clear that the RTT Act is applicable to both drugs and biologics but not medical devices.<sup>34</sup> Such eligible investigational drugs are exempt from select misbranding and new drug approval requirements, provided they comply with regulations pertaining to investigational drugs.<sup>35</sup>

If a sponsor or individual who “manufactures, distributes, prescribes, or dispenses” a drug introduces or delivers that drug for introduction into interstate commerce, or provides an eligible investigational drug,” then that entity or person can charge for direct costs of the particular drug, including costs to manufacture, acquire, and ship and handle.<sup>36</sup> The drug is exempt from labeling for adequate directions for use,<sup>37</sup> but is subject to labeling for INDs<sup>38</sup> and promotion of INDs.<sup>39</sup> The sponsor, manufacturer, prescriber, dispenser, or other individual entity is also exempt from liability with respect to acts or omissions under the RTT Act unless it engages in “reckless or willful misconduct, gross negligence, or an intentional tort.”<sup>40</sup> The RTT Act does expressly provide that private actions under state product liability, tort, consumer protection law, and warranty law are not impacted.<sup>41</sup>

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32. 21 U.S.C. § 360bbb-0a(a)(2).

33. See *Right to Try*, *supra* note 14.

34. The RTT Act references both 21 U.S.C. § 355 (pertaining to new drugs) and the Public Health Service Act, 21 U.S.C. § 351 (pertaining to biologics). 21 U.S.C. § 360bbb-0a(a)(2)(C).

35. Specifically, 21 U.S.C §§ 352(f), 353(b)(4), 355(a), and 355(i). 21 U.S.C. § 360bbb-0a(b) (2018).

36. 21 U.S.C. § 360bbb-0a(b) (referencing 21 CFR §§312.6–8(d)(1)).

37. 21 U.S.C. § 360bbb-0a(b) (referencing 21 U.S.C. § 352(f)).

38. 21 U.S.C. § 360bbb-0a(b) (referencing 21 CFR § 312.6).

39. 21 U.S.C. § 360bbb-0a(b) (referencing 21 CFR § 312.7).

40. 21 U.S.C. § 360bbb-0a(b)(1)(B).

41. See Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina *Right to Try Act of 2017*, Pub. L. No. 115-176, § 3(4), 132 Stat. 1372, 1374 (2018) (codified as amended at 21 U.S.C. 360bbb-0).

While the RTT Act excludes the FDA from the process, expressly creating an “alternative pathway”<sup>42</sup> for patients, several sections of the RTT Act reference the FDA.<sup>43</sup> Congress prohibits the FDA from using any clinical outcome to delay or adversely affect review or approval unless the Secretary of Health and Human Services makes a determination that use is critical to establishing the safety of the drug or the sponsor requests the use of such outcomes.<sup>44</sup> As described by the FDA, the limited role of the agency in the right to try process is “receipt and posting of certain information submitted regarding Right to Try use.”<sup>45</sup> Annual reporting of any use of the drug, including doses supplied, number of patients treated, uses for which the drug is made available, and any known serious adverse events is to be posted on the FDA website.<sup>46</sup> The agency states on its website that it “will post a consolidated annual summary report of Right to Try Act use.”<sup>47</sup> As of July 2020, such a report is not yet available on the FDA’s website.

The RTT Act has been widely criticized by bioethicists, patient groups, physicians, lawyers, and scientists for several significant reasons.<sup>48</sup> At a very basic level, critics argue that it gives patients

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42. *Id.*

43. *Id.* § 2–3.

44. 21 U.S.C. § 360bbb-0a(c)(1).

45. See *Right to Try*, *supra* note 14.

46. 21 U.S.C. § 360bbb-0a(d)(2).

47. See *Right to Try*, *supra* note 14.

48. See, e.g., D. Carrieri, F.A. Peccatori, and G. Boniolo, *The Ethical Plausibility of the “Right To Try” Laws*, 122 CLIN. REV. ONCOLOGY 64, 66 (2018) (citing M.J. Rubin ad K.R. Matthews, *The Impact of Right to Try Laws on Medical Access in the United States*, 66 THE BAKER INST. POL’Y REP. 1, 8–10 (2016)); Nicole Karlis, *Patient Advocacy Groups Scratch Their Heads Over Trump’s Right to Try Act*, SALON (June 1, 2018, 5:22 PM), <https://www.salon.com/2018/06/01/patient-advocacy-groups-scratch-their-heads-over-trumps-right-to-try-act> (characterizing advocacy groups as perplexed by the bill and at Trump’s statement that it will save hundreds of thousands of lives); Rachel Roubein, *40 Patient Advocacy Groups Oppose Right to Try Drug Bill*, THE HILL (Feb. 6, 2018, 4:07 PM), <https://thehill.com/policy/healthcare/372600-40-patient-advocacy-groups-oppose-right-to-try-drug-bill> (discussing letter to House from 40 patient advocacy groups who say the bill would “likely do more harm than good”); Michael D. Becker, *I’m the Ideal Person to Support the Right to Try. But I Can’t – It’s a Disaster in the Making*, STATNEWS (Feb. 1, 2019), <https://www.statnews.com/2018/02/01/right-to-try-cancer-fda> (highlighting a terminally ill patient perspective that RTT would “make things worse” focusing on costs and impact on insurance and hospice coverage); James Hamblin, *The Disingenuousness of “Right to Try”*, THE ATLANTIC (June 2, 2018), <https://www.theatlantic.com/health/archive/2018/06/right-to-try/561770/>; David Gorski, *Right to Try is Now Law. Let Patients Beware!*, SCIENCE-BASED MED. (Jun. 4, 2018), <https://sciencebasedmedicine.org/right-to-try-is-now-law-let-patients-beware/>; Holly Fernandez Lynch et al., *Promoting Patient Interests in Implementing the Federal Right to Try Act*, 320 JAMA 869, 869–70 (2018). However, despite intense opposition, there was



false hope.<sup>49</sup> Even the name itself implies that it grants an affirmative right rather than the mere option and process to officially request treatment. The legislation does not compel drug sponsors to acquiesce.<sup>50</sup> More significantly, the right to try process does not involve the oversight and active involvement of the FDA, which could harm patients.<sup>51</sup> Major patient advocacy groups argue that the current expanded access mechanisms are effective in providing critically ill patients a safe method of receiving unapproved therapies and that removing FDA oversight poses the same dangers that FDA law has evolved to counteract.<sup>52</sup> Patient advocacy groups also cite ethical concerns with the inability to provide patients seeking access to unapproved therapies the same protections that patients in clinical trials are afforded.<sup>53</sup>

Likewise, physicians have also expressed concern with the bill's removal of FDA oversight, urging that removal of FDA oversight could allow patients to become "victims to the likes of snake oil salesmen offering 'treatments' that could kill rather than cure."<sup>54</sup> Doctors urge that the elimination of the FDA from the process effectively removes the mechanism by which the success of treatments is monitored, weakening the role of the agency and compromising both patient safety and the public trust.<sup>55</sup> Physicians who are familiar with the FDA's expanded access policies emphasize that the RTT Act is redundant as it is not the FDA that obstructs patient access to unapproved treatments, but rather drug developers and manufacturers.<sup>56</sup> Legal commentators similarly criticize the RTT

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some patient advocacy support for the bill. See, e.g., Larry Luxner, *Rare Disease Groups, Patients Differ on Right to Try Bill Before U.S. Congress*, ALS NEWS TODAY (Feb. 12, 2018), <https://alsnewstoday.com/2018/02/12/rare-disease-groups-patients-differ-on-right-to-try-bill-before-us-congress>.

49. Wallis, *supra* note 13.

50. *Id.*

51. Right to Try Coalition Letter to Speaker of the House Paul Ryan and Minority Leader Nancy Pelosi (Feb. 6, 2018) ("Both [S.204 and H.R.878] remove the Federal Drug Administration from the initial approval process for accessing an investigational therapy outside of a clinical trial.") (on file with the International Society for Stem Cell Research) [hereinafter *Right to Try Coalition Letter*].

52. *Id.*

53. *Id.*

54. Alexandra Sifferlin, *The 'Right-To-Try' Bill has Passed Congress. Here's Why Doctors are Concerned*, TIME (Feb. 5, 2018, 2:15 PM), <https://time.com/5132892/right-to-try-bill-terminal-illness>.

55. *Id.*; see also Right to Try Coalition Letter, *supra* note 51.

56. See Right to Try Coalition Letter, *supra* note 51 ("When access to a therapy is denied to a patient, it is generally the company that denies the request. . .").

Act for removing informed consent and Institutional Review Board (“IRB”) protections, failing to restrict costs and provide mechanisms or incentives for insurance coverage, and eliminating FDA-granted incentives to provide investigational drugs, among other things.<sup>57</sup>

Practically speaking, it is also unclear whether pharmaceutical sponsors will even utilize the RTT Act or whether they will instead continue to coordinate with the FDA’s expanded access program. With recent streamlining of FDA procedures, drug sponsors report satisfaction with the FDA’s mechanisms.<sup>58</sup> The RTT Act does not remedy the reputational fallout resulting from incidents involving investigational drugs,<sup>59</sup> and the industry may be more inclined to involve the FDA. There is a dearth of information available about instances in which the new RTT Act route has been successful absent the creation of the annual reports by the FDA.<sup>60</sup> An academic medical oncology online resource noted in October 2019 that two patients have secured access to an investigational drug using the RTT Act process: one for brain cancer and the other for amyotrophic lateral sclerosis.<sup>61</sup>

### III. EXPANSION OF PATIENT ACCESS AND PATIENT INPUT

The right to try involves a theoretical expansion of access for terminally ill patients to investigational new drugs that bypasses existing FDA expanded access policies and mechanisms.<sup>62</sup> With recent legislative changes in the 21st Century Cures Act, there are also new provisions involving an expansion in patient input to FDA decision-making processes.<sup>63</sup> Therefore, there are two forms of expansion at

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57. See, e.g., Holly Fernandez Lynch et al., *Promoting Patient Interests in Implementing the Federal Right to Try Act* 320 JAMA 869, 869–70 (2018); Alison Bateman-House and Christopher T. Robertson, *The Federal Right to Try Act of 2017 – A Wrong Turn for Access to Investigational Drugs and the Path Forward*, 178 JAMA INTERNAL MED. 321, 321–22 (2018).

58. Brandon Brown et al., *Assessment of the Right-to-Try Law: The Pros and the Cons*, 59 J. OF NUCLEAR MED. 1492, 1492 (2018).

59. See Wallis, *supra* note 13.

60. See *Right to Try Is Working*, RIGHT TO TRY, <https://righttostry.org/right-to-try-is-working> (last visited June 8, 2020) (note there are few success stories uploaded).

61. Perelman Sch. of Med. at the Univ. of Pa., *How Oncologists Can Ethically Navigate the “Right to Try” Law*, MEDICAL XPRESS (Oct. 22, 2019), <https://medicalxpress.com/news/2019-10-oncologists-ethically-right-to-try-drug-law.html>.

62. Wallis, *supra* note 13.

63. See Kyle T. Edwards, *Good and Bad Patient Involvement: Implementing the Patient-Involvement Provisions of the 21st Century Cures Act at the FDA*, 128 YALE L.J. FORUM 1077, 1086 (2019).

the FDA regarding investigational new products: expanded *access* for patients to investigational drugs and devices through the expanded access program and expanded *input* from patients about drug and device products under review at the FDA.

A. *Expanded Patient Access to Investigational Products*

Expanded access requests, sometimes referred to as “compassionate use” requests, are routinely channeled through the FDA’s Expanded Access Program, which provides access to INDs in certain circumstances.<sup>64</sup> Codified in 1987, the expanded access program has been adjusted over time to streamline the process and increase transparency in agency decisions. The expanded access assessments focus on whether and to what extent individuals facing serious or life-threatening diseases or disorders should be able to access experimental drug treatments that have not yet received FDA approval under the touchstone measures of safety and effectiveness. The federal statute provides for such access to INDs, which is further set forth in FDA regulations.<sup>65</sup> In October 2017, the FDA published guidance for the industry titled *Individual Patient Expanded Use Access Applications: Form FDA 3926*. This guidance introduced a more streamlined process for physician submissions of individual patient requests for compassionate use of experimental drugs undergoing active clinical trials<sup>66</sup> by building on a well-established system of assessment by the FDA, providing a specific format for submission, and reducing the associated paperwork to two pages.<sup>67</sup>

As the 2017 guidance states, under the applicable criteria in the regulations,<sup>68</sup> the FDA must evaluate several key aspects. First, the FDA must determine that the patient has a serious or immediately life-threatening disease or condition and that there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.<sup>69</sup> Second, the FDA must determine

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64. *Expanded Access*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/news-events/public-health-focus/expanded-access> (last updated Apr. 27, 2020).

65. 21 C.F.R. § 312.1 (“This part contains procedures and requirements governing the use of investigational new drugs . . .”).

66. *Guidance for Industry: Individual Patient Expanded Access Applications: Form FDA 3926*, U.S. FOOD & DRUG ADMIN. (June 2016), <https://www.fda.gov/media/91160/download> [hereinafter *Form FDA 3926*].

67. *Id.*

68. 21 C.F.R. §§ 312.305(a), 312.310(a).

69. 21 C.F.R. § 321.305(a)(1).

that the patient cannot obtain the investigational drug under another IND or protocol.<sup>70</sup> Third, the FDA must determine that the potential patient benefit justifies the potential risks of the treatment's use and that those potential risks are not unreasonable in the context of the disease or condition to be treated.<sup>71</sup> The FDA must also determine that providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.<sup>72</sup> Further, the treating physician must determine that the probable risk of the investigational drug to the patient is not greater than the probable risk from the disease or condition.<sup>73</sup>

The goal of the recent draft guidance process and accompanying form is to make the submission process easier on physicians requesting access for patients.<sup>74</sup> The FDA's draft guidance document provides that the physician must first confirm that the manufacturer is willing to supply the drug.<sup>75</sup> The physician must include a letter of authorization (“LOA”) in the request which then allows right of reference to information submitted to the FDA by the drug sponsor.<sup>76</sup> Contents of a request include patient initials, date of submission, clinical information, patient treatment information, the LOA from the drug manufacturer, a physician's qualification statement and information such as name, address, contact information, as well as a request for authorization to use Form FDA 3926, and a certification statement and signature.<sup>77</sup> The physician is then considered a sponsor-investigator and subject to human subject protections contained in 21 C.F.R. 50 and IRB requirements in 21 C.F.R. 56.<sup>78</sup> Both informed consent and IRB authorization must be obtained prior to initiation unless the request is for an emergency individual use.<sup>79</sup> Treatment with the IND may proceed once the FDA notifies the physician, or within thirty days after the FDA receives

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70. *Id.*; see also 21 C.F.R. § 321.310(a)(2).

71. 21 C.F.R. § 321.305(a)(2).

72. 21 C.F.R. § 321.305(a)(3).

73. 21 C.F.R. § 312.310(a)(1).

74. See *Form FDA 3926*, at 1–3.

75. *Id.* at 5.

76. *Id.*

77. 21 C.F.R. § 312.23(a)(1).

78. *Form FDA 3926*, at 5–6.

79. *Id.* at 6.

the completed draft form (once finalized by the FDA).<sup>80</sup> The draft guidance includes a draft Form 3926 as Appendix I.<sup>81</sup>

The recent changes have undoubtedly improved the expanded access program, as the procedure has long been fraught with complaints about process, transparency, and outcomes. Complaints include extensive preparation time for physicians, lengthy FDA review times, a lack of reporting on drug sponsor determinations, uncertainty on coverage for the drugs, effect on clinical trial enrollment, and liability issues.<sup>82</sup> Despite these complaints, the FDA approves over 99% of more than one thousand requests per year.<sup>83</sup> The FDA reports on expanded access requests on its website.<sup>84</sup> However, even if an access request is granted by the FDA, neither the statute nor the regulations mandate that the drug sponsor provide the investigational drug.<sup>85</sup> Of note, not a single product liability case has resulted from provision of access to an investigational product through the FDA's expanded access program.<sup>86</sup>

#### *B. Reconciling the Right to Try with the FDA's Expanded Access Program*

The RTT Act intentionally establishes a system that bypasses historical mechanisms of patient access to investigational products through the FDA's expanded access program. Ultimately, the RTT Act will likely have little or no impact on patient access to investigational drugs because it does not disturb the existing expanded access program; it only creates an alternative pathway. There are also early indications that the pharmaceutical industry is reluctant to provide access through the RTT Act process rather than the established expanded access program. There are also several significant problems that the RTT Act pathway introduces.

First, the RTT Act eliminates the FDA from the process, relegating their role to one of merely publishing annual reported data

80. *Id.* at 6–7.

81. *Id.* at 6 (“Form FDA 3926 . . . may be found on FDA’s website at <https://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm>.”).

82. See Jonathan J. Darrow et al., *Practical, Legal, and Ethical Issues in Expanded Access to Investigational Drugs*, 372 *NEW ENG. J. MED.* 279, 282, 284 (2015).

83. Bateman-House & Robertson, *supra* note 57, at 321; Holbein et al., *supra* note 24, at 115.

84. See *Expanded Access*, *supra* note 64.

85. M.E. Blair Holbein et al., *Access to Investigational Drugs: FDA Expanded Access Programs or “Right-to-Try” Legislation?*, 8 *J. CLINICAL & TRANSLATIONAL SCI.* 526, 526 (2015).

86. Lynch et al., *supra* note 57, at 870.

on use of the RTT Act pathway submitted by industry.<sup>87</sup> While the RTT Act requires informed consent, nowhere does it define and describe the process; it is not robust “informed consent” as required by FDA regulations, which mandates IRB approval and express requirements as contained in the Code of Federal Regulations.<sup>88</sup> Stripping away long-established informed consent threatens patient safety and transparency. It also significantly reduces the quality and amount of information given to patients.

Second, and relatedly, without the FDA involved, there are no requirements for rigorous analysis and reporting of clinical outcomes from use of investigational drugs.<sup>89</sup> In fact, the RTT Act prohibits the FDA from using clinical data derived from right to try uses as part of review and approval of products.<sup>90</sup> The FDA currently holds the position that it maintains the ability to institute clinical holds on an investigational product in the face of clinical data, which then would cause the drug to be outside the scope of the right to try definition, halting a patient’s ability to maintain access.<sup>91</sup> It remains to be seen whether courts will agree with the FDA on this position based on Congressional intent and the statutory language. One scholar offers that “because of the requisite confidentiality in the drug development process, the FDA is often the only repository of detailed information about a test outside the manufacturer.”<sup>92</sup> A failure to integrate important outcome data, including adverse events, into product review seriously compromises patient safety.

Third, language in the RTT Act allows the manufacturer or distributor of the investigational drug to charge for the product, thereby opening the floodgates to exorbitant costs for hopeful patients.<sup>93</sup> The RTT Act lacks any insurance coverage provisions, forcing patients to pay out of pocket for both the drug itself and for costs, including travel and accommodations during treatments, as

87. Holbein et al., *supra* note 85, at 526.

88. See Jennifer Piel, *Informed Consent in Right-To-Try Cases*, 44 J. AM. ACAD. PSYCHIATRY L. 290, 295 (2016).

89. Gail A. Van Norman, *Expanding Patient Access to Investigational Drug Single Patient Investigational New Drug and the “Right to Try”*, 3 J. AM. C. CARDIOLOGY: BASIC TRANSLATIONAL SCI. 280, 290 (2018).

90. Steven Joffe & Holly Fernandez Lynch, *Federal-Right-to-Try Legislation—Threatening the FDA’s Public Health Mission*, 378 NEW ENG. J. MED. 695, 696 (2018).

91. 21 U.S.C. § 355(i)(3).

92. M.E. Blair Holbein et al, *Right Now, In the Right Way: U.S. Food and Drug Administrations’ Expanded Access Program and Patient Rights*, 2 J. CLIN. & TRANSL. SCI. 115, 115 (2018).

93. Bateman-House & Robertson, *supra* note 57, at 321.

well as any follow-up medical care.<sup>94</sup> The language allowing for the collection of direct costs has the potential to create a hefty price tag for the access alone.<sup>95</sup> The expanded access program requires the manufacturer to acquire authorization from the FDA to charge the patient; the FDA will authorize billing when the sponsor demonstrates that it could not conduct the clinical trial without charging for the drug because of extraordinary cost to that sponsor.<sup>96</sup>

Fourth, the liability exemptions will likely not be enough to sway sponsors to utilize that route to provide access to patients. Under both the FDA's expanded access program and RTT Act, a manufacturer is not mandated to provide access to the product, and many, if not most, will refuse access to avoid liability entirely.<sup>97</sup> The right to try exemption from liability is not unlimited; there may still be a cause of action for reckless or willful misconduct, gross negligence, or intentional tort.<sup>98</sup> The RTT Act also expressly states that private actions under state product liability, tort, consumer protection, and warranty laws are not impacted by the exemption from liability.<sup>99</sup> This language will likely be tested by the courts if a relevant scenario arises, given the almost complete lack of safety tracking, deep analysis of adverse events information, and patient protection. The industry will likely adhere to a "devil that you know" position, continuing to work with the FDA through the expanded access program and well-established mechanisms.

### C. Expanded Patient Input

The FDA has a history of involving patients in the regulatory process, beginning in the late 1980s with the creation of HIV/AIDs patient groups and the subsequent inclusion of patient representatives on advisory committees in 1991.<sup>100</sup> Patient input initiatives

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94. Holbein et al., *supra* note 85, at 526.

95. Kelly Folkers et al., *Federal Right to Try: Where Is It Going?*, 49 HASTINGS CTR. REP. 26, 27–8 (2019).

96. *Charging for Investigational Drugs Under an IND – Questions and Answers*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/media/85682/download> (last visited June 8, 2020); 21 C.F.R. § 312.8(b)(1)(iii).

97. Holbein et al., *supra* note 85, at 526; *see also* Right to Try Coalition Letter, *supra* note 51.

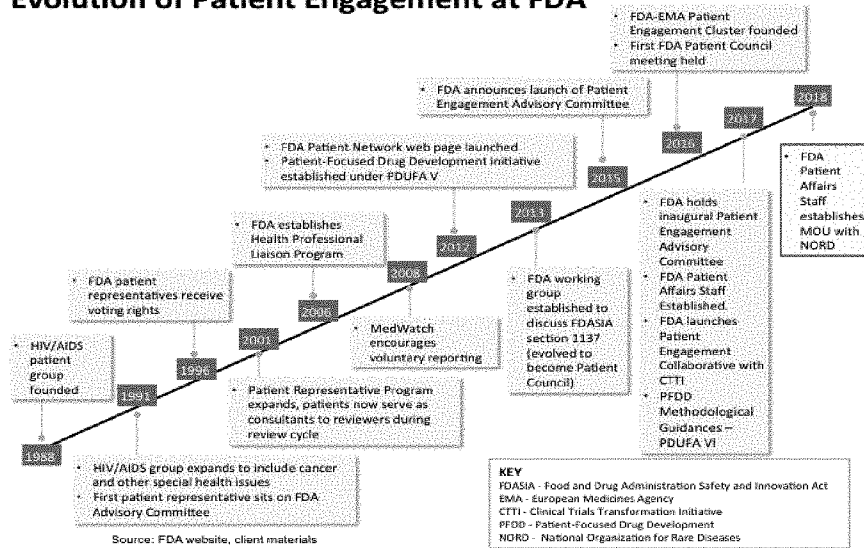
98. *See* Pub. L. 115–176, § 2(b), 132 Stat. 1374 (2018) (codified as amended at 21 U.S.C. 360bbb–0a).

99. *Id.*

100. *Evolution of Patient Engagement at FDA*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/patients/learn-about-fda-patient-engagement/evolution-patient-engagement-fda-text-description> (last updated Apr. 23, 2019).

have developed concurrently with increasing patient advocacy representation in the form of patient advocacy groups and alliances. Figure 1 illustrates FDA activity engaging patients.

**Figure 1**<sup>101</sup>  
**Evolution of Patient Engagement at FDA**



The FDA recently noted:

Patient groups have evolved from patient support, advocacy and basic disease research funding organizations, to being more active in medical product development and assessment. Patients are committed to contributing their views, data, and resources to increase patient-centric medical product innovation, assessment, and regulatory decision-making, and we are committed to assuring that our decisions and actions are informed by patient perspectives.<sup>102</sup>

Most recently, the 21st Century Cures Act introduced additional directives to the FDA to facilitate patient engagement in the

101. *Learn About FDA Patient Engagement*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/patients/learn-about-fda-patient-engagement> (last updated May 8, 2019).

102. CTR. FOR DEVICES AND RADIOLOGICAL HEALTH, U.S. FOOD & DRUG ADMIN., 2016-2017 STRATEGIC PRIORITIES 7.



drug and device approval process.<sup>103</sup> These provisions serve to move “engagement” into the regulatory process in several ways. Various sources trace the close involvement and support of patient advocacy groups with the pharmaceutical industry in the 21st Century Cures Act’s ultimate success.<sup>104</sup> Figure 2 identifies several select sections of the legislation that task the FDA with taking affirmative actions both to bolster patient input as part of the regulatory process itself and to speed the review and market entry of promising products.

**Figure 2: 21st Century Cures Act Provisions<sup>105</sup>**

<u>Section</u>	<u>Description</u>
3001-3004	FDA required to include patient experience data statement at time of drug approval, issue guidance on methods of collection, and report on review of patient experience data.
3011	Creates review mechanism at FDA for biomarkers and other drug development tools.
3021	FDA required to hold public meeting and issue guidance on adaptive designs and statistical modeling for new drug applications.
3022	FDA required to evaluate use of real-world evidence to support new indication of approved drug or postmarket requirements.
3024	FDA may waive or alter informed consent for minimal risk clinical trials.
3031	FDA may rely on qualified data summaries to support new indication for approved drug.
3051	Creates new breakthrough medical device pathway to market.

103. FDA SCI. BD., PROPOSED FDA WORK PLAN FOR 21<sup>ST</sup> CENTURY CURES ACT INNOVATION ACCOUNT ACTIVITIES (2017).

104. See, e.g., Sy Mukherjee, *Everything You Need to Know About the Massive Health Reform Law that Just Passed Congress*, FORTUNE (Dec. 7, 2016), <https://fortune.com/2016/12/07/congress-passes-21st-century-cures> [hereinafter *Everything You Need to Know About the Massive Health Reform Law that Just Passed Congress*].

105. 21st Century Cures Act, Pub. L. No. 114-255, §§ 3001–3004, 3011, 3021–22, 3024, 3031, 3051, 3053, 3058, 130 Stat. 1033, 1083–91, 1095–1100, 1126–1126, 1128–1129 (2016) (codified as amended at 21 U.S.C. 360bbb).

3053	Creates process for use of standards in medical device review.
3058	FDA required to consider least burdensome means for showing reasonable assurance of safety and effectiveness.

Taken together, these provisions expand the scope of information and stakeholders involved in drug review and approval.<sup>106</sup> The legislation requires the FDA to include patient experience data along with review of a sponsor application for approval.<sup>107</sup> This patient experience data is considered data collected by any person that is “intended to provide information about patients’ experience with a disease or conditions.”<sup>108</sup> This includes the impact of the disease or condition, or the accompanying therapy, and preferences regarding treatment.<sup>109</sup> The law also directs the FDA to issue guidance within eighteen months of enactment on methods to collect such information from patients and on use of such information in drug development.<sup>110</sup> The FDA must also publish a report on agency review of patient experience data and use in regulatory decision-making.<sup>111</sup> Many question how the agency will integrate patient experience data into product information that is circulated to consumers and health care professionals; some urge that it will require a separate label to facilitate consumer comprehension of the information.<sup>112</sup>

Congress also requires the FDA to establish a system of qualification for drug development tools, where qualification assures that the tool “can be relied upon to have a specific interpretation

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106. Discussion of these provisions is adapted from Jordan Paradise, *21<sup>st</sup> Century Citizen Pharma*, 44 AM. J. L. & MED. 309, 321–23 (2018).

107. 21st Century Cures Act, Pub. L. No. 114-255, § 3001(b), 130 Stat. 1033, 1084 (2016) (codified as amended at 21 U.S.C. 360bbb-8c). Patient experience data is defined as data that is “collected by any persons (including patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers)” and “intended to provide information about patients’ experience with a disease or condition, including (A) the impact of such disease or condition, or a related therapy, on patients’ lives; and (B) patient preferences with respect to treatment of such disease or condition.” *Id.* § 3001(c), 130 Stat. at 1084.

108. *Id.* § 3001(c)(2).

109. *Id.*

110. *Id.* § 3002(a)–(b).

111. *Id.* § 3004.

112. Sue Sutter, *Patient Experience Data May Require Separate Label, Genentech Suggests*, PINK SHEET 10 (Sept. 25, 2017), <https://pink.pharmaintelligence.informa.com/PS122249/Patient-Experience-Data-Section-Added-To-US-FDA-Drug-Reviews>.

and application in drug development and regulatory review.”<sup>113</sup> Congress urges the FDA to prioritize the qualification of drug development tools based on considerations of severity, rarity, or prevalence of the disease as well as public health priorities.<sup>114</sup> The law contemplates that the process involves a letter of intent, qualification plan, and full qualification package for FDA review.<sup>115</sup> Specific provisions direct the FDA to implement such a qualification process, along with expert consultation, for biomarkers.<sup>116</sup> A biomarker is defined as “a characteristic (such as a physiologic, pathologic, or anatomic characteristic or measurement) that is objectively measured and evaluated as an indicator of normal biologic processes, pathologic processes, or biological responses to a therapeutic intervention.”<sup>117</sup> Legal experts implore the FDA to fully utilize expert consultants in review of biomarker qualification requests, similar to advisory committees for substantive products.<sup>118</sup>

Furthermore, the FDA is tasked with establishment of a program to utilize real world evidence in the assessment of new drug indications and postmarket approval studies.<sup>119</sup> Congress defines real world evidence as “data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than randomized clinical trials.”<sup>120</sup> The FDA is given two years to establish a draft framework for such a program and begin implementation.<sup>121</sup> Congress enumerates required framework contents, which include sources of real world evidence (such as “ongoing safety surveillance, observational studies, registries, claims, and patient-centered outcomes research activities”), gaps in data collection, standards and methodologies for collection of real world evidence, and priority areas.<sup>122</sup> In implementing the program, the FDA must consult with several entities, including regulated industry, medical professional

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113. *Qualification Process for Drug Development Tools: Guidance for Industry and FDA Staff*, U.S. FOOD & DRUG ADMIN. (Nov. 12, 2019), <https://www.fda.gov/media/133511/download>.

114. 21 U.S.C. § 357(a)(2)(C).

115. *Id.* § 357(a)(1).

116. *Id.* § 357(a).

117. *Id.* § 357(e)(1).

118. See David E. Paul & Catherine Clements, *Getting by With A Little Help from Their Friends: FDA Using External Experts to Enhance Biomarker Qualification and Enhance Precision Medicine*, 72 FOOD & DRUG L. J. 660, 661 (2017).

119. See generally 21 U.S.C. § 355g (2016).

120. *Id.* § 355g(b).

121. *Id.* § 355g(c)(1).

122. *Id.* § 355g(c)(2).

organizations, academia, patient advocacy organizations, consumer organizations, and disease research foundations.<sup>123</sup>

Finally, the legislation creates a breakthrough medical device category that accelerates device review and approval.<sup>124</sup> These provisions mimic the breakthrough therapy designation introduced in the Food and Drug Administration Safety Innovation Act of 2012 (“FDASIA”) applying to drugs and biologics.<sup>125</sup> FDASIA established an expedited review mechanism and mandatory time frames for FDA response to applicant requests for breakthrough therapy designation; the FDA published a guidance for industry in May 2014 detailing the process.<sup>126</sup> Several long-standing FDA policies likewise support accelerated timeframes for drug products, including Fast Track designation, accelerated approval, and priority review designation.<sup>127</sup> The provisions in the 21st Century Cures Act pertaining to medical devices similarly set forth a process for breakthrough status for medical devices.<sup>128</sup> The FDA had previously developed an

123. *Id.* § 355g(c)(3).

124. *Id.* § 360e-3.

125. See Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), Pub. L. No. 112-144, § 902, 126 Stat. 993, 1086-1087 (2012) (codified as amended at 21 U.S.C § 356). Breakthrough therapy status signals that the drug is progressing through clinical trials subject to the statutory provisions provided for breakthrough therapies, not that the drug has been approved by the FDA. See U.S. FOOD & DRUG ADMIN., HEALTH & HUMAN SERV., GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS – DRUGS AND BIOLOGICS 10 (2014) [hereinafter GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS], <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf>. The FDA defines a breakthrough therapy as a drug “intended alone or in combination with one or more other drugs to treat a serious or life threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.” See *Fact Sheet: Breakthrough Therapies*, U.S. FOOD & DRUG ADMIN. (Mar. 28, 2018), <https://www.fda.gov/RegulatoryInformation/LawsEnforcedbyFDA/SignificantAmendments-to-the-FDCA/FDASIA/ucm329491.htm>.

126. Food and Drug Administration Safety and Innovation Act § 902(a); GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS 10–15, *supra* note 125.

127. See GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS, *supra* note 125, at 1, 7–8. A table within the FDA’s breakthrough therapy guidance document compares the four expedited mechanisms. *Id.*

128. See 21 U.S.C. § 360e-3. Congress directs the FDA to focus breakthrough status on medical devices “that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions . . . that represent breakthrough technologies . . . for which no approved or cleared alternatives exist . . . that offer significant advantages over existing approved or cleared alternatives, including the potential, compared to existing approved alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients’ ability to manage their own care (such as

Innovation Pathway, piloted in 2011, an expedited access pathway in 2015, and a Priority Review program as a means to facilitate faster development and review of promising medical devices.<sup>129</sup> The FDA implementation activity is set forth in Figure 3.

**Figure 3: FDA Implementation of Required Guidance**<sup>130</sup>

Guidance Requirement	Public Meeting	Draft Guidance	Final Guidance
Methods to collect patient and caregiver input on disease burden and existing therapies	Dec. 2017	June 2018	Mar. 2020
Processes to identify impacts most important to patients	Dec. 2018	June 2019	Mar. 2021
Approaches to identify and develop methods to measure patient impacts in clinical trials	Dec. 2019	June 2020	Dec. 2021
Methods and standards to collect and analyze clinical outcome assessments	June 2019	June 2020	Dec. 2021
Procedures for submission of proposed guidance regarding patient experience data	—	Mar. 2018	Dec. 2019
Timeframe for FDA response to drug development qualification program submissions for patient-reported outcomes	—	Dec. 2019	Sept. 2020

through self-directed personal assistance), or establish longterm clinical efficiencies; or . . . the availability of which is in the best interest of patients.” *Id.*

129. U.S. FOOD & DRUG ADMIN., HEALTH & HUMAN SERV., BREAKTHROUGH DEVICES PROGRAM: GUIDANCE FOR INDUSTRY AND FOOD AND DRUG ADMINISTRATION STAFF 1–2 (2018), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/breakthrough-devices-program>.

130. U.S. FOOD & DRUG ADMIN., HEALTH & HUMAN SERV., PLAN FOR ISSUANCE OF PATIENT-FOCUSED DRUG DEVELOPMENT GUIDELINES UNDER 21<sup>ST</sup> CENTURY CARES ACT at 8 (May 2017), <https://www.fda.gov/media/105979/download>.

Projected use of relevant patient experience data to inform regulatory decision-making, including in risk-benefit assessment	June 2019	June 2020	Dec. 2021
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The 21st Century Cures Act, along with FDA efforts, have affirmatively invited patient voices into the regulatory process. It remains to be seen how this process will be implemented, and how the agency will respond to increasing patient perspectives and patient-generated information in contrast to long-standing requirements for product approval. There are also critical questions regarding relationships between patient advocacy groups and the regulated industry, with many drug companies actively funding these groups or partnering with them on research initiatives. The Kaiser Health Network recently published a report detailing relationships among patient advocacy groups and the pharmaceutical industry.<sup>131</sup> Notably, pharmaceutical industry donations to patient advocacy groups are not subject to Sunshine laws. There is concern about a perceived lack of attention from patient advocacy groups on combating high drug costs, which may be the result of close financial ties with the industry.<sup>132</sup> Some commentators also warn that advocacy groups may exert pressure on the FDA to accelerate access with less data on safety and efficacy prior to market, straying from traditional clinical trial models.<sup>133</sup>

131. Emily Kopp et al., *Pre\$cription for Power*, KAISER HEALTH NEWS, <https://khn.org/patient-advocacy/#> (last visited Mar. 6, 2020). Key points reveal the following: 14 companies gave \$116M to patient advocacy groups in 2015, compared to \$63M in lobbying activities; 594 patient advocacy groups accepted money from pharma; and 15 patient advocacy groups relied on pharma for at least 20% of yearly revenue. *Id.*

132. See Laura Karas et al., *Pharmaceutical Industry Funding to Patient-Advocacy Organization: A Cross-National Comparison of Disclosure Codes and Regulation*, 42 HASTINGS INT’L & COMP. L. REV. 453, 453–456 (2019). “In general, the Sunshine Act requires applicable manufacturers of drugs, devices, biologicals, or medical supplies to report annually to the Secretary of HHS certain payments or other transfers of value to physicians and teaching hospitals.” Thomas Sullivan, *Physician Payment Sunshine Act Final Rule: Reporting Requirements*, POLICY & MEDICINE, <https://www.policymed.com/2013/02/physician-payment-sunshine-act-final-rule-reporting-requirements.html> (last updated May 6, 2018).

133. See Caroline Chen, *FDA Repays Industry by Rushing Risky Drugs to the Market*, PROPUBLICA (Jun. 26, 2018, 5:00 AM), <https://www.propublica.org/article/fda-repays-industry-by-rushing-risky-drugs-to-market>; see also Susannah L. Rose, *Patient Advocacy Organizations: Institutional Conflicts of Interest, Trust, and Trustworthiness*, 41 J L MED. ETHICS 680, 681–82 (2013).

#### IV. ACCELERATION OF CLINICAL TRIALS, PRODUCT REVIEW, AND APPROVAL

Many therapeutic biologics or drugs are developed to treat serious or life-threatening diseases for which no other products are available; they may also qualify for expedited development and review programs such as Fast Track designation, priority review, accelerated approval, Orphan Drug status, and breakthrough designation.<sup>134</sup>

Fast Track designation is provided under the Food and Drug Administration Modernization Act (“FDAMA”) for a product that is intended for the treatment of a serious or life-threatening condition and demonstrates the potential to address unmet medical needs for such a condition.<sup>135</sup> The applicant must apply for the Fast Track designation when it submits the IND, or at any time prior to the approval of the Biologics License Application (“BLA”).<sup>136</sup> The benefits of receiving Fast Track designation include the availability of meetings to seek FDA input into development plans, rolling submission where the BLA is submitted in sections as it becomes available rather than waiting for all sections to be submitted together at the end, the use of surrogate endpoints, priority review, and accelerated approval.<sup>137</sup> The FDA may withdraw the designation if clinical development data shows that the product no longer meets the criteria for the designation, as is the case when data shows that there is no anticipated advantage over existing therapy,<sup>138</sup> for example.

Priority review and standard review are classifications that the Center for Drug Evaluation and Research (“CDER”) and Center for Biologics Evaluation and Research (“CBER”) use to prioritize the review depending on the product’s estimated therapeutic

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134. See Jordan Paradise, *Introduction to Biologics*, in *THE FUNDAMENTALS OF LIFE SCIENCES LAW: DRUGS, DEVICES, AND BIOTECH*, 71 (Kristian A. Werling et al. eds., 2nd ed. 2014).

135. 21 U.S.C. § 356; see also FOOD & DRUG ADMIN., HEALTH & HUMAN SERV., GUIDANCE FOR INDUSTRY: FAST TRACK DRUG DEVELOPMENT PROGRAMS—DESIGNATION, DEVELOPMENT, AND APPLICATION REVIEW 1 (Jan. 2006) [hereinafter, GUIDANCE FOR INDUSTRY: FAST TRACK DRUG DEVELOPMENT], [http://www.msk.nclinnovations.org/medregulations/v1/html/Guidance/Guidance\\_Fast%20Track%20Development.pdf](http://www.msk.nclinnovations.org/medregulations/v1/html/Guidance/Guidance_Fast%20Track%20Development.pdf).

136. GUIDANCE FOR INDUSTRY: FAST TRACK DRUG DEVELOPMENT, *supra* note 135, at 8.

137. See *id.* at 10–15.

138. See *id.* at 9–10.

value.<sup>139</sup> Priority review is given to a product that, if approved, will bring significant improvement over marketed products.<sup>140</sup> Improvement can be demonstrated by: (1) evidence of increased effectiveness; (2) elimination or substantial reduction of a treatment-limiting drug reaction; (3) documented enhancement of patient compliance; or (4) evidence of safety and effectiveness of a new sub-population.<sup>141</sup> If not classified as priority review, the product will receive standard review. Under FDAMA, a priority review sets the target date for the FDA to complete all aspects of a review and make the approval decision at six months after the filing date, while a standard designation sets the target date at ten months.<sup>142</sup> Additionally, orphan drug status is assigned to drugs that treat rare diseases or disorders impacting 200,000 people or less.<sup>143</sup> The status serves as an incentive to research and innovate for treatments impacting small populations; the FDA prioritizes review of such products using the Priority Review program and also provides seven years of exclusivity for those that gain approval.<sup>144</sup>

Accelerated approvals are available for drugs or biologics that are indicated for serious or life-threatening illnesses and that confer meaningful therapeutic benefits over existing treatments, such as the ability to treat patients unresponsive to or intolerant of available therapy, or improved patient response over available therapy.<sup>145</sup> Under 21 C.F.R. § 601.41, the FDA may grant marketing approval for a biological product on the basis of adequate and well-controlled clinical trials which establish that the biological product has an effect on a surrogate endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity.<sup>146</sup>

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139. See CTR. FOR DRUG EVALUATION, RESEARCH, AND REVIEW, U.S. FOOD & DRUG ADMIN., MAPP 6020.3, REVIEW DESIGNATION POLICY: PRIORITY (P) AND STANDARD (S) 1–2 (2013), <https://www.fda.gov/media/72723/download>.

140. See *id.*

141. *Id.* at 6–7.

142. For further details, see U.S. FOOD & DRUG ADMIN., CBER, SOPP 8405: COMPLETE REVIEW AND ISSUANCE OF ACTION LETTERS, (2004), <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Processes/SOPPs/ucm073481.htm> (last visited June 1, 2013).

143. 21 C.F.R. § 316.3(b)(10) (“Orphan drug means a drug intended for use in a rare disease or condition as defined in section 526 of the act . . .”).

144. See 21 C.F.R. §§ 316.3(b)(12), 316.31.

145. 21 C.F.R. § 314.500.

146. 21 C.F.R. § 601.41.



Products receiving accelerated approvals are subject to additional postmarket studies to further evaluate the product and to verify its clinical benefits, especially when there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or as to the relation of the observed clinical benefit to the ultimate outcome.<sup>147</sup>

Finally, breakthrough designation was introduced by Congress in 2012 to add to these existing accelerated programs.<sup>148</sup> The FDA defines a breakthrough therapy as a drug “intended alone or in combination with one or more other drugs to treat a serious or life threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.”<sup>149</sup> Breakthrough therapy status signals that the drug is progressing through clinical trials subject to the statutory provisions provided for breakthrough therapies, not that the drug has been approved by the FDA.<sup>150</sup>

These routes of “faster” clinical trials, review, and approval are utilized by the FDA frequently, either alone or in combination.<sup>151</sup> While each route has its own designation and derives from a specific grant of authority in the statute, they are all, collectively, “accelerated” mechanisms. They are also associated with particular incentives, including periods of product exclusivity and priority review vouchers to be redeemed either with a future product or sold to another drug company for a hefty profit.<sup>152</sup> Recent empirical research suggests that the existence of these programs may be having a negative impact on product quality and safety, as well as on public

147. See 21 C.F.R. § 314.510-314.560.

148. Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), Pub. L. No. 112-144, § 902, 126 Stat. 993, 1086–1087 (2012) (codified as amended at 21 U.S.C. 356).

149. *Fact Sheet: Breakthrough Therapies*, U.S. FOOD & DRUG ADMIN. (Mar. 28, 2018), <https://www.fda.gov/RegulatoryInformation/LawsEnforcedbyFDA/SignificantAmendmentsToTheFDCA/FDASIA/ucm329491.htm>.

150. See GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS, *supra* note 125 at 10.

151. See *id.* at 1, 7.

152. See 21 C.F.R. §§ 316.3(b)(12), 316.31. Orphan drug status is accompanied by seven years of market exclusivity, during which the FDA will not approve a generic version of that drug. See *id.* Priority review vouchers are available both for rare tropical diseases and for rare pediatric diseases. The GAO recently conducted a study on the impact of the PRV programs on drug development. See GOVERNMENT ACCOUNTABILITY OFFICE, DRUG DEVELOPMENT: FDA’S PRIORITY REVIEW VOUCHER PROGRAMS 1, 2 (2020), <https://www.gao.gov/products/gao-20-251>.

perceptions of the FDA as a proper gatekeeper.<sup>153</sup> There is specific concern that the impact behind the term “FDA Approved” is eroding.<sup>154</sup>

In a January 2020 article, Darrow, Avorn, and Kesselheim explored FDA approval trends over the last four decades (1983–2018) and concluded that “legislation and regulatory initiatives have substantially changed drug approval at the FDA.”<sup>155</sup> Some of their statistics are particularly compelling. The number of new drug approvals that were supported by at least two pivotal clinical trials decreased from 80.6% to 52.8% from 1995–1997 to 2015–2017, while FDA drug review times decreased from over three years to less than one year from 1983 to 2017.<sup>156</sup> For new drugs, annual approval rates varied, on average, from 34% between 1990–1999, 25% between 2000–2009, to 41% between 2010–2018.<sup>157</sup> New approvals receiving orphan drug designation rose from 18% between 1984–1995 to 41% between 2008–2018.<sup>158</sup> In addition, the median number of generic drug approvals increased from 284 per year prior to 2012, to 488 per year between 2013–2018.<sup>159</sup> Kesselheim and co-authors had previously reported that of 174 new drug approvals between January 2012 and December 2016, 60% were assigned to one or more expedited programs, including 52% priority review, 36% Fast Track, 17% breakthrough, and 15% accelerated approval.<sup>160</sup> They also reported that the median time from the application for IND to FDA approval for drugs with at least one expedited route to market was 0.9 years shorter than a drug without any such mechanism.<sup>161</sup>

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153. Linda Carroll, *FDA Approval May Not be As Rigorous as it Once Was*, REUTERS (Jan. 14, 2020, 5:42 PM), <https://www.reuters.com/article/us-health-fda/fda-approval-may-not-be-as-rigorous-as-it-once-was-idUSKBN1ZD2TC>.

154. *Id.*

155. Jonathan J. Darrow et al., *FDA Approval and Regulation of Pharmaceuticals, 1983–2018*, 323 JAMA 164, 164 (2020). The Orphan Drug Act was enacted in 1983, followed by Fast Track provisions (1987), Accelerated Approval (1992), Priority Review (1992), and Breakthrough status (2012). *See id.* at 169, Box 2, for a helpful chronological chart of legislation.

156. *Id.* at 164.

157. *Id.*

158. *Id.*

159. *Id.*

160. Thomas J. Hwang et al., *The FDA’s Expedited Programs and Clinical Development Times for Novel Therapeutics*, 318 JAMA 2137, 2137 (2017).

161. *Id.* at 2138 (noting that the median development time decreased from 8 years to 7.1 years).

Another study reports specifically on breakthrough therapy designation following its introduction in the 2012 legislation.<sup>162</sup> Between 2012-2017, the FDA approved 46 new drugs and biologics with breakthrough status.<sup>163</sup> Of those 46 total products, 46 also received priority review, 30 received orphan drug status, 24 received Fast Track status, and 18 underwent accelerated approval.<sup>164</sup> More than half of the approvals were based on a single pivotal trial and average premarket development times were less than five years.<sup>165</sup> The authors conclude that the findings suggest “pivotal trials supporting these approvals commonly lacked randomization, double-blinding and control groups, used surrogate endpoints, and enrolled a small number of patients.”<sup>166</sup> These accumulating statistics suggest that accelerated routes to market are measurably impacting the scope of clinical trials and FDA review times.

## V. EXTENSION OF CLINICAL TRIALS TO POSTMARKET

Amendments to the Federal Food, Drug, and Cosmetic Act in 2007 introduced new statutory provisions that bolster the FDA’s post-approval authority including Risk Evaluation and Mitigation Strategy authority and extension of clinical trials or limited studies following product approval.<sup>167</sup> Prior to the legislative changes, the FDA often imposed “phase 4” requirements on drug sponsors, including additional clinical trials or collection of specific data.<sup>168</sup> However, there were no corresponding penalties or enforcement authority for violation of these requirements. Specifically, section 505(o) authorizes the FDA to require postmarket clinical trials for any drug product.<sup>169</sup> Violations of the statute trigger civil money

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162. Jeremy Puthumana et al., *Research Letter: Clinical Trial Evidence Supporting FDA Approval of Drugs Granted Breakthrough Therapy Designation*, 320 JAMA 301 (2018).

163. *Id.* at 301. Another article notes that between 2012 and Dec. 2016, the FDA assigned breakthrough therapy designation to 165 investigational drugs. Hwang et al., *supra* note 160, at 2138.

164. Puthumana et al., *supra* note 162, at 302.

165. *Id.*

166. *Id.*

167. 21 U.S.C. § 355-1(a)(1).

168. *How the FDA Drug Approval Process Works*, DPAC (Feb. 20, 2018), <http://www.diabetespac.org/fda-drug-approval-process>.

169. 21 U.S.C. § 355(o)(3). The FDA has also issued final guidance on their authority under these provisions. U.S. FOOD & DRUG ADMIN., HEALTH & HUMAN SERV., GUIDANCE FOR INDUSTRY: POSTMARKETING STUDIES AND CLINICAL TRIALS – IMPLEMENTATION OF SECTION 505(O)(3) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT 7 (Apr. 2011), <https://www.fda.gov/media/133746/download>.

penalties and subject manufacturers to litigation under misbranding provisions within the Food, Drug and Cosmetic Act.<sup>170</sup> Civil money penalties are capped at \$250,000 per violation and cannot exceed \$1 million for all violations in a single proceeding.<sup>171</sup> Where a violation continues after the agency provides written notice, the civil penalty is:

\$250,000 for the first 30-day period (or any portion thereof) that the responsible person continues to be in violation, and such amount shall double for every 30-day period thereafter that the violation continues, not to exceed \$1,000,000 for any 30-day period, and not to exceed \$10,000,000 for all such violations adjudicated in a single proceeding.<sup>172</sup>

The Secretary of the U.S. Department of Health and Human Services is instructed to consider whether the responsible person is making efforts to correct the violations when determining the amount of civil penalty.<sup>173</sup>

A search of the FDA website reporting on these postmarket requirements and commitments issued under Section 505(o)(3) identifies 502 such requirements imposed by both the Center for Drug Evaluation and Research (“CDER”) and the Center for Biologic Evaluation and Research since the passing of the legislation in 2007.<sup>174</sup> As noted in the approval letter for Sarepta Therapeutics’ new drug product Exondys-51 (eteplirsen), the FDA expressly states in the documentation of approval when they are exercising this authority:

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if

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170. 21 U.S.C. § 333(b).

171. 21 U.S.C. § 333(b).

172. 21 U.S.C. § 333(f)(4)(A)(ii).

173. 21 U.S.C. § 333(f)(4)(B).

174. *Postmarket Requirements and Commitments*, U.S. FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm> (last accessed June 13, 2020).

FDA makes certain findings required by the statute.<sup>175</sup>

The FDA approved Exondys-51 (eteplirsen), the first treatment for Duchenne Muscular Dystrophy (“DMD”), in September 2016 after prolonged disputes within the agency.<sup>176</sup> DMD is a severe form of muscular dystrophy associated with progressive muscle weakness and loss, manifesting in males between the ages of three and five.<sup>177</sup> DMD affects 1 in 3,500 boys in the U.S., classifying it as a rare, or Orphan, disease under the statute. The Director of the CDER, Dr. Janet Woodcock, ultimately approved the product despite advisory board recommendations.<sup>178</sup> The decision was controversial, as FDA staff and advisory committee members had urged that the drug had not been shown to be effective in clinical trials consisting of only twelve patients, with no placebo control group.<sup>179</sup> In an uncommon move, then-FDA Commissioner Robert Califf issued a public memo defending Dr. Woodcock’s decision.<sup>180</sup>

The drug’s approval was coupled with robust postmarket trial requirements imposed on Sarepta Therapeutics to further measure carcinogenicity in animals with required reporting deadlines looming in Fall 2020.<sup>181</sup> In addition to 505(o)(3) requirements for postmarket studies, Exondys-51 was also granted accelerated approval, Fast Track, Priority review, and Orphan Drug status along with a rare pediatric priority review voucher.<sup>182</sup> The drug costs approximately \$300,000 a year and will treat approximately 13% of

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175. Letter from Janet Woodcock, M.D., Director, Ctr. for Drug Evaluation and Research, to Sarepta Therapeutics, Inc. (Sept. 19, 2016) (on file with Food & Drug Admin.).

176. 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>.

177. W. Douglas Biggar, *Duchenne Muscular Dystrophy*, 27 PEDIATRICS IN REV. 83, 84 (2006).

178. Jeff Buchanan, *Bio Execs Talk Patient Advocacy, Duchenne Approval at BioForward Panel*, EXOME (Sept. 28, 2016), <https://www.xconomy.com/wisconsin/2016/09/28/bio-execs-talk-patient-advocacy-duchenne-approval-at-bioforward-panel>.

179. See Robert Weisman, *FDA Approves Sarepta’s Disputed Drug, Overruling Staffers and Advisors*, BOS. GLOBE (Sept. 19, 2016, 5:23 PM), <https://www.bostonglobe.com/business/2016/09/19/fda-approves-duchenne-drug-overturning-staff-and-advisers/mKVY1HQ0Fn1Mcs2WJQWS0J/story.html>.

180. Mukherjee, *supra* note 176.

181. Weisman, *supra* note 179.

182. Letter from Woodcock, M.D. to Sarepta Therapeutics, *supra* note 175.

patients with a specific mutation associated with DMD.<sup>183</sup> The debate and review of the drug was informed by intense patient participation. Public meetings in April 2016 were attended by hundreds of patient advocates.<sup>184</sup> Reporters described the meetings as “emotionally charged” when young, wheelchair-bound patients described living with the disease and the need for treatment.<sup>185</sup> Notably, the FDA expanded public discussion from sixty minutes to 2.5 hours.<sup>186</sup>

In a stunningly similar manner, the FDA recently approved Vyondys-53, a second DMD drug from Sarepta, in December 2019.<sup>187</sup> Again, FDA staff and experts originally recommended against approval, but Sarepta filed an appeal and resubmitted their new drug application.<sup>188</sup> Vyondys-53 is approved to treat the 8% of patients with a second genetic mutation.<sup>189</sup> The product was granted accelerated approval, Priority review, and Orphan Drug status and received a rare pediatric review voucher.<sup>190</sup> The FDA likewise required a slate of postmarket studies to verify clinical benefit, carcinogenicity, and immune response related to kidney side effects.<sup>191</sup> Testing to support such studies must be completed by 2024, during which time the drug may enter the market conditionally.<sup>192</sup> Sarepta indicates that its cost will be on par with Exondys-51, at about \$300,000 per month.<sup>193</sup>

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183. Weisman, *supra* note 179. The cost breaks down to \$1,680 for 2 milliliters.

184. Robert Weisman, *Muscular Dystrophy Drug Advocates Plan to Pack Crucial Meeting*, BOS. GLOBE (Apr. 18, 2016, 7:30 PM), <https://www.bostonglobe.com/business/2016/04/18/drug-advocates-plan-pack-crucial-meeting/OMB3xupTONfQm61CmDptTM/story.html>.

185. Weisman, *supra* note 179.

186. Natalie Grover, *Sarepta shares sink as FDA staff stay sour on muscle drug*, REUTERS (Apr. 21, 2016, 7:55 AM), <https://www.reuters.com/article/us-sarepta-fda/sarepta-shares-sink-as-fda-staff-stay-sour-on-muscle-drug-idUSKCN0XIIMO>.

187. Letter from Bill Dunn, M.D., Acting Director, Ctr. for Drug Evaluation and Research, to Sarepta Therapeutics, Inc. (Dec. 12, 2019) (on file with Food & Drug Admin.) [hereinafter *Letter from Bill Dunn, M.D. to Sarepta Therapeutics*].

188. Ned Pagliarulo and Jonathan Gardner, *In Stunning Twist, FDA Approves Sarepta’s Duchenne Drug It Rejected*, BIOPHARMADIVE (Dec. 12, 2019), <https://www.biopharmadive.com/news/fda-surprise-approval-sarepta-vyondys-53-duchenne-drug/569015>.

189. *Id.*

190. Letter from Bill Dunn, M.D. to Sarepta Therapeutics, *supra* note 187.

191. *Id.*

192. *Id.*

193. Marta Figueiredo, *FDA, in Reversal, Approves Vyondys 53 to Treat Duchenne Patients with Exon 53 Mutations*, MUSCULAR DYSTROPHY NEWS, (Dec. 13, 2019), <http://muscular dystrophynews.com/2019/12/13/vyondys-53-for-duchenne-md-with-exon-53-mutations-fda-approval>.

## VI. “FASTER” FORWARD

As a result of Congressional action through legislation, and agency policy and regulation, patients are getting earlier access to drug products through a variety of mechanisms. Whether this access is through FDA expanded access or the RTT Act, one or several of the accelerated mechanisms of review and approval, or extension of clinical trials into the postmarket space to accommodate for collection of safety and efficacy information following product approval, the timeline for any given product may be “faster” than the framework Congress set forth in the Kefauver-Harris Act in 1962.<sup>194</sup> The question becomes whether this seeming erosion of the historical framings of safety and efficacy has implications for patient health and product safety going forward. In the abstract, it is difficult to determine whether “faster” is introducing any challenges or tensions on those fronts and whether there may be a tipping point; after all, the FDA’s enduring conflict is the split mission in its enabling act to both protect the public health and to speed innovations. However, several issues warrant prospective attention as the FDA continues to utilize these mechanisms to speed up access and implement recent legislative directives to expand patient input in the regulatory process. This article identifies a few of these issues and reserves careful analysis to future scholarship.

First, as the scope of “substantial evidence” of “adequate and well-controlled studies” changes and the sources of information supporting review and approval expands, how useful and usable will patient experience data and real-world evidence be? What mechanisms can the FDA implement to verify experiences from an objective standpoint? And, ultimately, how will consumers and physicians understand and utilize this information if offered publicly with FDA approval decisions?

Second, what are the measurable impacts of increasing use of accelerated approval mechanisms, with the FDA often designating several mechanisms together to speed up both the timeframe for completion of clinical trials and the eventual FDA review time? Certainly, there must be implications of “faster” for patient safety with products being approved based on less data. A growing scholarship is exploring these issues, though more work needs to be

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194. AGATA DABROWSKA & SUSAN THAUL, HOW FDA APPROVES DRUGS AND REGULATES THEIR SAFETY AND EFFECTIVENESS, FAS 1–2 (May 8, 2018), <http://www.fas.org/sgp/crs/misc/R41983.pdf>.

done.<sup>195</sup> In order to collect and analyze this accumulating data, there must be transparent reporting mechanisms and databases to aggregate the information. Are current reporting procedures, public availability of these reports, and scrutiny and analysis of the post-market information by the FDA satisfactory? In addition, with the increasing use of 505(o) to require studies of aspects of concern to the FDA to be completed following a conditional approval, are important pre-market safety efficacy measures being relegated to a later time, after market? And how does the FDA feed the data and results from those studies back into the regulatory process? For example, has there been a resulting increase in withdrawals of approvals or indications resulting from those 505(o) studies?

Third, there are also informational gaps about the operation of faster routes to market and what it means about the level of clinical trials and premarket testing associate with the product. As noted explicitly by the FDA, “[b]ecause each of these approaches implies speed, there can be confusion about the specific meaning of each and the distinctions among them.”<sup>196</sup> Scholarship documents these misconceptions and misunderstandings on behalf of both patients and physicians.<sup>197</sup> Physicians, patients, and drug sponsors are also questioning the difference between the right to try process versus expanded use. How do we address this widespread misunderstanding, particularly by prescribers who serve as learned intermediaries? Are there particular educational modes and outlets or labeling approaches for approved products to inform relevant stakeholders?

Finally, tied directly to the pervasive problem of soaring drug prices, there are also questions about how these mechanisms are impacting effective patent life and the carefully-balanced calculus of patent term extension.<sup>198</sup> Some scholarship suggests that a

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195. See, e.g., Puthumana et al., *supra* note 162; Hwang et al., *supra* note 160; Caroline Chen, *FDA Increasingly Approves Drugs without Conclusive Proof They Work*, PBS NEWS HOUR (June 26, 2018), <https://www.pbs.org/newshour/health/fda-increasingly-approves-drugs-without-conclusive-proof-they-work>.

196. *Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review> (last accessed June 13, 2020).

197. Puthumana et al, *supra* note 162, at 301 (citing Aaron S. Kesselheim et al., *Physician’s Knowledge about FDA Approval Standards and Perceptions of the ‘Breakthrough Therapy’ Designation*, 315 JAMA 1516 (2016)); T. Krishnamurti et al., *A Randomized Trial Testing U.S. Food and Drug Administration ‘Breakthrough’ Language*, 175 JAMA INTERNAL MED. 1856 (2015).

198. 35 U.S.C. § 156.



status such as Fast Track diminishes patent life and serves as a disadvantage to the longevity of a product.<sup>199</sup> On the other hand, other sources indicate that less review and approval time available may translate into longer effective patent life and increased opportunities for monopolistic behavior by the industry. The relationship between recent trends for “faster” access and patent implications is ripe for focused scrutiny.

In conclusion, the RTT Act suffers from both structural and implementation problems and is unlikely to upend successful, longstanding FDA expanded access procedures. As a result of Congressional directives and FDA policy over the last several decades, there are various other mechanisms for “faster” access to investigational products, each raising their own collective questions about product safety and efficacy. While the value of these “faster” mechanisms cannot be overstated, there is also reason to continue to assess outcomes and implications.

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199. George C. Best, & Shaun R. Snader, *Accelerated FDA Review: Risks to Patent Term*, 4 FDLI UPDATE 43, 43 (2009).