
AN EXAMINATION OF THE RIGHT TO TRY ACT OF 2017 AND INDUSTRY'S POTENTIAL PATH MOVING FORWARD

SYLVIA ZAICH*

TABLE OF CONTENTS

INTRODUCTION	332
I. A BRIEF HISTORY OF THE FDA AND THE CURRENT DRUG DEVELOPMENT PROCESS	336
A. THE ORIGINS OF THE FDA'S REGULATORY FRAMEWORK.....	336
B. THE DRUG DEVELOPMENT PROCESS	338
II. CHALLENGES TO THE REGULATORY FRAMEWORK AND AN OVERVIEW OF THE EXPANDED ACCESS PROGRAM.....	341
A. PRIOR PRE-APPROVAL ACCESS CHALLENGES	341
1. 1970s: Laetrile, the FDCA, and <i>Rutherford v. United States</i>	341
2. 1980s–1990s: The Reagan Administration and the HIV/AIDS Epidemic	343
3. 2000s: Pre-Approval Access, a Proposal, and <i>Abigail Alliance v. Von Eschenbach</i>	344
B. THE EXPANDED ACCESS PROGRAM.....	347

*. Executive Senior Editor, *Southern California Law Review*, Volume 92; J.D. Candidate 2019, University of Southern California Gould School of Law; B.S., Journalism and Political Science 2011, Northwestern University, Medill School of Journalism. I would like to thank Professor Michael H. Shapiro for encouraging me to pursue this topic, which first sparked my interest in 2013. His feedback and insights on early drafts was invaluable. Special appreciation and thanks to my parents, Jon and Anna, for their love and support even after reviewing multiple drafts; to my friends and classmates, and in particular Aly, for allowing me to talk through my ideas on numerous occasions; and to my niece and nephew for their superb editing skills! I would also like to thank the Volume 92 editors of the *Southern California Law Review* for their careful editing and invaluable feedback, especially Nick Thomas, Jay Simmons, and Chris Phillips. Lastly, I would like to report working for Weber Shandwick where I represented biopharmaceutical and medical device clients (2011–2014) and working for Adaptive Biotechnologies (2014–2016).

1. How a Physician Requests Expanded Access for Individual Patient Use	348
2. How Companies Evaluate an Individual Patient Request	350
3. How the FDA Evaluates an Individual Patient Request	353
III. THE RIGHT-TO-TRY MOVEMENT	357
A. THE MOVEMENT'S RATIONALE FOR RIGHT TO TRY AND SUCCESS AT THE STATE LEVEL	358
1. The Right-to-Try Movement's Rationale	358
2. The Movement's Success at the State Level	362
B. THE FDA'S RESPONSE.....	366
1. Clarifying the FDA's Use of Clinical Outcomes.....	366
2. Demystifying Manufacturers' Eligibility Criteria	368
3. Increasing Awareness of Expanded Access	369
4. Streamlining the Individual Patient Request Process	369
C. THE PUSH FOR A FEDERAL RIGHT TO TRY	374
IV. THE RIGHT TO TRY ACT OF 2017.....	377
A. THE LAW	377
1. Who is Eligible?	377
2. When Would an Investigational Drug Qualify?	378
3. What are the Reporting Obligations?	379
4. When Can the FDA Use Clinical Outcomes?.....	379
B. INDUSTRY'S POTENTIAL PATH MOVING FORWARD	382
1. Even with the Right to Try Act, Most Companies Will Continue to Use Expanded Access.....	382
2. Charting Industry's Path Forward	392
CONCLUSION	399
APPENDIX	402

INTRODUCTION

In 2013, a petition started to circulate the Internet, urging the CEO of BioMarin Pharmaceutical to provide its investigational drug BMN-673 to then forty-five-year-old attorney Andrea Sloan, who was undergoing treatment for late stage ovarian cancer.¹ With standard treatments no longer an option, her physicians proposed trying BMN-673, one of a new class of cancer drugs called PARP inhibitors developed by BioMarin. The advanced

1. *BioMarin Pharmaceutical: Give Andrea Sloan (@andi_sloan) Access to the Cancer Drug That Could Save Her Life*, CHANGE.ORG, [hereinafter CHANGE.ORG] <https://www.change.org/p/biomarin-pharmaceutical-give-andrea-sloan-andi-sloan-access-to-the-cancer-drug-that-could-save-her-life> (last visited Feb. 6, 2019).

nature of Sloan's cancer disqualified her from enrolling in a clinical trial, so instead she and her physicians sought access to BMN-673 through the U.S. Food & Drug Administration's ("FDA") expanded access program, which allows pre-approval use of drugs outside of the clinical trial setting.²

The FDA confirmed Sloan was a candidate for expanded access use, but that confirmation did not guarantee use. That decision was left to the discretion of the company. BioMarin declined to provide BMN-673 because the drug was still in early phase of development: "It would be unethical and reckless to provide [BMN-673 to] end-stage refractory ovarian cancer patients outside a clinical trial."³ This decision sparked the Change.org petition that ultimately secured more than 230,000 signatures.⁴ Even with this overwhelming public support, BioMarin maintained its position. A different company, which was developing a similar drug, eventually provided Sloan with access on the condition that it remain unidentified. Sloan started the treatment, but her cancer had progressed, and she died shortly thereafter.⁵

Sloan's expanded access experience is not unique. A number of patients, with the support of their friends and families, launched similar online campaigns, seeking access to investigational medicines after becoming frustrated with companies' unwillingness to accommodate expanded access requests for investigational drugs.⁶ Some were successful;

2. William Hudson, *In Cancer Drug Battle, Both Sides Appeal to Ethics*, CNN (Sept. 28, 2013, 5:38 PM), <http://www.cnn.com/2013/09/28/health/compassionate-drug-use>. Expanded access is sometimes also referred to as either "compassionate use" or "pre-approval access."

3. *Id.* At the time of Sloan's request, BioMarin had only completed a phase I trial in thirty-nine patients. Johann Sebastian De Bono et al., *First-in-Human Trial of Novel Oral PARP Inhibitor BMN 673 in Patients with Solid Tumors*, AM. SOC'Y CLINICAL ONCOLOGY (June 3, 2013), <https://meetinglibrary.asco.org/record/83852/abstract>.

4. CHANGE.ORG, *supra* note 1; Andrea Ball, *Austin Woman Dies After Battle for Access to Experimental Cancer Drug*, AUSTIN AM.-STATESMAN (Jan. 3, 2014), <https://www.statesman.com/NEWS/20140103/Austin-woman-dies-after-battle-for-access-to-experimental-cancer-drug> (noting her "Facebook page—Andi's Army—ha[d] more than 15,000 followers").

5. 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>.

6. See, e.g., Elizabeth Cohen, *Company Denies Drug to Dying Child*, CNN (Mar. 11, 2014, 2:57 PM), <http://www.cnn.com/2014/03/10/health/cohen-josh>; accord Tirrell, *supra* note 5; Amanda Woerner, *Dying 25-Year-Old Fights for Compassionate Use Access to Cancer Treatment*, FOX NEWS (Mar. 26, 2014), <http://www.foxnews.com/health/2014/03/26/dying-25-year-old-fights-for-compassionate-use-access-to-cancer-treatment>. With the enactment of the federal Right to Try Act, some patients and their families are once again turning to social media to request access to investigational drugs through right to try. See Sumathi Reddy, *The 'Right to Try' Law Says Yes, the Drug Company Says No*, WALL ST. J. (June 6, 2018, 5:56 PM), <https://www.wsj.com/articles/family-battling-a-rare-disease-sees-roadblocks-despite->

others were not. These campaigns, including Sloan's, increased public awareness and dialogue regarding terminally ill patients' ability to access investigational medicine and helped spark a national legislative movement promoting such individuals' "right to try."⁷

In 2015, Texas was the twenty-first state to adopt right-to-try legislation.⁸ The Texas bill was named in Andrea Sloan's memory. These laws, despite often having bipartisan support, have been divisive, with supporters claiming that the right to try offers "real hope,"⁹ and critics maintaining that the right to try is merely political theatrics and ultimately will do more harm than good for individual patients.¹⁰ Forty-one states have adopted right-to-try laws since the movement first launched in 2014.¹¹ That success sparked a push for a federal right-to-try law.

President Donald J. Trump voiced his support for such legislation in his

right-to-try-law-1528293923 (discussing how—after a company declined to provide an investigational drug because an expanded access program was not yet available—given the limited clinical data in only a small number of patients, the parents of a toddler—both of whom were doctors—launched a Change.org petition in June 2018 that collected more than 100,000 signatures in just two weeks).

7. Erin Mershon, *'Right-to-Try' Law Intended to Weaken the FDA, Measure's Sponsor Says in Blunt Remarks*, STAT NEWS (May 31, 2018), <https://www.statnews.com/2018/05/31/right-to-try-ron-johnson>.

8. TEX. HEALTH & SAFETY CODE ANN. § 489 (West 2015); Eric Janez, *Andrea Sloan Bill Signed into Law*, KXAN (June 12, 2015), <http://kxan.com/2015/06/12/andrea-sloan-bill-signed-into-law>.

9. Kenneth Artz, *U.S. House Approves Federal Right to Try Bill*, HEARTLAND INST. (Apr. 25, 2018), <https://www.heartland.org/news-opinion/news/u-s-house-approves-federal-right-to-try-bill> (quoting Rep. Andy Biggs (R-Ariz.)); see also Christina Sandefur, *Safeguarding the Right to Try*, 49 ARIZ. ST. L.J. 513, 521 (2017) (arguing right-to-try laws are a "major change" from expanded access). See generally CHRISTINA CORIERI, GOLDWATER INST., EVERYONE DESERVES THE RIGHT TO TRY: EMPOWERING THE TERMINALLY ILL TO TAKE CONTROL OF THEIR TREATMENT (2014), https://goldwaterinstitute.org/wp-content/uploads/cms_page_media/2015/1/29/Right%20To%20Try.pdf (proposing the right-to-try legislation).

10. Ron Leuty, *The Right to Try: Terminally Ill Patients Say Trying Experimental Drugs Offers Hope. But Is It Just False Hope?*, S.F. BUS. TIMES (June 8, 2017, 5:15 PM), <https://www.bizjournals.com/sanfrancisco/news/2017/06/08/biotech-2017-right-to-try-laws-biomarin-fda-ca.html>. See generally Rebecca Dresser, *The "Right to Try" Investigational Drugs: Science and Stories in the Access Debate*, 93 TEX. L. REV. 1631 (2015) (examining the right to try movement and the role of patient stories in the debate); Lisa Kearns & Alison Bateman-House, *Who Stands to Benefit? Right to Try Law Provisions and Implications*, 51 THERAPEUTIC INNOVATION & REG. SCI. 170 (2017) (arguing the laws are not pro-patient); Rebecca Dresser, *"Right to Try" Laws: The Gap Between Experts and Advocates*, 45 HASTINGS CTR. REPORT, May-June 2015, at 9–10 [hereinafter Dresser, *The Gap*] (proposing ways to shift public debate regarding right to try in favor of existing programs).

11. Press Release, Goldwater Inst., Alaska Becomes 41st State to Enact Right to Try Legislation (July 13, 2018), <http://righttotry.org/alaska-becomes-41st-state-to-enact-right-to-try-legislation> (Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kentucky, Louisiana, Maine, Maryland, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, South Dakota, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, Wisconsin, and Wyoming).

2018 State of the Union address: “People who are terminally ill should not have to go from country to country to seek a cure—I want to give them a chance right here at home. It is time for the Congress to give these wonderful Americans the ‘right to try.’”¹² That endorsement was the final nudge Congress needed. On May 30, 2018, President Trump signed the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 (“Right to Try Act”).¹³

This Note proceeds in four parts. Part I briefly looks back at the FDA’s history and the impact of two significant drug crises in establishing the agency’s current framework before explaining the current drug development process. Part II recounts previous challenges to this regulatory framework, which ultimately led to the development of the current expanded access program. Part II also examines the current expanded access program and, more specifically, the evaluation criteria applied by three of its key decisionmakers: the treating physician; the manufacturer; and the FDA.

Part III traces the beginnings of the right to try movement, examining the rationale for the laws and exploring how social media and increased direct-to-consumer advertising of approved drugs possibly created an opening for widespread support of these laws. Part III also explores why the FDA’s efforts to address criticisms of the expanded access program were unable to dissuade enactment of the Right to Try Act. Part IV provides an overview of the Right to Try Act and how the Act differs from expanded access. Part IV further explores why, in general, mainstream industry likely will not adopt the right-to-try pathway, before arguing that pharmaceutical and biotechnology companies should avoid maintaining their current positions regarding pre-approval access, and instead address some of the

12. Donald J. Trump, President of the United States, State of the Union Address (Jan. 30, 2018), <https://www.whitehouse.gov/briefings-statements/president-donald-j-trumps-state-union-address>. Vice President Mike Pence, who signed into law the Indiana Right to Try Act, is also a public proponent of right-to-try legislation. *E.g.*, Vice President Mike Pence (@vp), TWITTER (Aug. 3, 2017, 12:21 PM), <https://twitter.com/vp/status/893190193829875713> (“Right to Try is about giving terminally ill patients hope & a chance. Proud of @POTUS’ & @SenRonJohnson’s work to help pass it in Senate.”); Vice President Mike Pence (@vp), TWITTER (Mar. 13, 2018, 2:12 PM) [hereinafter Vice President Mike Pence, March 13 Tweet], <https://twitter.com/vp/status/973668021028950017> (“Always great to see Jordan McLinn & his mother Laura McLinn, 2 great Hoosiers who have been fierce advocates for the Right to Try legislation the House will consider today. This bipartisan bill is about restoring hope to patients w/ terminal illnesses & it’s the right thing to do.”).

13. Press Release, White House, President Donald J. Trump to Sign Right to Try Legislation Fulfilling the Promise He Made to Expand Healthcare Options for Terminal Americans (May 30, 2018) [hereinafter White House Press Release], <https://www.whitehouse.gov/briefings-statements/president-donald-j-trump-sign-right-try-legislation-fulfilling-promise-made-expand-healthcare-options-terminal-americans>.

criticisms raised during the right-to-try movement by (1) revising their existing expanded access policies and (2) improving clinical trial access.

I. A BRIEF HISTORY OF THE FDA AND THE CURRENT DRUG DEVELOPMENT PROCESS

To better understand the rationale for the FDA's regulatory framework and the role it has "effectively balanc[ing] the interests of those patient populations who would benefit from having greater access to investigational drugs, with the broader interests of society in having safe and effective new therapies approved for marketing and widely available,"¹⁴ Part I of this Note reviews how the FDA's authority developed in response to two significant drug safety crises and provides a primer on the current drug development process.

A. THE ORIGINS OF THE FDA'S REGULATORY FRAMEWORK

The origins of the FDA can be traced back to the 1800s, but two drug safety crises prompted the development of the agency's current regulatory framework. The deaths of more than one hundred people from an untested drug formulation led to the enactment of the Federal Food, Drug, and Cosmetic Act of 1938 ("FDCA"), which required manufacturers to show "that any new drug was safe before it could be marketed."¹⁵ The initial effectiveness of the FDCA was limited. If the agency did not respond to a new drug application¹⁶ within sixty days, the drug was automatically approved for public consumption.¹⁷ The FDCA also did not require

14. Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75,160, 75,160 (Dec. 14, 2006) (to be codified at 21 C.F.R. pt. 312).

15. CTR. FOR DRUG EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMIN., THE HISTORY OF DRUG REGULATION IN THE UNITED STATES 2, 7 (2006), <https://www.fda.gov/downloads/AboutFDA/WhatWeDo/History/ProductRegulation/PromotingSafeandEffectiveDrugsfor100Years/UCM114468.pdf>; Michelle Meadows, *Promoting Safe and Effective Drugs for 100 Years*, U.S. FOOD & DRUG ADMIN. Jan.–Feb. 2006, <https://www.fda.gov/downloads/AboutFDA/WhatWeDo/History/FOrgsHistory/CDER/UCM586463.pdf>. The marketing application had to include information regarding "all clinical investigations . . . the drug's components and composition, methods of manufacture including facilities and controls, and copies of both the packaging and labeling of the new drug." SUZANNE WHITE JUNOD, U.S. FOOD & DRUG ADMIN., FDA AND CLINICAL DRUG TRIALS: A SHORT HISTORY 6 (2008), <https://www.fda.gov/downloads/AboutFDA/History/ProductRegulation/UCM593494.pdf>.

16. A new drug application "is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the U.S. The data gathered during the animal studies and human clinical trials . . . become part of the NDA." *New Drug Application (NDA)*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/newdrugapplicationnda/default.htm> (last updated Mar. 29, 2016).

17. Federal Food, Drug and Cosmetic Act, Pub. L. No. 75-717, § 505(c), 52 Stat. 1040, 1052

standardized drug testing.¹⁸ This remained the regulatory environment—despite efforts by some to address these shortcomings—until the second drug safety crisis of the twentieth century.

In 1960, the manufacturer of the then-popular sedative thalidomide submitted a marketing application for the drug in the United States.¹⁹ The FDA refused to grant approval over concerns about inadequate and deficient safety data.²⁰ The manufacturer had distributed “more than two and a half million tablets . . . to approximately 20,000 patients” in the United States for clinical testing, but few, if any, of these individuals were actually monitored after receiving the drug.²¹ The drug was eventually linked to an “epidemic of congenital malformations.”²² The global thalidomide crisis motivated politicians to reconsider legislation that would have “tightened restrictions surrounding the surveillance and approval process for drugs.”²³

Two years later, in 1962, Congress passed the Kefauver-Harris Amendment “to assure the safety, effectiveness, and reliability of drugs.”²⁴ This amendment eliminated the FDCA’s de facto approval loophole and extended the review period to 180 days.²⁵ Even more significant, the Kefauver-Harris Amendment “laid the groundwork for the [current multi-phased] system of clinical trials”²⁶ by requiring a manufacturer to submit “substantial evidence” of an investigational drug’s safety and efficacy with its marketing application.²⁷

(1938).

18. JUNOD, *supra* note 15, at 6–7. The randomized, controlled trial is now considered to be the “gold standard” of clinical research. *See generally* Laura Bothwell et al., *Assessing the Gold Standard—Lessons from the History of RCTs*, 374 NEW ENG. J. MED. 2175 (2016) (describing how randomized, controlled trials rose to prominence and transformed medical research).

19. The drug’s sales equaled those of aspirin. Bara Fintel et al., *The Thalidomide Tragedy: Lessons for Drug Safety and Regulation*, HELIX (July 28, 2009), <https://helix.northwestern.edu/article/thalidomide-tragedy-lessons-drug-safety-and-regulation>.

20. *Id.*

21. *Id.*

22. TOM BRODY, CLINICAL TRIALS: STUDY DESIGN, ENDPOINTS AND BIOMARKERS, DRUG SAFETY, AND FDA AND ICH GUIDELINES 783 (2nd ed. 2016). More than 8,000 babies were born missing limbs, blind, or intellectually disabled as a result of the drug. *Id.*

23. Fintel et al., *supra* note 19.

24. Kefauver-Harris Amendment, Pub. L. No. 87-781, 76 Stat. 780 (1962).

25. *Id.* § 104(c), 76 Stat. at 784.

26. Jeremy A. Green & Scott H. Podolsky, *Reform, Regulation, and Pharmaceuticals—The Kefauver-Harris Amendments at 50*, 367 NEW ENG. J. MED. 1481, 1481 (2012). *See also infra* Section II.A for further discussion of the clinical trial process.

27. Kefauver-Harris Amendment §§ 102(d), 103(b), 76 Stat. at 780–81, 783. To meet this requirement, a manufacturer needs to conduct “adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience.” *Id.* at § 102(d), 76 Stat.

B. THE DRUG DEVELOPMENT PROCESS

A manufacturer or other protocol sponsor,²⁸ before conducting a clinical trial, must first submit an investigational new drug (“IND”) application.²⁹ The IND provides an overview of the biopharmaceutical company’s general investigational plan and clinical trial protocols for the drug.³⁰ The plan must provide:

- (a) [t]he rationale for the drug or research study;
- (b) the indication(s) to be studied;
- (c) the general approach to be followed in evaluating the drug;
- (d) the kinds of clinical trials to be conducted in the first year . . . ;
- (e) the estimated number of patients . . . ; and
- (f) any risks of particular severity or seriousness anticipated on the basis of the toxicological data in animals or prior studies in humans with the drug or related drugs.³¹

The IND gives the FDA the information it needs to assess the safety of the proposed phase I trials and the “scientific quality of [the proposed phase II and III trials] and the likelihood that the [trials] will yield data capable of meeting statutory standards for marketing approval.”³²

In phase I, a manufacturer assesses the drug’s safety and determines the appropriate dosage for subsequent trials.³³ The participants are typically

at 780–81.

28. A sponsor can be an individual physician or researcher, company, or institution that is responsible for the initiation, management, and possibly funding of the clinical trial. INT’L COUNCIL FOR HARMONISATION OF TECH. REQUIREMENTS FOR PHARM. FOR HUMAN USE (ICH), GUIDANCE FOR INDUSTRY: E6 GOOD CLINICAL PRACTICE: CONSOLIDATED GUIDANCE 7 (2016) [hereinafter E6 GOOD CLINICAL PRACTICE].

29. 21 C.F.R. § 312.20 (2018) (listing IND requirements). The FDA defines “[a]n Investigational New Drug Application [(‘IND’) as] a request for authorization . . . to administer an investigational drug or biological product to humans.” *Investigational New Drug (IND) or Device Exemption (IDE) Process (CBER)*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/biologicsbloodvaccines/developmentapprovalprocess/investigationalnewdrugindordeviceexemptionideprocess/default.htm> (last updated Jan. 19, 2018). A company must secure an IND prior to shipping a drug interstate or administering any investigational drug not the subject of an approved marketing application. *Id.*

30. 21 § 312.23(a)(3)(iv). A clinical trial protocol describes “the objective(s), design, methodology, statistical considerations, and organization of a trial . . . [and] usually gives the background and rationale for the trial.” E6 GOOD CLINICAL PRACTICE, *supra* note 28, at 6.

31. 21 C.F.R. § 312.23(a)(3)(iv).

32. *Id.* § 312.22(a). The number of clinical trials necessary during each phase of clinical development can vary depending on the disease and availability of current treatments. It is estimated about seventy trials are needed during clinical development. RICK NG, DRUGS: FROM DISCOVERY TO APPROVAL 140 (2005).

33. BIOTECH. INNOVATION ORG., CLINICAL DEVELOPMENT SUCCESS RATES 2006–2015, at 13 (2016) [hereinafter CLINICAL DEVELOPMENT SUCCESS RATES 2006–2015], <https://www.bio.org/sites/d>

healthy volunteers but depending on the condition may be patient volunteers.³⁴ The enrollment size of these trials is small. A single phase I trial might enroll anywhere between twenty to eighty volunteers.³⁵ The Biotechnology Innovation Organization (“BIO”) estimates that approximately 60% of drugs advance from phase I to phase II clinical trials.³⁶

In phase II, the investigational drug is tested in patient volunteers who have the disease or condition.³⁷ This commonly involves a randomized clinical trial in which patients are randomly assigned either the investigational drug or some other treatment—“either an inactive substance (placebo), or a different drug that is usually considered the standard of care for the disease”—without knowing which treatment they are receiving.³⁸ The manufacturer then compares the effectiveness of the investigational drug to the effectiveness of the alternative treatment.³⁹ Phase II clinical trials are also required to assess the drug’s “common short-term side effects and risks.”⁴⁰ In general, this is the stage of development with the “lowest success rate”—almost 70% of drugs fail to move beyond phase II.⁴¹

The pre-approval development process culminates with phase III clinical trials,⁴² which are intended to produce “statistically significant data about the safety, efficacy and overall benefit-risk relationship of the investigational medicine.”⁴³ This data is an integral component of the new

efault/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%
%20Biomedtracker,%20Amplion%202016.pdf; *see also* 21 C.F.R. § 312.21 (describing the three phases of clinical development); BRODY, *supra* note 22, at 321 (noting phase I trials for cancer therapies are designed to identify the “minimal dose that can cause significant toxicity” given the assumption that “the most appropriate dose” is just below the “dose that produces unacceptable toxicity”).

34. 21 C.F.R. § 312.21(a).

35. U.S. FOOD & DRUG ADMIN., 22 CASE STUDIES WHERE PHASE 2 AND PHASE 3 TRIALS HAD DIVERGENT RESULTS 2 (2017) [hereinafter 22 CASE STUDIES], <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM535780.pdf>; PHARMA. RESEARCH & MFRS. OF AM., BIOPHARMACEUTICAL RESEARCH & DEVELOPMENT: THE PROCESS BEHIND NEW MEDICINES 13 (2015) [hereinafter BIOPHARMACEUTICAL RESEARCH & DEVELOPMENT], http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf.

36. CLINICAL DEVELOPMENT SUCCESS RATES 2006–2015, *supra* note 33, at 10.

37. BIOPHARMACEUTICAL RESEARCH & DEVELOPMENT, *supra* note 35, at 13.

38. *Id.*

39. *See id.*

40. 21 C.F.R. § 312.21(b) (2018).

41. CLINICAL DEVELOPMENT SUCCESS RATES 2006–2015, *supra* note 33, at 7.

42. A company will sometimes conduct phase IV studies post-approval. BIOPHARMACEUTICAL RESEARCH & DEVELOPMENT, *supra* note 35, at 16.

43. *Id.* at 13.

drug application a manufacturer submits to the FDA.⁴⁴ To obtain statistically significant data, these studies often require a substantial number of volunteers—sometimes upwards of 5,000 volunteers depending on the disease or condition.⁴⁵

The recruitment process throughout clinical development can take several years and be very expensive, with manufacturers often struggling to fully enroll their clinical trials.⁴⁶ The low accrual rates can be the result of strict inclusion and exclusion criteria.⁴⁷ Still, manufacturers can be resistant to making the criteria less restrictive and more inclusive,⁴⁸ perhaps because less-standardized patients might make it harder to parse through data, extend the length or size of a clinical trial, increase the risk of adverse events potentially impacting a drug's safety profile and potentially its approval, and make clinical development more expensive.⁴⁹

The estimated time from discovery to FDA approval of a drug is now

44. 21 C.F.R. § 314.50 (describing the requirements for submitting a new drug marketing application); *id.* § 601.2 (describing the requirements for submitting a biologics license application). The new drug application must “tell the drug’s whole story” so that the FDA can decide

[1] [w]hether the drug is safe and effective in its proposed use(s), and whether the benefits of the drug outweigh the risks[;] [2] [w]hether the drug’s proposed labeling (package insert) is appropriate, and what it should contain[;] [3] [w]hether the methods used in manufacturing the drug and the controls used to maintain the drug’s quality are adequate to preserve the drug’s identity, strength, quality, and purity.

New Drug Application (NDA), *supra* note 16.

45. BIOPHARMACEUTICAL RESEARCH & DEVELOPMENT, *supra* note 35, at 13.

46. See Benjamin Carlisle et al., *Unsuccessful Trial Accrual and Human Subjects Protections: An Empirical Analysis of Recently Closed Trials*, 12 CLINICAL TRIALS 77, 81 (2015) (“19% of trials registered as newly closed in 2011 either terminated due to failed accrual or completed with less than 85% of their expected [enrollment.]”); Aylin Sertkaya et al., *Key Cost Drivers of Pharmaceutical Clinical Trials in the United States*, 13 CLINICAL TRIALS 117, 117 (2016) (finding the three main causes of high clinical trial expenses were clinical procedures, administrative staff, and site monitoring); Gina Kolata, *A Cancer Conundrum: Too Many Drug Trials, Too Few Patients*, N.Y. TIMES (Aug. 12, 2017), <https://nyti.ms/2vsMRXf>. There are even companies that manufacturers hire to increase volunteer enrollment. See, e.g., *Putting Our Focus to Work*, PRAXIS, <https://www.gopraxis.com/experience> (last visited Feb. 8, 2019) (providing various case studies of successful clinical trial enrollment campaigns).

47. ASCO and Friends of Cancer Research Release *Comprehensive Recommendations to Broaden Eligibility Criteria for Cancer Clinical Trials*, AM. SOC’Y OF CLINICAL ONCOLOGY (Oct. 2, 2017) [hereinafter *ASCO and Friends*], <https://www.asco.org/advocacy-policy/asco-in-action/asco-and-friends-cancer-research-release-comprehensive> (noting factors, including age, comorbidities—such as heart disease, liver dysfunction, or kidney disease—advanced stage of disease, prior history of cancer, and HIV/AIDS).

48. *Id.*

49. Edward Kim et al., *Broadening Eligibility Criteria to Make Clinical Trials More Representative: American Society of Clinical Oncology and Friends of Cancer Research Joint Research Statement*, 35 J. CLINICAL ONCOLOGY 3737, 3742 (2017). See generally Susan Jin et al., *Re-Evaluating Eligibility Criteria for Oncology Clinical Trials: Analysis of Investigational New Drug Applications in 2015*, 35 J. CLINICAL ONCOLOGY 3745 (2017) (discussing the problems with eligibility criteria and finding that current criteria is too narrow in cancer clinical trials).

at least ten years. The cost of development is estimated between \$10 million and \$2.6 billion, with the higher estimate factoring in costs associated with investigational drugs that never advance beyond clinical development.⁵⁰ These costs are then passed on to patients, with some cancer therapies costing upwards of \$375,000.⁵¹ “The U.S. spent nearly \$88 billion treating cancer in 2014, with patients paying nearly \$4 billion out-of-pocket.”⁵² All of that spending, however, does not necessarily translate into positive outcomes for every patient.⁵³

II. CHALLENGES TO THE REGULATORY FRAMEWORK AND AN OVERVIEW OF THE EXPANDED ACCESS PROGRAM

A. PRIOR PRE-APPROVAL ACCESS CHALLENGES

The tension—highlighted most recently by the right-to-try movement—between ensuring patients have access to potentially groundbreaking medicines as soon as possible and ensuring that these therapies are both safe and effective is not nascent. There have been three significant pre-approval access challenges—starting with *Rutherford v. United States* in 1975—to the FDA’s regulatory framework since the enactment of the Kefauver-Harris Amendment.

1. 1970s: Laetrile, the FDCA, and *Rutherford v. United States*

In 1975, a few individuals with terminal cancer filed a lawsuit seeking to enjoin the FDA from obstructing the interstate shipment and sale of the alternative treatment laetrile because it was not approved by the FDA.⁵⁴ The

50. BIOPHARMACEUTICAL RESEARCH & DEVELOPMENT, *supra* note 35, at 1 (“The overall probability of clinical success . . . is estimated to be less than 12%.”); *see also* CLINICAL DEVELOPMENT SUCCESS RATES 2006–2015, *supra* note 33, at 7 (“[O]nly 9.6% of drug development programs successfully make it to market.”); Joseph A. DiMasi, Henry G. Grabowski & Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20, 20 (2016); Matthew Herper, *The Cost of Developing Drugs Is Insane. That Paper that Says Otherwise Is Insanely Bad*, FORBES (Oct. 16, 2017, 10:58 AM), <https://www.forbes.com/sites/matthewherper/2017/10/16/the-cost-of-developing-drugs-is-insane-a-paper-that-argued-otherwise-was-insanely-bad>.

51. Michelle Cortez, *The ‘Right to Try’ Could Cost Dying Patients a Fortune*, BLOOMBERG (June 20, 2018, 10:44 AM) [hereinafter Cortez, *Cost Dying Patients*], <https://www.bloomberg.com/news/articles/2018-06-20/the-price-to-try-a-drug-could-be-300-000-for-dying-patients>.

52. Liz Szabo, *Widespread Hype Gives False Hope to Many Cancer Patients*, KAISER HEALTH NEWS (Apr. 27, 2017), <https://khn.org/news/widespread-hype-gives-false-hope-to-many-cancer-patients>.

53. *See id.*

54. *United States v. Rutherford*, 442 U.S. 544, 548 (1979). Laetrile, derived from apricot pits, had been touted as an anti-cancer drug despite limited clinical studies examining its safety and efficacy. Barron H. Lerner, *McQueen’s Legacy of Laetrile*, N.Y. TIMES (Nov. 15, 2005), <http://www.nytimes.com/2005/11/15/health/mcqueens-legacy-of-laetrile>.

district court ordered the FDA to allow patients pre-approval access.⁵⁵ On appeal, the U.S. Court of Appeals for the Tenth Circuit referred the issue to the FDA,⁵⁶ which found laetrile was a new drug within the meaning of the FDCA and could be barred from interstate sale until the necessary safety and efficacy data was submitted for FDA review and received FDA approval.⁵⁷ The district court vacated that decision on statutory and constitutional grounds,⁵⁸ and the FDA appealed.⁵⁹ The Tenth Circuit—rather than relying on the district court’s reasoning—held instead that the FDCA’s “‘safety’ and ‘effectiveness’ terms” did not apply to individuals with terminal cancer diagnoses.⁶⁰

The case was eventually heard by the Supreme Court, which decided in favor of the agency’s FDCA interpretation.⁶¹ The Court held the FDCA made “no special provision for drugs used to treat terminally ill patients” based on the statute’s plain language.⁶² The Court also explained that it could not imply a statutory exception because the “legislative history and consistent administrative interpretation” of the FDCA did not support one.⁶³

55. *Rutherford*, 442 U.S. at 548 (citing *Rutherford v. United States*, 399 F. Supp. 1208, 1215 (W.D. Okla. 1975)).

56. *Id.* at 549 (citing *Rutherford v. United States*, 542 F.2d 1137 (10th Cir. 1976)).

57. *Rutherford v. United States*, 438 F. Supp. 1287, 1289 (W.D. Okla. 1977). A new drug is one “not generally recognized, among experts . . . as safe and effective for use under conditions prescribed, recommended, or suggested in the labeling.” 21 U.S.C. § 321(p)(1) (2018).

In addition to determining that laetrile was a new drug, the FDA also concluded that the Kefauver-Harris Amendment’s grandfather clause did not apply. *Rutherford*, 438 F. Supp. at 1289. The grandfather clause exempted drugs from the effectiveness requirement if they were on the day prior to enactment of the Kefauver-Harris Amendments (1) “commercially used or sold in the United States,” (2) not a new drug under section 201(p) of the 1938-version of the FDCA, and (3) not “covered by an effective application” under section 505 of the 1938-version of the FDCA. *See* Kefauver-Harris Amendment § 107(4).

58. *Rutherford*, 438 F. Supp. at 1294, 1300–01 (finding FDCA’s grandfather clause exempted laetrile from any pre-market approval requirement and that regardless of the statutory interpretation the right to “use a nontoxic substance” was encompassed within one’s “constitutional right of privacy”).

59. *Rutherford v. United States*, 582 F.2d 1234, 1235 (10th Cir. 1978).

60. *Id.* at 1236. The court was not persuaded by the FDA’s argument that a non-effective drug used in the treatment of a life-threatening disease was also not safe. *Id.* at 1236–37. The court also expressly declined to address the lower court’s constitutional findings. *Id.* at 1237.

In another case involving laetrile, a physician and several other co-defendants appealed misdemeanor convictions “for conspiracy to sell and prescribe an unapproved drug laetrile”—a violation of California Health and Safety Code section 1707.1—as unconstitutional. The California Supreme Court held, however, that “a right of access to drugs not recognized by the government as effective” was not a fundamental right recognized by the California or U.S. Constitutions. *People v. Privitera*, 591 P.2d 919, 925 (Cal. 1979).

61. *United States v. Rutherford*, 442 U.S. 544, 551 (1979).

62. *Id.* (explaining how FDCA section 505 requires FDA approval of a new drug unless the drug qualifies for grandfather clause exemption or is being administered through a clinical trial).

63. *Id.* at 552.

2. 1980s–1990s: The Reagan Administration and the HIV/AIDS Epidemic

After President Ronald Reagan’s election in 1980, his administration ushered in widespread deregulation efforts across all areas of government.⁶⁴ Those efforts included (1) amending the FDCA, which the administration viewed as unnecessarily delaying drug approvals, and (2) establishing a defined program for terminally patients seeking access to investigational drugs for treatment rather than research purposes.⁶⁵ The FDA, in response to the administration’s latter concern, proposed codifying the agency’s existing informal pre-approval access procedures.⁶⁶ Those efforts became even more urgent with the HIV/AIDS epidemic though the agency’s efforts and the administration’s initial concern regarding pre-approval access were not aimed directly at aiding individuals with HIV/AIDS.⁶⁷

The FDA promulgated several significant changes not only to improve patient access outside of the clinical trial setting to drugs still in clinical development, but also to reduce the length of time between discovery and final FDA approval. The latter issue being one in which the interests of activists and manufacturers aligned, as both advocated for changes to the regulatory framework.⁶⁸ First, the FDA amended its regulations in 1987 to allow widespread access to an investigational drug outside of the clinical trial setting through a “treatment protocol.”⁶⁹ The agency continued to apply an informal standard for individual requests until the Food & Drug

64. The deregulation efforts of the Trump administration, which include the Right to Try Act, arguably closely mirror, if not surpass, the deregulation efforts of the Reagan administration. See Paul Bedard, *Trump Ahead of Reagan’s Record in Cutting Regulations*, WASH. EXAMINER (Oct. 3, 2017, 7:16 AM), <https://www.washingtonexaminer.com/trump-ahead-of-reagans-record-in-cutting-regulations>.

65. Lewis A. Grossman, *AIDS Activists, FDA Regulation, and the Amendment of America’s Drug Constitution*, 42 AM. J.L. & MED. 687, 700–01 (2016).

66. *Id.* at 699–700 (citing Proposed New Drug, Antibiotic, and Biologic Drug Product Regulations, 48 Fed. Reg. 26,720, 26,742 (June 9, 1983) (codified at 2 C.F.R. pt. 312)).

67. *Id.* at 701–02, 706.

68. *Id.* at 694, 704–07 (“AIDS activism was the first mass movement for freedom of therapeutic choice within orthodox scientific medicine.”); see also REBECCA DRESSER, *WHEN SCIENCE OFFERS SALVATION: PATIENT ADVOCACY AND RESEARCH ETHICS* 48–49, 52–55 (2001) (citing individual autonomy, the anticipated hastened development of improved treatments as a result of more clinical involvement, and justice by way of non-exclusionary participation as reasons to change the regulatory framework).

69. A protocol sponsor could request that an investigational drug be made available for widespread use if the drug was intended for the treatment of a “serious or immediately life-threatening disease” for which there was “no comparable or satisfactory alternative drug or other therapy available.” 21 C.F.R. 312.34 (1987). The FDA also required the manufacturer to be actively investigating the drug in a “controlled clinical trial” or to have completed testing, and “actively pursuing marketing approval” of the therapy with “due diligence.” *Id.* A sponsor requesting access for a “substantial population” of patients with a serious disease would likely need to submit data from phase III trials. *Id.*

Administration Modernization Act of 1997 codified the expanded access program, which specifically addressed the need for a formal individual patient request process.⁷⁰ Second, the FDA created the Accelerated Approval pathway⁷¹ and introduced a striated review framework⁷² to speed up the availability of promising new drugs intended for the treatment of serious diseases or conditions. Subsequent congressional action in 1997 and 2012 armed the FDA with two additional means to further reduce the time from initial development of a drug to its approval.⁷³

3. 2000s: Pre-Approval Access, a Proposal, and *Abigail Alliance v. Von Eschenbach*

There was not another significant challenge to the drug development and approval process until an organization, seeking to improve terminally ill patients' abilities to obtain investigational drugs, proposed a "three-tiered approval system."⁷⁴ The first approval tier would have allowed limited

70. Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75,147, 75,148 (proposed Dec. 14, 2006) (to be codified at 21 C.F.R. pt. 312); Grossman, *supra* note 65, at 735. The current individual patient expanded access program is separately discussed in Section II.B.

71. The Accelerated Approval pathway enables a drug for the treatment of a serious condition to be approved based on a "surrogate endpoint." U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS—DRUGS AND BIOLOGICS 1–7 (2014) [hereinafter EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS], <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf>. Although a surrogate endpoint is not always indicative of the viability of a treatment, it "may be used instead of stronger indicators, such as longer survival or improved quality of life, because the results of the trial can be measured sooner." *Surrogate Endpoint*, NAT'L CANCER INST., <https://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=729831> (last visited Feb. 8, 2019). The FDA has approved more than 100 new drug applications submitted through the accelerated approval pathway since its introduction in 1992. See U.S. FOOD & DRUG ADMIN., CDER DRUG AND BIOLOGIC ACCELERATED APPROVALS BASED ON A SURROGATE ENDPOINT (2018), <https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/NDAandBLAApprovalReports/UCM404466.pdf>.

72. With the striated review framework, an investigational drug will either receive "Priority" or "Standard Review." The FDA will grant an investigational drug Priority Review when it "treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness." See EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS, *supra* note 71, at 24. The designation requires the FDA to review a marketing application within six months of receiving the submission rather than the standard ten-month review. *Id.* at 8.

73. In the last twenty years, the FDA has introduced two other approaches to address concerns regarding the lengthy approval process—Fast Track and Breakthrough Therapy. See Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 112, 111 Stat. 2296, 2309–10 (1997); Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 902, 126 Stat. 993-1132 (2012). For more background regarding these two expedited designations, see EXPEDITED PROGRAMS FOR SERIOUS CONDITIONS, *supra* note 71, at 9–15.

74. Karyn Hede, *Patient Group Seeks Overhaul of FDA Clinical Trial System in Court*, 98 J. NAT'L CANCER INST. 1268, 1268 (2006); see also Citizen Petition of the Abigail Alliance and the Washington Legal Foundation to the Food and Drug Administration, U.S. Dept. of Health and Human Services, *In re*

marketing of investigational drugs following completion of phase I trials.⁷⁵ The organization—the Abigail Alliance for Better Access to Developmental Drugs (the “Abigail Alliance”)⁷⁶—claimed terminally ill patients with no other treatment options faced a “different risk-benefit tradeoff” and should have the option to try investigational drugs.⁷⁷ The FDA rejected this proposal, explaining that this approach “would upset the appropriate balance” by “giving almost total weight to the goal of early availability and giving little recognition to the importance of marketing drugs with reasonable knowledge . . . of their likely clinical benefit and their toxicity.”⁷⁸

The Abigail Alliance, agency rejection in hand, filed an action against the FDA.⁷⁹ The organization sought to block the agency’s policy prohibiting the pre-approval sale of drugs to individuals with terminal conditions.⁸⁰ The Abigail Alliance argued that the FDA’s policy “violate[d] terminally ill patients’ constitutional privacy and liberty rights, as well as their due process rights to life.”⁸¹ The district court found these claims legally unpersuasive.⁸²

Tier 1 Initial Approval Program to Expedite the Availability of Lifesaving Drugs (June 11, 2003) [hereinafter *Abigail Alliance Citizen Petition*].

75. *Abigail Alliance Citizen Petition*, *supra* note 74, at 5.

76. The Abigail Alliance for Better Access to Developmental Drugs (the “Abigail Alliance”) was founded in November 2001 following the death of twenty-one-year-old Abigail Burroughs from squamous cell carcinoma of the head and neck. *About*, ABIGAIL ALL. FOR BETTER ACCESS TO DEV. DRUGS, <https://www.abigail-alliance.org/p/about.html> (last visited Feb. 8, 2017). Burroughs’s story is similar to that of Andrea Sloan’s. After traditional chemotherapy and radiation failed, Burroughs attempted to enroll in multiple clinical trials but did not meet the eligibility requirements. While she was ultimately able to enroll in a clinical trial, her cancer had progressed, and she died shortly thereafter. Peter Hart, *Abigail Alliance Case Discussed: Balancing Study Drugs, Safety*, UNIV. PITT. TIMES (Feb. 19, 2009), <http://www.utimes.pitt.edu/?p=8605>; Peter D. Jacobson & Wendy E. Parmet, *A New Era of Unapproved Drugs: The Case of Abigail Alliance v. Von Eschenbach*, 297 JAMA 205, 205 (2007). The investigational drug that Burroughs sought, cetuximab, was at the time only being studied in patients with colorectal cancer. *Id.* In 2011—ten years after Burroughs’s death—cetuximab was approved by the FDA for the treatment of patients with late-stage head and neck cancer. Ben Leach, *Cetuximab Approved by FDA for Patients with Late-Stage Head and Neck Cancer*, ONCLIVE (Nov. 7, 2011), <http://www.onclive.com/web-exclusives/cetuximab-approved-by-fda-for-patients-with-late-stage-head-and-neck-cancer>.

77. *Abigail Alliance Citizen Petition*, *supra* note 74, at 9.

78. *Abigail All. for Better Access to Dev. Drugs v. McClellan*, 2004 U.S. Dist. LEXIS 29594 at *4, *20–21 (D.D.C. 2004) (citing Letter from Peter J. Pitts, Associate Commissioner for External Relations, Department of Health and Human Services, to Frank Burroughs, President Abigail Alliance for Better Access to Developmental Drugs (Apr. 25, 2003)).

79. *Id.* at *5.

80. *Id.*

81. *Id.* The Abigail Alliance reasoned that if companies were allowed to profit from sales of investigational drugs to terminally ill patients, they would be more apt to provide terminally ill patients access under compassionate use. *Id.*

82. *Id.* at *25–36. The court concluded that no recognized fundamental right was involved because the “plaintiffs have stated the holdings of *Glucksberg*, *Cruzan*, and *Griswold* too broadly in their attempt

But a United States Court of Appeals for the District of Columbia Circuit (“D.C. Circuit”) panel, in a 2–1 split, agreed with the group, holding that the due process clause protected the right of terminally ill patients to decide whether to use investigational drugs that the FDA had determined were safe enough for additional clinical trials after reviewing results from phase I clinical trials.⁸³ The panel directed the district court to determine whether the FDA’s policy was narrowly tailored to serve a compelling governmental interest.⁸⁴

The FDA’s request for an en banc hearing was granted before a lower court could apply strict scrutiny.⁸⁵ The court en banc flatly rejected the panel’s decision.⁸⁶ The court expressed “serious doubt” about the constitutional validity of the Abigail Alliance’s articulated right: a “fundamental right of access for the terminally ill to experimental drugs.”⁸⁷ To establish its articulated right, the Abigail Alliance needed to illustrate a tradition of accessibility to drugs that were not proven to be safe or effective.⁸⁸ The en banc court found that “FDA regulation of post-phase I drugs [was] entirely consistent with [the United States’] historical tradition of prohibiting the sale of unsafe drugs.”⁸⁹ The en banc court also disputed the group’s effectiveness argument, noting the existence of “at least some drug regulation prior to [the Kefauver-Harris Amendment] address[ing] efficacy.”⁹⁰ The en banc court also dismissed the Abigail Alliance’s

to apply the privacy and liberty rights to the instant case,” and that there was no authority supporting “the proposition that the due process right to life extends to requiring affirmative access by terminally ill patients to investigational drugs.” *Id.* at *31–32. Therefore, the FDA policy was rationally related to a legitimate state interest. *Id.*

83. *Abigail All. for Better Access to Dev. Drugs v. Von Eschenbach*, 445 F.3d 470, 486 (D.C. Cir. 2006). Of note, the court distinguished this action from *Rutherford v. United States* by emphasizing that in this action, terminally ill patients were seeking investigational drugs that had successfully completed phase I trials. *Id.* at 486.

84. *Id.*

85. *See Abigail All. for Better Access to Dev. Drugs v. Von Eschenbach*, 469 F.3d 129, 132 (D.C. Cir. 2006).

86. *Abigail All. for Better Access to Dev. Drugs v. Von Eschenbach*, 495 F.3d 695, 711–12, 714 (D.C. Cir. 2007). Only the author of the panel’s majority opinion dissented. *Id.*

87. *Id.* at 703. The en banc court noted that the Alliance’s “claimed right depends on a regulatory determination that the drug is safe for testing, prompting an obvious question: How can a constitutional right be defined by an administrative regulation that is subject to change?” *Id.* at 702 n.6.

88. *Id.* at 702–03.

89. *Id.* at 703 n.7, 704–06 (discussing the long history of drug regulation in England, the adoption of drug-dispensing legislation by the Virginia colony, and enactment of various other legislation regulating unsafe drugs in Louisiana, Alabama and Georgia).

90. *Id.* at 706–07 (explaining that if lack of government interference was sufficient, “it would be easy to employ such a premise to support sweeping claims of fundamental rights”). The court posited that a more “plausible explanation for the limited efficacy regulation” was the fact that “[t]he history of the effectiveness requirement in drug regulation is inextricably linked to the advent of the randomized,

argument that the right to self-preservation—based on the common law doctrine of necessity, the tort of intentional interference with rescue, and the right to self-defense—created a constitutionally protected right in this context.⁹¹ The court concluded that the Abigail Alliance’s articulated right was not fundamental.⁹² The court held that “the FDA’s policy of limiting access to investigational drugs [was] rationally related to the legitimate state interest of protecting patients, including the terminally ill, from potentially unsafe drugs with unknown therapeutic effects.”⁹³

Two years after the D.C. Circuit’s decision in *Abigail Alliance*, the FDA finally issued revised expanded access regulation clarifying the process by which an individual patient could request expanded access.⁹⁴ The current expanded access program is discussed in greater detail below.

B. THE EXPANDED ACCESS PROGRAM

The expanded access program, as discussed, was designed to address concern that some individuals may not have an opportunity to try a promising therapy given the sometimes ten-year path to formal regulatory approval. The expanded access program allows some patients with serious or immediately life-threatening diseases to use “an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.”⁹⁵ The program is available for individual patient use,

controlled clinical trial as the cornerstone of medical research . . . , [which] would not become widely recognized until the twentieth century.” *Id.* at 706 n.12 (quoting Jennifer Kulynych, *Will FDA Relinquish the “Gold Standard” for New Drug Approval? Redefining “Substantial Evidence” in the FDA Modernization Act of 1997*, 54 FOOD & DRUG L.J. 127, 131 (1999)).

91. *See id.* at 707–10.

92. *Id.* at 713.

93. *Id.* The en banc court further substantiated its reasoning with previous Supreme Court decisions upholding the FDCA and prior circuit court decisions rejecting “arguments that the Constitution provides an affirmative right of access to particular medical treatments reasonably prohibited by the Government.” *Id.* at 710–13 (citing *Gonzales v. Raich*, 545 U.S. 1, 28 (2005); *United States v. Rutherford*, 442 U.S. 544, 552 (1979)); *see also id.* at 711 n.18 (citing *Mitchell v. Clayton*, 995 F.2d 772, 775 (7th Cir. 1993); *N.Y. State Ophthalmological Soc’y v. Bowen*, 854 F.2d 1379, 1389 (D.C. Cir. 1988); *Carnohan v. United States*, 616 F.2d 1120, 1122 (9th Cir. 1980); *Rutherford v. United States*, 616 F.2d 455, 457 (10th Cir. 1980)).

94. Expanded Access to Investigational Drugs for Treatment Use, 74 Fed. Reg. 40,900, 40,942–45 (Aug. 13, 2009) (codified at 21 C.F.R. pts. 312, 316). While the *Abigail Alliance* case made its way through the judicial system in 2006, the FDA announced proposed rules to clarify the individual patient expanded access program. Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75,147, 75,148 (proposed Dec. 14, 2006) (to be codified at 21 C.F.R. pt. 312).

95. *Expanded Access*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm> (last updated Nov. 8, 2018).

intermediate-size patient use, and widespread patient use.⁹⁶ In addition to the patient, there are three other important decisionmakers. Section II.B.1 describes how a physician would initiate an expanded access request for an individual patient. Sections II.B.2 and II.B.3 then discuss the criteria used by biopharmaceutical companies and the FDA to determine eligibility in the individual-patient setting.

1. How a Physician Requests Expanded Access for Individual Patient Use

Prior to initiating an expanded access request for a patient, the requesting physician must first conclude that “the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition.”⁹⁷

After this determination is made, the physician must then seek a letter of authorization (“LOA”) from the manufacturer.⁹⁸ The request must be made by a physician. The LOA allows the FDA to refer to the requested investigational drug’s IND file instead of requiring the requesting physician to obtain confidential information regarding the drug’s pharmacology, toxicology, chemistry, or manufacturing process.⁹⁹ As evidenced by Andrea Sloan’s unsuccessful request, this has been the greatest source of frustration for patients seeking expanded access use. Aside from Pfizer, most companies do not disclose how many requests they receive or grant each year.¹⁰⁰ This

96. *Expanded Access Categories for Drugs (Including Biologics)*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm431774.htm> (last updated Jan. 4, 2018).

97. 21 C.F.R. § 312.310(a)(1) (2018); *Expanded Access to Investigational Drugs for Treatment Use*, 71 Fed. Reg. 75,147, 75,153 (Dec. 14, 2006) (codified at 21 C.F.R. pt. 312).

The evidence needed to make this determination for expanded access for an individual patient will vary. For a patient with an immediately life-threatening condition, the evidentiary burden could be very low—little if any clinical evidence to suggest a potential benefit or possibly only animal data to support safety of the use. For a patient with a serious, but not immediately life-threatening, condition who could expect to enjoy a reasonable quality of life for an extended time without any treatment, the evidentiary burden would be higher.

Id. § 312.310(a)(1).

98. *Expanded Access: Information for Physicians*, U.S. FOOD & DRUG ADMIN. [hereinafter *Information for Physicians*], <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm429624.htm> (last updated Dec. 17, 2018).

99. *IND Applications for Clinical Treatment: Contents and Format*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm363005.htm> (last updated Dec. 23, 2015). The criteria used by a manufacturer to determine whether to provide a letter of authorization (“LOA”) is covered in Section II.B.2.

100. *Compassionate Use and Expanded Access*, PFIZER [hereinafter *Pfizer Policy*], <https://www.pfizer.com/purpose/medicine-access/compassionate-use> (last visited Feb. 8, 2019) (“In 2017, the PfizerCAREs portal received 4,818 requests from 59 countries, of which 98% were approved.”); see also *Criteria for Consideration of Access*, GENENTECH [hereinafter *Genentech Policy*],

step of the process can also be lengthy as current FDA regulation does not impose a time restraint.¹⁰¹ So even if a company acknowledges receipt of a request within two-to-three business days,¹⁰² the company is not required to expediently review that request, which often involves multiple parties within a company.¹⁰³

If the company agrees to grant use and provides a LOA, the requesting physician would then submit an application form to the FDA. The FDA asks the physician to provide an overview of the patient's clinical history, the rationale for the expanded access request, and the proposed treatment plan.¹⁰⁴ The FDA has up to thirty days to review the application and provide feedback.¹⁰⁵ A 2017 U.S. Government Accountability Office ("GAO") report found that the FDA's median response time was no more than nineteen days for non-emergency situations.¹⁰⁶

While the FDA reviews the application, the physician must also obtain approval from his or her institution's or hospital's institutional review board ("IRB").¹⁰⁷ The requesting physician can also request a waiver from the

<https://www.gene.com/patients/investigational-medicines/criteria> (last visited Feb. 8, 2019). See generally U.S. GOV'T ACCOUNTABILITY OFFICE, GAO-17-564, INVESTIGATIONAL NEW DRUGS: FDA HAS TAKEN STEPS TO IMPROVE THE EXPANDED ACCESS PROGRAM BUT SHOULD FURTHER CLARIFY HOW ADVERSE EVENTS DATA ARE USED 16 (2017) [hereinafter GAO-17-564, INVESTIGATIONAL NEW DRUGS], <https://www.gao.gov/assets/690/685729.pdf> (discussing findings of an FDA survey of nine manufacturers, in which manufacturers reported receiving between thirty-nine and 800 individual patient expanded access requests).

101. Steve Usdin, *FDA to Facilitate Access to Unapproved Drugs*, BIOCENTURY (Dec. 14, 2018, 5:34 PM), <https://www.biocentury.com/biocentury/regulation/2018-12-14/how-fda-plans-help-patients-get-expanded-access-unapproved-drugs>.

102. See generally *Company Directory*, REAGAN-UDALL FOUND., <http://navigator.reaganudall.org/company-directory> (last visited Feb. 8, 2019).

103. See *infra* Appendix.

104. *Information for Physicians*, *supra* note 98. An abbreviated form was introduced by the FDA in 2016 after complaints that the previous form, which was required for all expanded access categories, was overly complex and time consuming. See discussion *infra* Section III.B.

105. 21 C.F.R. § 312.20(c) (2018). A patient may start treatment thirty days after the FDA's receipt of the IND submission, or earlier if the FDA informs the treating physician that expanded access use can start. *Id.* § 312.20(c); FDA, EXPANDED ACCESS: INFORMATION FOR PATIENTS, <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/ucm20041768.htm> (last updated Dec. 14, 2018). The criteria used by the FDA to determine whether to grant expanded access is covered in Section II.B.3.

106. GAO-17-564, INVESTIGATIONAL NEW DRUGS, *supra* note 100, at 20.

107. U.S. FOOD & DRUG ADMIN., INDIVIDUAL PATIENT EXPANDED ACCESS APPLICATIONS: FORM FDA 3926 GUIDANCE FOR INDUSTRY 6 (2017), <https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm432717.pdf>. "An [institutional review board ("IRB")] means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of biomedical research involving human subjects. The primary purpose of IRB review is to assure that the rights and welfare of human subjects

FDA, which would allow the expanded access request to be reviewed by either the IRB chair or another designated member.¹⁰⁸ The physician must also discuss the expanded access requirements with the patient and secure the patient's informed consent to treatment.¹⁰⁹

2. How Companies Evaluate an Individual Patient Request

The expanded access regulation does not prescribe the criteria a manufacturer should use when determining whether to grant an expanded access request.¹¹⁰ Industry groups Pharmaceutical Research and Manufacturers of America (“PhRMA”) and BIO, however, have each separately published guiding principles for the groups' respective members that closely mirror the evaluation criteria used by the FDA.¹¹¹ PhRMA recommends that manufacturers consider five factors: (1) whether the individual has exhausted all available treatment options for a serious or life-threatening illness; (2) whether “[t]he investigational drug [is] under active clinical development”; (3) whether “[t]he patient is ineligible for, or otherwise unable to participate in, clinical trials”; (4) whether “[t]he potential benefit to the patient [outweighs the] potential risk”; and (5) whether approving the request would interfere with the “successful completion of the clinical trial process.”¹¹²

A survey of twenty biopharmaceutical companies' eligibility criteria¹¹³

are protected.” *Id.* at 6 n.10.

108. 21 C.F.R. § 312.10 (2018); *see also* Scott Gottlieb, *Expanded Access: FDA Describes Efforts to Ease Application Process*, FDA VOICE (Oct. 3, 2017), <https://www.fda.gov/NewsEvents/Newsroom/FDAVoices/ucm612009.htm>.

109. *Information for Physicians*, *supra* note 98.

110. There is also no guidance on who within a biopharmaceutical company should make that decision. In general, most companies delegate decisionmaking authority to their medical or clinical team. *See infra* Appendix.

111. *See* PHARM. RESEARCH AND MFRS. OF AM., PRINCIPLES ON THE CONDUCT OF CLINICAL TRIALS AND COMMUNICATION OF CLINICAL TRIAL RESULTS 28–29 (2015) [hereinafter PRINCIPLES ON THE CONDUCT OF CLINICAL TRIALS], http://phrma-docs.phrma.org/sites/default/files/pdf/042009_clinical_trial_principles_final_0.pdf; *BIO Principles on Expanded Access to Investigational, Unapproved Medicines*, BIOTECH. INNOVATION ORG. [hereinafter *BIO Principles on Expanded Access*], <https://www.bio.org/articles/bio-principles-expanded-access-investigational-unapproved-medicines> (last visited Feb. 8, 2019); *see also* Bill Chin, *Newly Implemented Expanded Access Principles Support Commitment to Patients*, PHRMA: THE CATALYST (June 3, 2015), <https://catalyst.phrma.org/newly-implemented-expanded-access-principles-support-commitment-to-patients>. The evaluation criteria of the FDA, respectively, are discussed in Section II.B.3.

112. PRINCIPLES ON THE CONDUCT OF CLINICAL TRIALS, *supra* note 111, at 28–29.

113. The Appendix surveys the expanded access criteria of the top twenty pharmaceutical companies by global sales. *Top Pharma List: Top 25 Pharma Companies by Global Sales*, PMLIVE, http://www.pmlive.com/top_pharma_list/global_revenues (last visited Feb. 8, 2019). For additional analysis of expanded access policies, *see* Emily Jung et al., *Prevalence of Publicly Available Expanded*

illustrates that most large companies offering expanded access have adopted criteria modeled off either PhRMA or BIO's guidelines, with only slight variations.¹¹⁴ In general, companies include criteria limiting expanded access to patients with serious or life-threatening conditions. The extent to which a patient must have tried standard treatment options and must not have other treatment options available varies. A few companies require the patient to have tried standard treatments unsuccessfully and to not have other treatment options available. Other companies just require that the patient does not have other treatment options available. The real difference in this language, however, might be just semantics.

Of the companies surveyed, one also factored in a patient's ability to regularly travel to a treating site for observation and follow-up while receiving the investigational drug when deciding whether to grant an expanded access request.¹¹⁵ Likewise, manufacturers will not consider an expanded access request unless the drug is in active development (that is, the company cannot have discontinued the program), but some companies choose to define this criterion more narrowly than BIO or PhRMA.¹¹⁶ Take for examples, Merck, Amgen, and Allergan, which will not grant requests for a specific drug unless the company is actively developing the drug in the proposed intended use.¹¹⁷ The criteria used by Merck and a few other companies also requires that the company have plans to submit a marketing application.¹¹⁸

Given concerns about expanded access impacting clinical trial enrollment, companies are hesitant to grant an expanded access request unless the individual is unable to participate in a clinical trial. This criterion is generally left vague, but some companies provide specific factors that they will or will not consider.¹¹⁹ For example, under Genentech's criteria, an individual who lives too far away from a clinical trial center would not be considered ineligible for a clinical trial and therefore would not qualify for

Access Policies, 104 CLINICAL PHARM. & THERAPEUTICS 1016 (2018).

114. See *infra* Appendix. These policies were not widely available until the enactment of the 21st Century Cures Act ("Cures Act"). For a more in-depth discussion of the Cures Act, see *supra* Section III.B.

115. See *infra* Appendix.

116. *Id.* PhRMA and BIO do not define active clinical development. PRINCIPLES ON THE CONDUCT OF CLINICAL TRIALS, *supra* note 111, at 28; *BIO Principles on Expanded Access*, *supra* note 111.

117. See *infra* Appendix.

118. *Id.*

119. *Id.* This aligns with PhRMA's approach. PRINCIPLES ON THE CONDUCT OF CLINICAL TRIALS, *supra* note 111, at 28 ("Geographic limitations alone would generally not be considered a barrier to participation in clinical trials.").

expanded access based on this factor alone.¹²⁰ In contrast, Pfizer and Teva Pharmaceutical would consider geographic limitations as a factor affecting a patient's ability to participate in a clinical trial.¹²¹

All of the companies surveyed included a criterion requiring the potential benefits of the drug to outweigh the potential combined risks of the treatment and the disease to the individual patient.¹²² To make this risk-benefit assessment, PhRMA explains, "there should be sufficiently robust preliminary safety and efficacy data, including dosing information, to determine that the preliminary benefit-risk balance is positive for the specific indication for which the request is made."¹²³ While some companies keep this criterion vague to allow for greater discretion, a few companies' criteria specifically mentions a dosing requirement.¹²⁴ Although most companies' criteria did not distinguish between children and adults, one company's guidelines specifically require sufficient pediatric data to determine the appropriate dosage before it will grant expanded access use for a child.¹²⁵

Like the other criteria, almost all of the companies surveyed had some language in their expanded access guidelines addressing the clinical trial process and, more specifically, the need to ensure that pre-approval access use did not interfere with the clinical trial process.¹²⁶ A few companies specifically consider whether they have adequate drug supply for both their clinical trials and expanded access when making the determination.¹²⁷ While not specifically addressed, this criterion likely also considers the extent to which expanded access use might impact other aspects of clinical development, such as the FDA's use of adverse events occurring during expanded access use, when reviewing an investigational drug's marketing

120. *Genentech Policy*, *supra* note 100. This could have implications for some rural patients, who might have difficulties enrolling in a clinical trial given the distance and costs associated with travel. REBECCA A. ENGLISH ET AL., TRANSFORMING CLINICAL RESEARCH IN THE UNITED STATES: CHALLENGES AND OPPORTUNITIES 24 (2010), https://www.ncbi.nlm.nih.gov/books/NBK50892/pdf/Bookshelf_NBK50892.pdf.

121. *Pfizer Policy*, *supra* note 100; *see also* TEVA PHARM., EXPANDED ACCESS PROGRAMS 2 (2015), <https://www.tevapharm.com/files/policy.pdf>.

122. *See infra* Appendix.

123. PRINCIPLES ON THE CONDUCT OF CLINICAL TRIALS, *supra* note 111, at 29; *see also* *BIO Principles on Expanded Access*, *supra* note 111 (discussing similar requirements).

124. *See, e.g., Position on Expanded Access to Investigational Medicines*, ASTELLAS [hereinafter *Astellas Position*], <https://www.astellas.com/system/files/Position%20on%20Expanded%20Access%20E%202017-04-11.pdf> (last updated Apr. 2017).

125. *Allergan Pre-Approval Access Program*, ALLERGAN, <https://www.allergan.com/research-and-development/pre-approval-access> (last visited Feb. 8, 2019).

126. *See infra* Appendix.

127. *See, e.g., Genentech Policy*, *supra* note 100.

application.¹²⁸ A few companies also build in additional discretion by allowing their medical teams to establish additional criteria in light of a given drug's current development and available data.¹²⁹

As discussed, however, most companies do not disclose how many expanded access requests they receive or, of those, how many they grant.¹³⁰ This lack of disclosure makes it difficult for physicians, patients, or even the FDA to hypothesize how companies apply their criteria when reviewing an expanded access request. Two companies have made this type of information publicly available, but through different channels and with different levels of information. Pfizer, for example, discloses its overall expanded access approval rate on its website, but it does not explain the rationale for the small percentage of denials. By contrast, as part of a case study in the *Journal of the American Medical Association* (“JAMA”), Janssen released limited expanded access data regarding one investigational drug for a distinct period of time. That study reported the most common reason the company denied a request was an unfavorable risk-benefit profile.¹³¹

3. How the FDA Evaluates an Individual Patient Request

The FDA, as mentioned, must review all expanded access requests. When reviewing an expanded access request—whether for individual patient use, intermediate-size patient use, or widespread patient use—the FDA examines three threshold criteria: (1) patient eligibility; (2) risk-benefit analysis; and (3) impact on clinical trials.

a. Patient Eligibility

The patient or group of patients must have a “serious or immediately life-threatening disease or condition,” in which “no comparable or satisfactory alternative therapy” is available.¹³² An “immediately life-

128. See PRINCIPLES ON CONDUCT OF CLINICAL TRIALS, *supra* note 111, at 29; *BIO Principles on Expanded Access*, *supra* note 111. See also *infra* Section III.B for a discussion regarding the FDA's use of adverse events.

129. See *infra* Appendix.

130. See *supra* note 100 and accompanying text.

131. Arthur L. Caplan & Amrit Ray, *The Ethical Challenges of Compassionate Use*, 315 JAMA 979, 980 (2016).

Between July 1 and December 31, 2015, Janssen received 160 preapproval access requests for daratumumab. Of these, company physicians determined that [forty-three] had a benefit-risk profile that was not favorable, [twenty-eight] requests had not exhausted all approved alternative therapies or were eligible for expanded-access programs or clinical trials, and [thirteen] were excluded for other reasons (eg, incomplete data for assessment).

Id.

132. 21 C.F.R. § 312.305(a)(1) (2018).

threatening disease” is defined 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.”¹³³ A “serious disease” is defined as one “associated with morbidity that has substantial impact on day-to-day functioning.”¹³⁴ The FDA has previously authorized expanded access use for serious diseases like amyotrophic lateral sclerosis (“ALS”), narcolepsy, and Alzheimer’s disease.¹³⁵ In guidance from the FDA, the agency further clarifies its standard for a serious disease explaining: “short-lived and self-limiting morbidity will usually not be sufficient to qualify a condition as serious, but the morbidity need not be irreversible, provided it is persistent or recurrent.”¹³⁶ The FDA interprets no comparable or satisfactory therapy to “mean that there exists no other available therapy to treat the patient’s condition or that the patient has tried available therapies and failed to respond adequately or is intolerant to them.”¹³⁷

b. Risk-Benefit Analysis

The second requirement is that the “potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease.”¹³⁸ This criterion acknowledges “the need for the risks and benefits of drugs to be well characterized” before the FDA will grant an expanded access request for an individual or group of patients.¹³⁹ This criterion is not intended to establish a uniform minimum approval threshold; that determination is dependent on the expanded access category and the seriousness of the disease.¹⁴⁰

c. Impact on Clinical Trials

The availability of expanded access also hinges on the FDA’s determination that “providing the investigational drug . . . will not interfere with . . . clinical investigations that could support marketing approval.”¹⁴¹ While it is understandable that many patients would prefer to secure an

133. *Id.* § 312.300(b).

134. *Id.*

135. Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75,147, 75,151 (proposed Dec. 14, 2006) (codified at 21 C.F.R. pt. 312). Additional examples of diseases and conditions that would fit in this category include seizures, rheumatoid arthritis, and chronic depression. *Id.*

136. *Id.*

137. *Id.*

138. 21 C.F.R. § 312.305(a)(2).

139. Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. at 75,150.

140. *Id.* at 75,151.

141. 21 C.F.R. § 312.305(a)(3).

investigational drug outside of the confines of a clinical trial, especially given their randomized nature, expanded access use cannot “compromise enrollment in the trials” that would ultimately support a marketing application.¹⁴² This criterion attempts to address concerns that expanded access would reduce individuals’ willingness to participate in clinical trials, especially given evidence that approximately 3% of adults with cancer enroll in clinical trials.¹⁴³

* * *

The three expanded access categories each have additional category-specific criteria that the FDA must consider before granting a request (Table 1). With an individual patient expanded access request, the FDA must also conclude that “the patient cannot obtain the drug under another IND or protocol.”¹⁴⁴ This means that the patient is either ineligible to enroll in ongoing clinical trials based on eligibility criteria or unable to enroll for some other reason.¹⁴⁵

142. Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. at 75,151.

143. REBECCA A. ENGLISH ET AL., *supra* note 120, at 64.

144. 21 C.F.R. § 312.310(a)(2).

145. U.S. FOOD & DRUG ADMIN., EXPANDED ACCESS TO INVESTIGATIONAL DRUGS FOR TREATMENT USE—QUESTIONS AND ANSWERS: GUIDANCE FOR INDUSTRY 12 (2017) [hereinafter EXPANDED ACCESS: GUIDANCE FOR INDUSTRY], <https://www.fda.gov/downloads/drugs/guidances/ucm351261.pdf>.

TABLE 1. Expanded Access Category-Specific Criteria

<i>Individual Patient Use^a</i>	<i>Intermediate-Size Patient Use^b</i>	<i>Widespread Patient Use^c</i>
Drug not available through another IND or protocol	Sufficient evidence that drug is safe at proposed dose and duration to support a clinical trial in the number of patients expected to receive the drug and at least preliminary clinical evidence of efficacy or a plausible pharmacologic effect to make expanded access a reasonable therapeutic option	Ongoing investigation of drug in controlled clinical trial under an IND designed to support marketing application <i>or</i> all clinical trials completed <i>and</i> active pursuit of marketing approval with due diligence * * * <i>Serious disease or condition:</i> enough clinical safety and efficacy data to support expanded access use (for example, at least “compelling data” from completed phase I trials) <i>Immediately life threatening disease or condition:</i> available scientific evidence giving reasonable basis to determine drug may be effective for expanded access use and not expose patient to “unreasonable and significant risk” (for example, either phase III or II trials, but possibly earlier clinical data)

Notes: ^a 21 C.F.R. § 312.310(a) (2018); ^b *Id.* § 312.215(b); ^c *Id.* § 312.320(a).

The FDA approves most expanded access requests.¹⁴⁶ Between 2012 and 2015, the agency approved approximately 99% of the more than 5,000 single-patient expanded access requests it received.¹⁴⁷ The FDA does not just rubber-stamp these requests. The FDA made “meaningful changes in approximately 10 percent of these cases to enhance patient safety” such as adjusting dosage, increasing safety oversight, and strengthening informed consent.¹⁴⁸ FDA Commissioner Scott Gottlieb explained:

[t]he changes are based on the scientific and medical expertise of our staff, and informed by confidential information provided to FDA by product sponsors during the course of development. This information is often unavailable to the treating physician—and the larger medical community—and becomes available only after a drug is approved.¹⁴⁹

The real question is how many expanded access requests never reach the FDA because the manufacturer declines to provide a letter of authorization.¹⁵⁰

III. THE RIGHT-TO-TRY MOVEMENT

In 2014, the Goldwater Institute, a conservative and libertarian public policy think tank, launched a new initiative based on patients’ right to “some choice over their own destinies.”¹⁵¹ The think tank’s initial goal was to pass state laws giving terminally ill patients the right to obtain access to investigational drugs that have completed phase I clinical trials without

146. For additional discussion regarding why the FDA might deny a request for individual patient expanded access, see *id.* at 12.

147. GAO-17-564, INVESTIGATIONAL NEW DRUGS, *supra* note 100, at 17 (reporting FDA received more than 5,000 single-patient expanded access requests during this period). The FDA also granted 245 requests from trial sponsors for expanded access in the intermediate-size and treatment protocol setting. *Id.* (stating that the FDA allowed 95.1% of intermediate-size requests and 100% of treatment protocol requests to proceed). The FDA does not specifically track the number of patients who are treated under intermediate-size or treatment protocol applications. In 2006, the FDA estimated that since the formal implementation of the expanded access program, this number was around 100,000 patients. Expanded Access to Investigational Drugs for Treatment Use, 71 Fed. Reg. 75,147, 75,148 (Dec. 14, 2006) (codified at 21 C.F.R. pt. 312).

148. *Examining Patient Access to Investigational Drugs: Hearing Before the H. Comm. on Energy and Commerce*, 115th Cong. (2017) (statement of Scott Gottlieb, U.S. Food & Drug Admin. Comm’r), <https://www.hhs.gov/about/agencies/asl/testimony/2017-10/examining-patient-access-to-investigational-drugs.html>.

149. *Id.*

150. See *supra* note 6 and accompanying text.

151. *Examining Patient Access to Investigational Drugs: Hearing Before the H. Comm. on Energy and Commerce*, 115th Cong. 2 (2017) (statement of Rep. Andy Biggs (R-Ariz.)); see also Sandefur, *supra* note 9, at 528.

interference from the FDA.¹⁵² This goal was later expanded to secure the enactment of a federal law under the same premise.

Section III.A outlines and assesses the movement's rationale for proposing a new pre-approval access pathway before briefly discussing the movement's success at the state level. Section III.B examines the FDA's attempts to address the movement's claims and why those attempts by the agency were insufficient. Section III.C discusses the efforts by Senator Ron Johnson (R-Wis.) to secure enactment of federal right to try legislation.

A. THE MOVEMENT'S RATIONALE FOR RIGHT TO TRY AND SUCCESS AT THE STATE LEVEL

1. The Right-to-Try Movement's Rationale

The arguments for right to try can be distilled to three main claims: (1) the expanded access program is "so riddled with bureaucracy and delay that a patient's chances of obtaining potentially lifesaving treatment in time are practically negligible";¹⁵³ (2) the FDA is irreparably broken because it prevents individuals from using "potentially lifesaving medicines and treatments until those treatments receive final approval";¹⁵⁴ and (3) patients with life-threatening diseases should be allowed to try an investigational drug that has already passed the FDA's basic safety testing in phase I trials and remains within the FDA's approval process because they are "safe."¹⁵⁵

a. The Expanded Access Program Is Overly Bureaucratic and Slow

The Goldwater Institute specifically claimed that the expanded access program burdens people's right to try because: (1) the FDA has "unfettered authority to deny a terminal patient access . . . for a variety of reasons,

152. See generally GOLDWATER INST., RIGHT TO TRY MODEL LEGISLATION (2014), http://goldwaterinstitute.org/wpcontent/uploads/cms_page_media/2016/1/5/GoldwaterInstituteRighttoTryModel.pdf.

153. Sandefur, *supra* note 9, at 519.

154. *Id.* at 513.

155. *Id.* at 529–30. The Goldwater Institute attempted to root this final argument in a constitutional right to access while distinguishing it from the prior failed attempts to challenge FDA regulatory oversight in *Rutherford* and *Abigail Alliance*. Sandefur, *supra* note 9, at 513, 519 (suggesting that in *Abigail Alliance*, patients wanted the "authority to access drugs that had not yet been approved for safe use by the FDA"). That claim, however, that terminally ill patients have a fundamental right to use non-FDA approved drugs that have successfully completed phase I testing is the very same fundamental right the Abigail Alliance unsuccessfully advocated for in *Abigail Alliance v. Von Eschenbach*. *Abigail All. for Better Access to Dev. Drugs v. Von Eschenbach*, 495 F.3d 695, 701 (D.C. Cir. 2007) (examining "whether terminally ill patients have a fundamental right to experimental drugs that . . . passed Phase I clinical testing"). For additional background regarding *Rutherford* and *Abigail Alliance*, see *supra* Section II.A.

including nonmedical reasons”); (2) the application is overly burdensome and complicated for requesting physicians; and (3) the IRB review requirement prolongs and prevents access for patients undergoing treatment at non-academic centers outside of major metropolitan areas.¹⁵⁶

There are two problems with the first part of this claim. First, this claim completely ignores the GAO report findings, which suggest a contrary proposition.¹⁵⁷ Second, this claim fails to acknowledge that sign-off from the FDA is only the last step in the process.¹⁵⁸ Take Andrea Sloan’s story as an example. The FDA acknowledged Sloan was an appropriate candidate for expanded access, but BioMarin would not provide BMN-673.¹⁵⁹ While the FDA approves nearly all of the expanded access requests it receives, the perception is that the bigger obstacle is manufacturer cooperation.¹⁶⁰ Most companies do not publicly disclose the number of requests received or promote the number of times the company has approved an individual patient’s request.¹⁶¹ Of the company policies surveyed in Section II.B.2,¹⁶² only Pfizer publicized information on its website about the number of requests it received and how many were approved by the company.¹⁶³ The lack of collective disclosure by manufacturers—and the inability of the FDA to require manufacturers to provide this information—leaves the public and politicians with a myopic view of the expanded access program.

The FDA has since introduced Form FDA 3926 (“Individual Patient Expanded Access – Investigational New Drug Application”) and modified the IRB review requirement addressing the second and third part of this claim, which are both discussed in greater detail in Section III.B. These changes could improve accessibility to the expanded access program over time.

156. CORIERI, *supra* note 9, at 11.

157. *See supra* Section II.B.3.

158. *Id.*

159. *See supra* Introduction.

160. Gail A. Van Norman, *Expanding Patient Access to Investigational Drugs*, 3 JACC: BASIC TRANSLATIONAL SCI. 280, 291 (2018); *see also* GAO-17-564, INVESTIGATIONAL NEW DRUGS, *supra* note 100, at 17; Hudson, *supra* note 2. *But see* U.S. FOOD & DRUG ADMIN., EXPANDED ACCESS PROGRAM REPORT 21 (2018) [hereinafter EXPANDED ACCESS PROGRAM REPORT], <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM618903.pdf> (noting that manufacturers with active expanded access programs approve 40% to 95% of expanded access requests).

161. *See supra* Section II.B.2; *infra* Appendix.

162. *Top Pharma List: Top 25 Pharma Companies by Global Sales*, *supra* note 113.

163. *Pfizer Policy*, *supra* note 100.

b. The FDA Regulatory Framework Is Broken

The Goldwater Institute argued that the current regulatory framework is broken because it can take years before the FDA approves a drug. Yet instead of offering a solution to address the clinical trial process (for example, lobbying for legislation to support the use of different clinical trial designs,¹⁶⁴ or to incentivize companies to reconsider their rationale for certain inclusion and exclusion criteria that could provide data that more accurately reflects real-world patients¹⁶⁵)—which could potentially improve access to investigational drugs more broadly—the organization decided the easier path was pre-approval access legislation that cut-out the FDA. This strategy was shortsighted and arguably based on the Goldwater Institute’s overarching goal of limiting the FDA’s oversight of drugs for all patients and not just those drugs designed for the treatment of immediately life-threatening diseases.¹⁶⁶

The claim that the framework is “broken” also focuses on speed to the detriment of safety and efficacy. The need for adequate safety and effectiveness data can prolong the drug approval process,¹⁶⁷ however, even with these requirements, the FDA is consistently faster at approving investigational drugs than other regulatory authorities. For example,

[a]mong the 289 unique novel therapeutic agents [approved between 2001 and 2010], 190 were approved in both the United States and Europe (either by the EMA or through the mutual recognition process), of which 121 (63.7%) were first approved in the United States; similarly, 154 were approved in both the United States and Canada, of which 132 (85.7%) were first approved in the United States.¹⁶⁸

The speed with which a drug is approved, however, should not be the only

164. See Margot J. Fromer, *Accelerating Pediatric Drug Development: Master Protocols May be a Way to Go*, ASCO POST (Apr. 25, 2017), <http://www.ascopost.com/issues/april-25-2017/accelerating-pediatric-drug-development-master-protocols-may-be-a-way-to-go> (proposing a master protocol to aid pediatric research); Press Release, Memorial Sloan Kettering Cancer Ctr., *FDA Announces First Approval of Targeted Therapy Based on Basket Study* (Nov. 6, 2017), <https://www.mskcc.org/trending-topics/fda-announces-first-approval-targeted-therapy-based-basket-study> (discussing similar protocol used in the adult setting, which lead to FDA approval).

165. Kim et al., *supra* note 49, at 3742.

166. See generally MARK FLATTEN, GOLDWATER INST., *STUDIED TO DEATH: FDA OVERCAUTION BRINGS DEADLY CONSEQUENCES* (2018), <https://goldwaterinstitute.org/wp-content/uploads/2018/11/Studied-to-Death-web.pdf> (proposing additional means to reduce FDA oversight through conditional approval, reciprocal review upon approval from a foreign regulatory authority, and off-label promotion of approved drugs).

167. See *supra* Section I.B.

168. Nicholas S. Downing et al., *Regulatory Review of Novel Therapeutics—Comparison of Three Regulatory Agencies*, 366 NEW ENG. J. MED. 2284, 2284 (2012). Of note, this study was conducted prior to the creation of the Breakthrough Therapy designation. See *supra* note 73 and accompanying text.

priority—safety and efficacy are still important concerns. Some argue the agency is now underemphasizing these two criteria in its aim to ensure patients can access novel drugs more quickly.¹⁶⁹ A *JAMA* study found that “nearly a third of [drugs] approved [by the FDA] from 2001 through 2010 had major safety issues years after they were widely available to patients.”¹⁷⁰ A patient with a life-threatening disease or condition may understandably be frustrated by the lengthy development timeline, especially when a drug is touted as a potential “breakthrough” early on in its development cycle. However, pre-approval access without FDA oversight does not directly fix this lag between development and approval; it could make it worse for everyone if patients attempt to seek pre-approval access instead of enrolling in clinical trials.¹⁷¹

c. Patients Should Be Allowed to Use Investigational Drugs that Have Completed Phase I Clinical Testing

Finally, the Goldwater Institute’s claim that patients should be able to try investigational drugs because completion of phase I testing renders them safe fails to acknowledge that most investigational drugs are not approved by the FDA. The “overall likelihood of [FDA] approval . . . from Phase I for all developmental candidates [between 2006 and 2015] was 9.6%.”¹⁷² The successful completion of a phase I clinical trial also does not guarantee a drug’s safety, and in general, investigational drugs have the lowest successful transition rates at phase II.¹⁷³ Take the example of fialuridine. In 1993, five individuals enrolled in a phase II clinical trial studying the use of fialuridine in hepatitis B died, despite an earlier phase I clinical trial in which 25% of a twenty-four-patient trial were cured after receiving fialuridine for

169. Caroline Chen, *FDA Repays Industry by Rushing Risky Drugs to Market*, PROPUBLICA (June 26, 2018, 5:00 AM), <https://www.propublica.org/article/fda-repays-industry-by-rushing-risky-drugs-to-market>. Of note, some HIV/AIDS activists now argue that their efforts during the 1980s and 1990s “opened a Pandora’s box.” *Id.*

170. Sydney Lupkin, *Nearly 1 in 3 Recent FDA Drug Approvals Followed by Major Safety Actions*, KAISER HEALTH NEWS (May 9, 2017), <https://khn.org/news/1-in-3-recent-fda-drug-approvals-followed-by-major-safety-actions> (“It took a median time period of 4.2 years after the drugs were approved for these safety concerns to come to light, and issues were more common among . . . drugs that were granted ‘accelerated approval’ and drugs that were approved near the regulatory deadline for approval.”).

171. See *How Will the Federal Right to Try Law Impact Drug Development?*, CLINICAL LEADER (June 27, 2018) [hereinafter CLINICAL LEADER], <https://www.clinicalleader.com/doc/how-will-the-federal-right-to-try-law-impact-drug-development-0001>.

172. CLINICAL DEVELOPMENT SUCCESS RATES 2006–2015, *supra* note 33, at 3 (“Phase II clinical programs continue to experience the lowest success rate of the four development phases, with only 30.7% of developmental candidates advancing to Phase III.”); see also 22 CASE STUDIES, *supra* note 35, at 1.

173. See *supra* Section I.B.

twenty-eight days.¹⁷⁴ This example might seem extreme, but it still illustrates the risks associated with equating successful completion of a phase I trial with a broad endorsement of safety. As discussed, an approved drug's safety profile is also not fully understood until sometimes years after it is approved. The potential harm of an investigational drug, even to someone "facing imminent death," still needs to be considered before allowing an individual with a serious or life-threatening disease to use the investigational drug merely on the basis of completion of phase I testing.¹⁷⁵

In conclusion, the movement's rationales for these laws were misplaced and ill-guided. There is no doubt, however, that despite these claims, the Goldwater Institute was successful in securing the support necessary to pass both state and federal legislation.

2. The Movement's Success at the State Level

Post-*Abigail Alliance*, efforts were made to enact legislation to amend the expanded access program. While these federal bills failed to make it beyond congressional committee,¹⁷⁶ the state right-to-try bills, from the outset, gained more support. There are several possible reasons for this increased support. First, information regarding investigational drugs, especially data from medical meetings, has become more accessible with the Internet and social media.¹⁷⁷ This increased accessibility is good, but it also can lead to increased interest in investigational drugs—especially when a drug is deemed "revolutionary" by the medical community, even with

174. Larry Thompson, *The Cure that Killed: FIAU Destroyed a Deadly Virus. Then It Began to Destroy Patients.*, DISCOVER MAG. (Mar. 1, 1994), <http://discovermagazine.com/1994/mar/thecurethatkille345>.

175. Mark Flatten, *Dead on Arrival: Federal "Compassionate Use" Leaves Little Hope for Dying Patients*, RIGHTTO TRY (Feb. 24, 2016), <http://righttotry.org/dead-on-arrival> ("Those facing imminent death cannot access a drug while it is being tested, even if early results show that it works better than existing treatments, unless they are among the fortunate few who qualify for clinical trials. That amounts to a death sentence for most patients, even though their cure may have already been found."); see also Thompson, *supra* note 174.

176. *H.R. 6288 (112th): Patient Choice Act of 2012*, GOVTRACK, <https://www.govtrack.us/congress/bills/112/hr6288> (last visited Feb. 8, 2019) (proposing to allow "provisional approval" of drugs with Fast Track designation); *S. 3045 (110th): ACCESS Act*, <https://www.govtrack.us/congress/bills/110/s3046> (last visited Feb. 8, 2019) (proposing the creation of a "conditional approval system").

177. *See Debate: Benefits, Harms of Social Media Sharing from Medical Conferences*, HEMONC TODAY (Sept. 13, 2017), <https://www.healio.com/hematology-oncology/practice-management/news/online/%7Bfa961a3a-28d2-4909-a186-dbad928ddd03%7D/debate-benefits-harms-of-social-media-sharing-from-medical-conferences> (describing how non-attendees can follow along on Twitter or access abstracts and posts through conference databases); *Forums*, MYELOMA BEACON, <https://myelomabeacon.org/forum> (last visited Feb. 8, 2019) (including example of patient forum discussing treatment options).

limited safety and efficacy data.¹⁷⁸ Timothy Turnham, the former executive director at the Melanoma Research Foundation, explains: “There is a disconnect between what researchers think is statistically significant and what is really significant for patients . . . Patients hear ‘progress,’ and they think that means they’re going to be cured.”¹⁷⁹

Second, there has been an increase in direct-to-consumer advertising of approved specialty drugs for the treatment of conditions such as cancer and autoimmune disorders by pharmaceutical companies¹⁸⁰ and of specific practices areas such as oncology and organ transplantation by cancer hospitals.¹⁸¹ The United States is one of only a small number of countries which allows drug company advertising to not only mention an approved drug and its intended use, but also claims about its safety and efficacy.¹⁸² These advertisements—though meant to be scientifically accurate—can also sometimes have misleading effects on people’s perceptions of their individual health outcomes.¹⁸³ If patients’ perceptions are skewed when they see a television advertisement claiming an FDA-approved drug will give them “a chance to live longer,” it is reasonable to think that patients’ perceptions could be equally skewed about investigational drugs given that investigational drugs are often touted as “revolutionary” at medical meetings

178. See Sharon Begley, *Beware the Hype: Top Scientists Cautious About Fighting Cancer with Immunotherapy*, STAT NEWS (Sept. 25, 2016), <https://www.statnews.com/2016/09/25/cancer-immunotherapy-caution>; Joy Victory, *A Cancer Doctor Speaks Out: How Premature Hype About Experimental Drugs Fails Patients*, HEALTHNEWSREVIEW (Apr. 10, 2018), <https://www.healthnewsreview.org/2018/04/a-cancer-doctor-speaks-out-how-premature-hype-about-experimental-drugs-fails-patients>.

179. Szabo, *supra* note 52.

180. Ned Pagliarulo, *Viagra No More: The Changing Face of Drug Ads on TV*, BIOPHARMADIVE (Oct. 22, 2018), <https://www.biopharmadive.com/news/drug-ads-tv-pharma-changing-face-dtc-advertising/539982>; see also Kevin McCaffrey, *Merck’s DTC Ad for Keytruda Hints at More Cancer Brands Turning to TV*, MM&M (Feb. 12, 2017), <https://www.mmm-online.com/home/channel/commercial/mercks-dtc-ad-for-keytruda-hints-at-more-cancer-brands-turning-to-tv> (“From June 2013 to February [2017], pharma companies spent an estimated \$223 million on more than 42,000 airings for DTC ads . . . Before 2013, when the first Provenge DTC aired, it was unheard of for brands to use direct-to-consumer advertising for oncology drugs.”).

181. Kathryn Doyle, *Cancer Hospital Advertising Triples Since 2005*, REUTERS (July 11, 2016, 12:40 PM), <https://www.reuters.com/article/us-health-cancer-ads-idUSKCN0ZR2D6>.

182. C. Lee Ventola, *Direct-to-Consumer Pharmaceutical Advertising: Therapeutic or Toxic?*, 36 PHARMACY & THERAPEUTICS 669, 669, 673–82 (2011).

183. Stephanie M. Lee, *Cancer Hospital Ads Deceive Patients About Their Chances of Survival, New Report Finds*, BUZZFEED (Oct. 25, 2018, 4:01 PM), <https://www.buzzfeednews.com/article/stephaniemlee/cancer-treatment-center-misleading-ads>; Szabo, *supra* note 52 (“A TV commercial for the Bristol-Myers Squibb drug Opdivo projects the words ‘a chance to live longer’ on the side of skyscrapers, as a captivated crowd looks on. In much smaller type, a footnote reveals that lung cancer patients taking Opdivo lived just 3.2 months longer than others.”).

by the manufacturers, tweeted as “ground-breaking” by physicians, and reported as “life-saving” by media, as compared to the currently available treatment option.

Third, with social media, individual patients like Andrea Sloan have a more accessible, widely-used platform by which to raise awareness of their struggle to obtain these investigational drugs through expanded access.¹⁸⁴ In the past, publicized efforts to pressure manufacturers for expanded access were generally a coordinated effort led by advocacy groups, aimed at obtaining an investigational drug for more widespread use.¹⁸⁵ Individual patients were often left to phone calls and letter writing with slim chance of successfully obtaining an experimental treatment without a connection.¹⁸⁶ This changed with social media. The news media found these campaigns and latched onto Sloan’s and other patients’ stories with headlines like “Company Denies Drug to Dying Child” and “Merck Expands Cancer Drug Access but too Late for Denver Dad,” which only amplified the public’s frustration with expanded access.¹⁸⁷ The social media campaigns and media attention, in turn, increased pressure on politicians to fix the system and allow individuals access to investigational drugs.¹⁸⁸

184. Tim K. Mackey & Virginia J. Schoenfeld, *Going “Social” to Access Experimental and Potentially Life-Saving Treatment: An Assessment of the Policy and Online Patient Advocacy Environment for Expanded Access*, 14 *BIOMED CENT. MED.*, no. 17, 2016, at 1–10; see also Alison Bateman-House et al., *Findings on “Right to Try” Laws and Pre-Approval/Compassionate/Expanded Access to Investigational Medical Products*, N.Y.U. SCH. MED. (July 1, 2016) [hereinafter Bateman-House, *Findings*], https://med.nyu.edu/pophealth/sites/default/files/pophealth/RTT%20Findings%20FINAL%207_1.pdf (“The number of Change.org online petitions in support of individual requests has increased over the last several years.”).

185. See, e.g., Laura Fraser, *The Demonstration*, *GENENTECH* (Sept. 2016), <https://www.gene.com/stories/the-demonstration>.

186. E.g., Darshak M. Sanghavi, *The Pills of Last Resort*, *N.Y. TIMES MAG.* (Oct. 31, 2013), <https://www.nytimes.com/2013/11/03/magazine/how-dying-patients-get-access-to-experimental-drugs.html>.

187. Cohen, *supra* note 6; Sydney Lupkin, *Merck Expands Cancer Drug Access but too Late for Denver Dad*, *ABC NEWS* (Mar. 18, 2014), <http://abcnews.go.com/Health/merck-expands-cancer-drug-access-late-denver-dad/story?id=22954543>; Tirrell, *supra* note 5.

188. See Dresser, *The Gap*, *supra* note 10, at 10 (“To lawmakers and the public hearing these stories, it would be cruel to vote against a right to try law.”); Paige Winfield Cunningham, *The Health 202: How ‘Right to Try’ Caught Washington’s Eye*, *WASH. POST* (Feb. 1, 2018), <https://www.washingtonpost.com/news/powerpost/paloma/the-health-202/2018/02/01/the-health-202-how-right-to-try-caught-washington-s-eye/5a71fcc330fb041c3c7d755e> (discussing how the right-to-try movement’s success is in part due to patients and their families reaching out to their representatives); Richard Halstead, *BioMarin Denies ‘Compassionate Use’ of Experimental Drug, Considers Adding Cancer Patient to Clinical Trial*, *MARIN INDEP. J.* (Jul. 19, 2018, 3:17 AM), <https://www.marini.com/2013/09/06/biomarin-denies-compassionate-use-of-experimental-drug-considers-adding-cancer-patient-to-clinical-trial> (discussing how Rep. Jared Huffman (D-San Rafael, Cal.) was involved in a case after receiving “a flood of calls to his office”).

The Goldwater Institute initially targeted more conservative states like Colorado, Arizona, and Texas,¹⁸⁹ but the movement also gained traction and success in more liberal states like California and Oregon.¹⁹⁰ The state bills also often had little political opposition and were supported by members on both sides of the aisle.¹⁹¹ In total, forty states adopted right-to-try laws prior to the enactment of the federal Right to Try Act. With Alaska's enactment of its own right-to-try law in July 2018, that total is now forty-one states.¹⁹²

The goal of these state-level right-to-try laws, as discussed, is to enable terminally ill patients to bypass the FDA expanded access program and request pre-approval use directly from manufacturers, but there are variations in these laws' provisions regarding, among other things, cost

189. See COLO. REV. STAT. § 25-45-101-108 (2014); TEX. HEALTH & SAFETY CODE ANN. § 489.001-.151 (West 2015); ARIZ. REV. STAT. ANN. § 36-1311-1314 (2014); see also Patti Parson, *Colorado First State to Pass 'Right to Try,' or the 'Dallas Buyers' Club' Law*, PBS NEWS HOUR (May 19, 2014), <https://www.pbs.org/newshour/health/colorado-first-state-pass-right-try-dallas-buyers-club-law>.

190. See OR. REV. STAT. § 127 (2017); CAL. HEALTH & SAFETY CODE § 111548-111548.5 (West, Westlaw through 2018 Sess.).

191. Some of the state laws were sponsored by politicians with personal connections. Brady Dennis & Ariana Eunjung Cha, *"Right to Try" Laws Spur Debate Over Dying Patients' Access to Experimental Drugs*, WASH. POST (May 16, 2014), https://www.washingtonpost.com/national/health-science/right-to-try-laws-spur-debate-over-dying-patients-access-to-experimental-drugs/2014/05/16/820e08c8-dcfa-11e3-b745-87d39690c5c0_story.html (the Colorado law was co-sponsored by a Democrat whose brother benefited from a clinical trial); Michele Munz, *Missouri's "Right to Try" Law No Guarantee Patient Will Get Experimental Drugs*, ST. LOUIS POST-DISPATCH (May 20, 2015), https://www.stltoday.com/news/local/metro/missouri-s-right-to-try-law-no-guarantee-patientwill/article_05c07958-5217-5c3f-9f15-1a43c8a3e740.html (reporting the Missouri law was sponsored by a Republican lawmaker whose daughter died of cancer). Others, like California Assembly Majority Leader Ian Calderon, sponsored the right-to-try bill because it was "a logical companion to Death with Dignity." *Exploring a Right to Try for Terminally Ill Patients: Hearing Before the S. Comm. on Homeland Sec. & Gov't Affairs*, 114th Cong. 1-2 (2016) (statement of Ian C. Calderon, Majority Leader, Cal. State Assemb.), <https://www.hsgac.senate.gov/imo/media/doc/Testimony-Calderon-2016-09-22.pdf>. He explained before Congress:

I never saw the two issues as incompatible. I didn't want to limit the options for those diagnosed with a terminal illness, to only death, albeit a more controlled one. I felt strongly that if we were going to pass Death with Dignity, and thus make it easier for terminally ill patients to die in California, that we should also make it easier for these terminally ill patients to fight to live, by giving them access to potentially life-saving drugs and treatments, that have been deemed safe, but not yet approved by the FDA.

Id. at 2-3.

192. See *supra* note 11 (listing states that have adopted right-to-try laws).

recovery,¹⁹³ insurance coverage,¹⁹⁴ and informed consent.¹⁹⁵ The extent to which those variations now matter given the enactment of the Right to Try Act of 2017 is still not fully clear, but as discussed below, at least some are likely still applicable.

B. THE FDA'S RESPONSE

In response to the right-to-try advocates' criticisms, the FDA further clarified and modified aspects of the expanded access program to address its perceived shortcomings. The FDA also stepped up efforts to increase awareness and understanding of the expanded access program.

1. Clarifying the FDA's Use of Clinical Outcomes

A major issue for manufacturers—which face external pressure from investors, physicians, and patient groups to bring new drugs to market—concerns the potential impact an adverse event during expanded access use could have on an investigational drug's development and subsequent agency review.¹⁹⁶ This concern was likely overstated, particularly given that “clinical safety data from expanded access treatment” has only been considered in a “small number of cases” when determining an approved drug's label,¹⁹⁷ and that such a criterion has never been used to deny

193. Compare TEX. HEALTH & SAFETY CODE ANN. § 489.053(c) (West, Westlaw through 2017 Regular & First Called Sess.) (stating a company cannot charge a patient), with ARIZ. REV. STAT. ANN. § 36-1312(B)(2) (West, Westlaw through First Special & Second Regular 2018 Sess.) (stating a company can charge a patient “costs of or associated with the manufacture of the investigational drug”), and CAL. HEALTH & SAFETY CODE § 111548.2(b)(2) (West, Westlaw through 2018 Sess.) (same).

194. E.g., CAL. HEALTH & SAFETY CODE § 111548.2(c)(2) (West, Westlaw through 2018 Sess.) (stating insurance providers are allowed to choose not to cover the cost of the therapy or costs related to that treatment); OR. REV. STAT. § 127 (2017), https://www.oregonlegislature.gov/bills_laws/ors/ors127.html (same); COLO. REV. STAT. § 25-45-104(b)–(c) (2014) (stating insurance providers are also allowed to deny certain coverage for a period of up to six months after the commencement of treatment).

195. Compare CAL. HEALTH & SAFETY CODE § 111548.1(h)(1)(A)–(H), (h)(2) (stating a patient must be informed, among other things, of potential impact on hospice eligibility and at-home care), and COLO. REV. STAT. § 25-45-103(4) (West, Westlaw through Second Regular 2018 Sess.) (same), with ARIZ. REV. STAT. ANN. § 36-1311(1)(d) (2014) (including no definition of informed consent).

196. See Alexander Gaffney, *Company's Compassion Leads to Clinical Hold on Experimental Drug*, REG. FOCUS (Nov. 19, 2014), <http://www.raps.org/Regulatory-Focus/News/2014/11/19/20780/Companys-Compassion-Leads-to-Clinical-Hold-on-Experimental-Drug> (noting the FDA stopped enrollment of an expanded access treatment protocol after a patient died).

197. EXPANDED ACCESS: GUIDANCE FOR INDUSTRY, *supra* note 145, at 18. A drug label includes information “such as disease indications, target populations, drug–drug interactions, and [adverse drug reactions]. The label of a prescription drug is prepared by manufacturers and approved by the FDA and, thus, in its final form, reflects the collective input from regulators, drug manufacturers, and scientific experts.” Hong Fang et al., *FDA Drug Labeling: Rich Resources to Facilitate Precision Medicine, Drug Safety, and Regulatory Science*, 21 DRUG DISCOVERY TODAY 1566, 1566 (2016).

approval.¹⁹⁸ Still, the potential for an adverse event was often cited as an obstacle for patients seeking expanded access use.¹⁹⁹

The FDA attempted to address these concerns, even if arguably overstated, by clarifying its policy. The treating physician needs to report only “suspected [serious or unexpected] adverse reactions . . . if there is evidence to suggest a causal relationship between the drug and the adverse event.”²⁰⁰ The agency also noted that given the nature of expanded access use (in other words, an investigational drug administered outside of a controlled clinical trial to a terminally ill patient with multiple comorbidities), it would be difficult to often establish the necessary causal relationship.²⁰¹

This modification, however, did not address the other major concern raised by manufacturers: the lack of a readily available supply of the drug sought for expanded access.²⁰² The FDA cannot directly tackle this issue, but it could affect the drug supply indirectly through clinical trial policies promoting diversity and inclusion.²⁰³ This, in turn, could help some patients, who are willing to participate in a clinical trial but are instead driven to seek expanded access due to their failure to satisfy clinical eligibility requirements given age or certain comorbidities.²⁰⁴

198. EXPANDED ACCESS: GUIDANCE FOR INDUSTRY, *supra* note 145, at 18.

199. GAO-17-564, INVESTIGATIONAL NEW DRUGS, *supra* note 100, at 17.

200. Gottlieb, *supra* note 108; *see also* U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY AND INVESTIGATORS: SAFETY REPORTING REQUIREMENTS FOR INDS AND BA/BE STUDIES 29 (2012), <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM227351.pdf> (providing criteria regarding what might qualify as an adverse event).

201. EXPANDED ACCESS: GUIDANCE FOR INDUSTRY, *supra* note 145, at 18.

202. Shannon Firth, *FDA Head Expresses Doubt About ‘Right to Try’*, MEDPAGE TODAY (Oct. 4, 2017), <https://www.medpagetoday.com/washington-watch/fdageneral/68310> (FDA Commissioner Scott Gottlieb stated, “I think that the biggest obstacle to providing drugs through expanded access is the supply constraints”). Adequate supply is often a factor when evaluating an expanded access request. *See infra* Appendix. This is a genuine concern because a manufacturer initially only develops sufficient supply for its trials. *See Fraser, supra* note 185 (“[Genentech] was already in the process of trying to dramatically ramp up its production of Herceptin, encountering roadblocks in machinery, engineering and chemistry along the way.”).

203. U.S. FOOD & DRUG ADMIN., PUBLIC WORKSHOP: EVALUATING INCLUSION AND EXCLUSION CRITERIA IN CLINICAL TRIALS: WORKSHOP REPORT 10 (2018) [hereinafter PUBLIC WORKSHOP: EVALUATING INCLUSION AND EXCLUSION CRITERIA], <https://www.fda.gov/downloads/RegulatoryInformation/LawsEnforcedbyFDA/SignificantAmendmentstotheFDCAct/FDARA/UCM613054.pdf>.

204. *See Tirrell, supra* note 5 (explaining that fifteen-year-old Nathalie Traller was unable to enroll in clinical trials—despite meeting all of the eligibility criteria—because of her age).

2. Demystifying Manufacturers' Eligibility Criteria

A long-standing frustration for patients and their physicians was biopharmaceutical companies' lack of transparency regarding how they evaluated expanded access requests. Before the enactment of the 21st Century Cures Act ("Cures Act"), manufacturers were not required to disclose their evaluation processes.²⁰⁵ A few biopharmaceutical companies released their criteria after either coming under pressure from patients' social media campaigns, which requested expanded access, or observing the impact that such campaigns had on other, similar companies.²⁰⁶ Generally, however, this information was not easily available to patients or physicians.²⁰⁷

The Cures Act now requires manufacturers to disclose how they evaluate and respond to individual patient requests for access to investigational drugs.²⁰⁸ The following information must be included on a manufacturer's website: (1) contact information; (2) expanded access request procedures; (3) individual patient eligibility criteria; (4) anticipated response time; and (5) a link or other reference to information about the clinical trials of the drug for which expanded access is sought, available on ClinicalTrials.gov.²⁰⁹

Three primary issues have impacted the Cures Act's effectiveness. First, not all companies are in compliance with its provisions.²¹⁰ The Cures Act does not contain an enforcement mechanism to give the FDA the ability to penalize companies that do not publish policies. Second, the Cures Act

205. Juliet Eilperin & Carolyn Y. Johnson, *Obama, Paying Tribute to Biden and Bipartisanship, Signs 21st Century Cures Act Tuesday*, WASH. POST: POWERPOST (Dec. 13, 2016), <https://wapo.st/2gXhOsT>.

206. *E.g.*, Hal Barron, *A Scientific Application of Compassion*, GENENTECH (May 15, 2013), <https://www.gene.com/stories/a-scientific-application-of-compassion>. *But see* Press Release, Cancer Survivor Andrea Sloan, Ovarian Cancer Survivor Andrea Sloan Seeks Compassionate Use Exemption from BioMarin to Save Her Life (Aug. 29, 2013, 2:28 PM), <http://www.marketwired.com/press-release/ovarian-cancer-survivor-andrea-sloan-seeks-compassionate-use-exemption-from-biomarin-1825934.htm> ("Despite best efforts to contact BioMarin, the company has not been cooperative, merely sighting their lack of a policy on the issue.").

207. Ed Silverman, *21st Century Cures Would Require Pharma to Post Policies on Experimental Drugs*, STAT: PHARMALOT (Nov. 28, 2016), <https://www.statnews.com/pharmalot/2016/11/28/21st-century-experimental-drugs>.

208. *See generally* 21st Century Cures Act, 21 U.S.C. § 360bbb-0 (2018).

209. *Id.* § 360bbb-0(c).

210. *Examining Patient Access to Investigational Drugs: Hearing Before the H. Comm. Energy and Commerce*, 115th Cong. 4 (2017) (statement of the Alison Bateman-House, Assistant Professor, Division of Medical Ethics, Department of Population Health, N.Y.U. Langone Health) [hereinafter Bateman-House, *Examining Patient Access*] (explaining why an enforcement mechanism is necessary, given that there is "less than 100% compliance with the rule"). For additional discussion about compliance with respect to specific provisions in the Cures Act, see Jung et al., *supra* note 113.

does not require participation in expanded access—just that a company post its policies. Though most companies have guidelines similar to the ones previously detailed in Section II.B.2, a company is still allowed under the Cures Act to have a policy against providing expanded access, so long as that policy is available on the company’s website.²¹¹ And even if a company’s criteria mirrors that of PhRMA’s criteria, they are still subject to interpretation by that company’s employees. This could make it difficult to determine whether a physician’s request on behalf of a patient will be approved. Third, the Cures Act does not ensure timely response—just that a company post an anticipated response time. In general, that time frame represents the estimated time to an acknowledgment rather than an estimated time to a decision.²¹² The FDA seems posed to address this final issue but has not announced definite plans to institute a timing requirement.²¹³

3. Increasing Awareness of Expanded Access

The FDA has also attempted to dispel many of the misconceptions regarding expanded access and clarify the application process for physicians and patients, especially those outside of major academic medical centers. The Reagan-Udall Foundation for the FDA, for example, created the “Expanded Access Navigator.”²¹⁴ This website provides an overview of the application process from both a physician and patient perspective. The physician-specific section includes contact information for independent IRB committees should a physician’s institution not have its own IRB committee,²¹⁵ and a manufacturer directory listing companies’ expanded access criteria and their anticipated response time.

211. See *Expanded Access/Right to Try Act*, BRAINSTORM CELL THERAPEUTICS, <http://www.brainstorm-cell.com/patients-caregivers/expanded-accesscompassionate-use> (last visited Feb. 8, 2019) (stating the company currently does not offer expanded access).

212. *Company Directory*, *supra* note 102.

213. Usdin, *supra* note 101.

214. *About the Expanded Access Navigator*, REAGAN-UDALL FOUND., <http://navigator.reaganudall.org/about> (last visited Feb. 8, 2019) (“The Expanded Access Navigator, or EA Navigator, represents a unique partnership between the Reagan-Udall Foundation for the FDA, patient advocacy organizations, the pharmaceutical industry, and the federal government to provide clear, digestible information on single-patient EA.”).

215. See *id.* The addition of this resource (that is, connecting community physicians with regional IRB committees) could be a relatively simple way of helping alleviate potential application disparities between patients who are primarily treated at academic centers where physicians are more aware of clinical trials and expanded access, and patients who are primarily treated by a community physician who might have less familiarity and access to these resources.

4. Streamlining the Individual Patient Request Process

a. Form FDA 3926

Prior to the release of Form FDA 3926, a physician could spend up to one hundred hours in his or her attempt to secure expanded access use for a single patient.²¹⁶ Although a significant portion of that estimate likely included time spent negotiating with the manufacturer to obtain a LOA and coordinating with the IRB, physicians complained the application, comprised of Form FDA 1571 (“Investigational New Drug Application”) and Form FDA 1572 (“Statement of the Investigator”),²¹⁷ was unnecessarily complex and took upwards of eight hours to complete.²¹⁸

In 2016 the FDA rolled out a streamlined application, Form FDA 3926, to ease the application process.²¹⁹ This change was meant not only to reduce the burden on physicians already familiar with requesting expanded access, but also, more importantly, to encourage doctors less familiar with the regulatory process who may have been previously dissuaded from submitting an expanded access request for their patients because of the forms’ complexities.²²⁰ Form FDA 3926 only requires the physician to provide: (1) the patient’s initials; (2) the date of submission; (3) the type of submission; (4) clinical information; (5) treatment information; (6) a LOA; (7) the physician’s qualification statement; and (8) the physician’s name, address, and contact information.²²¹ The new two-page form takes forty-five minutes to complete—a time savings of more than 90%.²²² The

216. Zachary Brennan, *FDA Looks to Revitalize Compassionate Use Program with Simplified Form*, *Final Guidance*, REG. FOCUS (June 2, 2016) [hereinafter Brennan, *Revitalize Compassionate Use*], <https://www.raps.org/news-articles/news-articles/2016/6/fda-looks-to-revitalize-compassionate-use-program-with-simplified-form,-final-guidance>.

217. U.S. FOOD & DRUG ADMIN., INVESTIGATIONAL NEW DRUG APPLICATION (IND): FORM FDA 1571 [hereinafter FORM FDA 1571], <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083533.pdf> (last updated July 2018); U.S. FOOD & DRUG ADMIN., STATEMENT OF INVESTIGATOR: FORM FDA 1572, <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf> (last updated Feb. 2016).

218. EXPANDED ACCESS PROGRAM REPORT, *supra* note 160, at 5.

219. Statement, U.S. Food & Drug Admin., Statement from FDA Commissioner Robert Califf, M.D. on the Release of the Final Individual Patient Expanded Access Form (Jun. 2, 2017) [hereinafter Statement from FDA Commissioner Califf], <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm504579.htm>.

220. Brennan, *Revitalize Compassionate Use*, *supra* note 216.

221. *Id.* Form FDA 1571 has twenty-six fields and requires seven attachments. FORM FDA 1571, *supra* note 217. Form FDA 3926 has eight fields and requires one attachment. U.S. FOOD & DRUG ADMIN., INSTRUCTIONS FOR FILLING OUT FORM FDA 3926—INDIVIDUAL PATIENT EXPANDED ACCESS, INVESTIGATIONAL NEW DRUG APPLICATION (IND), <https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM504574.pdf> (last updated Apr. 2017).

222. *Id.*; *see also* EXPANDED ACCESS PROGRAM REPORT, *supra* note 160, at 5.

total application process is now estimated to take thirty hours with this new estimate likely factoring in the FDA's simplified IRB requirement.²²³

b. IRB Review

In October 2017, the FDA announced another change to the single-patient expanded access process. A requesting physician can now seek approval from a specifically assigned IRB or the IRB chairperson, rather than waiting for a full IRB review (in other words, a committee meeting where “a majority of the members are present”).²²⁴ This change was intended to reduce the time between when the patient and treating physician determine an investigational drug might be appropriate and when the treating physician's IRB approves that request, as well as to remove another potential hurdle for physicians outside of major academic centers.²²⁵

This modification attempts to strike the appropriate balance between oversight and timeliness as it recognizes the continued need for independent confirmatory review, while also acknowledging that full IRB review may be unnecessary in the individual patient expanded access setting, given that it could cause undue delays and potentially deter some community-based physicians from using the expanded access pathway. Yet this change also has at least one limitation and two potential drawbacks. With respect to the limitation, it is difficult to know whether hospitals will adopt this modification as it is permissive not mandatory. At least a few major centers appear to be utilizing it, though further research is necessary to determine the full extent of its adoption.²²⁶ To facilitate more widespread adoption, the FDA or the Reagan-Udall Foundation should work with those institutions effectively utilizing the less-stringent IRB review process to develop recommended criteria that other institutions could utilize.

223. EXPANDED ACCESS PROGRAM REPORT, *supra* note 160, at 16.

224. Gottlieb, *supra* note 108; EXPANDED ACCESS: GUIDANCE FOR INDUSTRY, *supra* note 145, at 6.

225. Gottlieb, *supra* note 108; *see also* FDA Simplifies IRB Requirements for Individual Patient Expanded Access, AM. SOC'Y CLINICAL ONCOLOGY (Oct. 3, 2017), <https://www.asco.org/advocacy-policy/asco-in-action/fda-simplifies-irb-requirements-individual-patient-expanded-access>. *But see* Kelly McBride Folkers & Alison Bateman-House, *Will New FDA Regulation on IRB Review Speed Patient Access to Experimental Drugs?*, HEALTH AFFAIRS BLOG (Dec. 11, 2017), <https://www.healthaffairs.org/doi/10.1377/hblog20171205.384786/full> (suggesting it is difficult to assess the actual impact of this change without “baseline data” regarding the role of IRB review in the expanded access process).

226. *E.g.*, *Expanded Access to Unapproved Drugs, Biologics, or Devices and Right to Try Laws*, U. CAL. IRVINE: OFF. RES., <https://www.research.uci.edu/compliance/human-research-protections/researchers/expanded-access-and-right-to-try.html> (last visited Feb. 8, 2019); *Investigational New Drugs and Biologics*, U. CAL. S.F.: OFF. ETHICS & COMPLIANCE, <https://irb.ucsf.edu/investigational-new-drugs-and-biologics> (last updated Apr. 13, 2018).

With respect to potential concerns, first, the modification to the IRB requirement potentially reduces the amount of independent oversight. The average IRB is composed of fourteen members, so before the change, an average of seven members would need to be present to constitute a full IRB review.²²⁷ This change places that decision in the hands of one chairperson or another designated member; this type of reduced oversight is typically reserved for research that poses “minimal risk” to the individual.²²⁸ Second, the FDA did not establish specific eligibility criteria for this waiver. Instead, the FDA has said “such a waiver is appropriate for individual patient expanded access INDs when the physician obtains concurrence by the IRB chairperson or another designated IRB member before treatment use begins.”²²⁹ This standard again places that decision in the hands of one person; the same person who also decides whether expanded access treatment is appropriate. To address these concerns, the FDA should closely monitor incoming expanded access requests to determine if reducing the number of IRB reviewers increases the number of denied FDA requests based on patients not meeting the eligibility criteria. As an initial step, the FDA could refer institutions incorrectly utilizing the waiver to other hospitals that are correctly applying the waiver criteria, and if that appears to not resolve this potential problem, the FDA should consider changing its policy to require at least two or three IRB members or one designated IRB member and a consulting physician specializing in the patient’s disease or condition.²³⁰

* * *

There were arguably three reasons that these modifications did not quell the right-to-try movement and those ultimately pushing for a federal law. First, the legislation—both at the state and federal level—was not aimed at improving pre-approval access for patients, but was instead meant “to

227. E.g., Joseph A. Catania et al., *Survey of U.S. Human Research Protection Organizations: Workload and Membership*, 3 J. EMPIRICAL RES. ON HUM. RES. ETHICS 57, 61–62 (2008); see also *IRB—Human Participants Committee Membership*, CORNELL UNIV. OFF. RES. INTEGRITY & ASSURANCE, <https://www.irb.cornell.edu/membership> (noting the university’s IRB committee is generally made up of twelve to eighteen voting members) (last visited Feb. 8, 2019).

228. See *Levels of Review: Expedited Research*, U. CAL. IRVINE: OFF. RES., <https://www.research.uci.edu/compliance/human-research-protections/researchers/levels-of-review.html#Expedited> (last visited Feb. 19, 2018) (anonymous surveys and chart reviews).

229. EXPANDED ACCESS: GUIDANCE FOR INDUSTRY, *supra* note 145, at 6.

230. The idea of a “consulting physician” builds from a few of the state right-to-try laws, including California, which still require a second physician to review and concur with the treating physician’s opinion, but not an IRB to review and approve the treating physician’s opinion. E.g., CAL. HEALTH & SAFETY CODE § 111548.1(a), (b)(4), (b)(6) (West, Westlaw through 2018 Sess.).

weaken” the FDA.²³¹ Congress did not even wait to assess the impact of the modifications before voting on the Right to Try Act, even though it had authorized the agency to release a report assessing the impact of some of these modifications in 2017.²³² That report, published after the enactment of the Right to Try Act, suggests that all of the key stakeholders, patients, physicians, manufacturers, and payers, have a positive perception of the program and the FDA’s role in pre-approval access decisions.²³³ The efforts to reduce some of the administrative burdens associated with expanded access appear to be well-received.²³⁴ In 2017 (the first full year Form FDA 3926 was available and the year the Expanded Access Navigator was launched), there were 1,151 single-patient expanded access requests, which was a 12% increase from 2016 (1,025 requests).²³⁵ Moreover, Congress did not thoroughly assess the effectiveness of the state right-to-try laws before moving forward with the federal law.

Second, the slow implementation of the FDA’s modifications likely further validated for some the right-to-try advocates’ argument that the FDA is too rigid and unresponsive. For example, the modifications to the application process were introduced more than two years after the right-to-try movement started.²³⁶

Third, the modifications, aside from the clarification regarding use of clinical outcomes, also did not address the other weakness of the expanded access program—uneven manufacturer participation.²³⁷ The movement’s

231. Mershon, *supra* note 7; Press Release, U.S. Senate Comm. on Homeland Sec. & Gov’t Affairs, Johnson to FDA: Agency Should Comply with Right to Try Law (May 31, 2018) [hereinafter Press Release, Johnson to FDA], <https://www.hsgac.senate.gov/media/majority-media/johnson-to-fda-agency-should-comply-with-right-to-try-law> (“This law intends to diminish the FDA’s power over people’s lives, not increase it. It is designed to work within existing FDA regulations, definitions, and approval processes. It is not meant to grant FDA more power or enable the FDA to write new guidance, rules, or regulations”); *see also* Alison Bateman-House & Christopher T. Robertson, Opinion, *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) (arguing that as-written the federal Right to Try Act was meant to undercut the FDA’s authority rather than to create a more effective pre-approval access pathway).

232. FDA Reauthorization Act of 2017, Pub. L. 115–52, § 610(a)(2), 131 Stat. 1005, 1052 (2017).

233. EXPANDED ACCESS PROGRAM REPORT, *supra* note 160, at 13.

234. *Id.* at 13–14.

235. *Expanded Access INDs and Protocols 2009–2017*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/newsevents/publichealthfocus/expandedaccesscompassionateuse/ucm443572.htm> (last updated Feb. 21, 2018). The number of requests between 2015 and 2016 increased 31% from 779 to 1,025. *Id.*

236. *See* Statement from FDA Commissioner Califf, *supra* note 219.

237. This is not just an expanded access problem. The right-to-try laws, both state and federal, do not compel manufacturer participation. *See infra* Section IV.A.

supporters argued a federal right-to-try law would improve manufacturer participation in pre-approval access.²³⁸

C. THE PUSH FOR A FEDERAL RIGHT TO TRY

Capitalizing on the success at the state level, proponents pushed for federal legislation,²³⁹ even though (1) there was little evidence to suggest that existing state laws had a real impact on patients' ability to secure pre-approval access,²⁴⁰ and (2) the effects of the FDA's modifications to the expanded access program were not fully evaluated.

The first proposed bill never made it out of committee,²⁴¹ but in 2016 Senator Ron Johnson (R-Wis.) started strategically laying the groundwork. As Chair of the U.S. Senate Committee on Homeland Security and Governmental Affairs, he convened a hearing to discuss how Congress could reform the regulatory framework to provide "more patients a chance to save

238. Sammy Caiola, *Federal Right to Try Proposal Could Make California Law More Effective*, CAPITAL PUB. RADIO (Jan. 31, 2018), <http://www.capradio.org/109381> (discussing the need for complementary federal legislation).

239. See Right to Try Act of 2015, H.R. 3012, 114th Cong. (as reported by H. Judiciary Subcomm. on Crime, Terrorism, Homeland Sec. & Investigations, July 29, 2015); see also Caiola, *supra* note 238.

240. Zachary Brennan, *Who's Actually Using 'Right-to-Try' Laws? A Texas Oncologist Explains His Experience*, REG. AFF. BLOG (Aug. 4, 2017), <https://www.raps.org/news-articles/news-articles/2017/8/who-s-actually-using-right-to-try-laws-a-texas-oncologist-explains-his-experience> ("The six patient testimonies provided to *Focus* by the libertarian Goldwater Institute . . . all focus on obtaining this same investigational cancer therapy outside of a clinical trial from the former director of therapeutic nuclear medicine at M.D. Anderson Cancer Center."); David Kroll, *Trump's Call for #RightToTry Experimental Drug Access: A Nothingburger for Patients and Families*, FORBES (Jan. 31, 2018, 12:51 PM), <https://www.forbes.com/sites/davidkroll/2018/01/31/trumps-call-for-rightto-try-experimental-drug-access-a-nothingburger-for-patients-and-families> (citing National Right to Try Movement, Meet Dr. Ebrahim Delpassand, FACEBOOK (Sept. 22, 2016), <https://www.facebook.com/RightToTry/videos/592616080918116>; and Richard Pazdur, U.S. Food & Drug Admin., NDA Approval Letter, NDA-208700 for Luthathera 4-5 (Jan. 26, 2018), https://www.accessdata.fda.gov/drugsatfda_docs/applletter/2018/208700Orig1s000ltr.pdf).

It's disingenuous of #RightToTry advocates to use [Dr. Delpassand's story] to justify non-FDA-reviewed patient access to drugs after Phase 1 preliminary safety studies, the very early stage of drug studies in humans. If you look specifically around 0:54 of the Right To Try video, Dr. Delpassand's disappointment on behalf of his patients was due to the FDA's denial of his broad expanded-use request—that is, after *Phase 3* safety and efficacy trials were completed and under FDA review. If one looks at the NDA approval letter, the FDA still had at least another year of questions and concerns about the drug since the April 28, 2016, NDA submission.

Kroll, *supra* (emphasis in original); see also Munz, *supra* note 191 (discussing how one man with ALS moved back to Missouri after the state passed its right-to-try law thinking that he would be able to obtain an investigational drug through the pathway, but the company declined).

241. H.R.3012—Right to Try Act of 2015, CONGRESS.GOV, <https://www.congress.gov/bill/114th-congress/house-bill/3012/actions> (last visited Feb. 11, 2018).

their lives.”²⁴² He introduced a right-to-try bill later that year,²⁴³ but this bill was blocked by Senate Minority Leader Harry Reid (D-Nev.) who objected over the bill’s lack of bipartisan support and nonexistent review through a formal hearing process.²⁴⁴ In January 2017, Senator Johnson reintroduced a federal right-to-try bill—the Trickett Wendler Right to Try Act of 2017 (“S. 204”).²⁴⁵ On August 3, 2017, the Senate passed the bill with no opposition, thus moving the debate over right to try to the U.S. House of Representatives.²⁴⁶

The fate of S. 204 remained in limbo for several months after an October hearing before the House Committee on Energy and Commerce.²⁴⁷

242. *Connecting Patients to New and Potential Life Saving Treatments: Hearing Before the S. Comm. on Homeland Sec. & Gov’t Affairs*, 114th Cong. (2016) (statement of Sen. Ron Johnson, Chairman, S. Comm. on Homeland Sec. & Gov’t Affairs), <https://www.hsgac.senate.gov/media/majority-media/chairman-ron-johnson-opening-statement-connecting-patients-to-new-and-potential-life-saving-treatments>. Of note, no one from the FDA was present at the hearing, which included the president and CEO of the Goldwater Institute, two patients, the now former executive director of the Rothman Institute of Innovation and Entrepreneurship at Fairleigh Dickinson University, who also authored the book *Innovation Breakdown: How the FDA and Wall Street Cripple Medical Advances*, and the executive director of the non-profit organization Kids v. Cancer. *Connecting Patients to New and Potential Life Saving Treatments*, U.S. SENATE COMMITTEE ON HOMELAND SECURITY & GOV’T AFF. (Jan. 25, 2016), <https://www.hsgac.senate.gov/hearings/connecting-patients-to-new-and-potential-life-saving-treatments>. See generally JOSEPH GULFO, *INNOVATION BREAKDOWN: HOW THE FDA AND WALL STREET CRIPPLE MEDICAL ADVANCES* (2014) (arguing the FDA is “horribly broken”).

Senator Ron Johnson convened a second hearing in September 2016 that included testimony from one patient, the California Assembly Majority Leader Ian Calderon, U.S. Representative Jim Neely (R-Mo.), the former president and CEO of Neuralstem, Inc., the executive director of the non-profit organization the Isaac Foundation, and the FDA’s Associate Commissioner for Public Health Strategy and Analysis Peter Lurie. *Exploring a Right to Try for Terminally Ill Patients*, U.S. SENATE COMMITTEE ON HOMELAND SECURITY & GOV’T AFF. (Sept. 22, 2016), <https://www.hsgac.senate.gov/hearings/exploring-a-right-to-try-for-terminally-ill-patients>.

243. Press Release, U.S. Sen. Comm. on Homeland Sec. & Gov’t Affairs, Johnson Introduces Trickett Wendler Right to Try Act (May 10, 2016), <https://www.hsgac.senate.gov/media/majority-media/johnson-introduces-trickett-wendler-right-to-try-act>.

244. Bill Glauber, *Johnson’s Right-to-Try Bill Blocked*, MILWAUKEE J. SENTINEL (Sept. 28, 2016), <https://www.jsonline.com/story/news/politics/2016/09/28/johnsons-right--try-bill-blocked/91225922>.

245. Press Release, U.S. Sen. Comm. on Homeland Sec. & Gov’t Affairs, Chairman Johnson Introduces Bill to Help Terminally Ill Patients (Jan. 24, 2017), <https://www.hsgac.senate.gov/media/majority-media/chairman-johnson-introduces-bill-to-help-terminally-ill-patients>.

246. Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, S. 204, 115th Cong. (as passed by Senate, Aug. 3, 2017).

247. *Examining Patient Access to Investigational Drugs: Hearing Before the H. Comm. on Energy & Commerce*, 115th Cong. (2017), <https://energycommerce.house.gov/hearings/examining-patient-access-investigational-drugs>. This hearing included testimony from Rep. Andy Biggs (R-Ariz.), FDA Commissioner Scott Gottlieb, the Director for Health Care from the U.S. Government Accountability Office, New York University Assistant Professor and Bioethicist Alison Bateman-House, one patient, the Director of Healthcare Policy from the Goldwater Institute, the president and CEO from Cognition

The momentum shifted in favor of the right-to-try movement, however, after President Trump singled out the proposed right-to-try law in his 2018 State of the Union address.²⁴⁸ This mention was enough to reenergize efforts in the House. In March 2018, the House Committee on Energy and Commerce introduced H.R. 5247, Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2018, a narrower right-to-try bill incorporating feedback from the FDA.²⁴⁹ H.R. 5247 failed an initial vote on March 13, but a week later, on March 21, 2018, the bill passed by a vote of 267–149, mostly along partisan lines.²⁵⁰

H.R. 5247 never reached the Senate floor.²⁵¹ With the Senate at a standstill, the House renewed discussions over S. 204.²⁵² In spite of ongoing criticism from industry, patient groups, and physicians,²⁵³ on May 22, 2018, the House passed S. 204 by a vote of 250–169, again on partisan lines.²⁵⁴ On May 31, 2018, President Trump signed the Right to Try Act and declared the law a victory for patients.²⁵⁵

Therapeutics, and the chairperson of the non-profit organization Friends of Cancer Research. *Id.*

248. Donald Trump, State of the Union Address, *supra* note 12.

249. Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2018, H.R. 5247, 115th Cong. (as passed by House, Mar. 21, 2018). H.R. 5247 was narrower than S. 204 because it would have required a requesting patient to have an immediately life-threatening disease and would have limited eligible drugs to those with an active IND application that were not subject to a clinical hold. *Id.* The bill would have also required the manufacturer to notify the FDA within seven days of granting a right-to-try request and to report adverse events. *Id.*

250. See *Actions Overview: H.R. 5247 — 115th Congress*, CONGRESS.GOV, <https://www.congress.gov/bill/115th-congress/house-bill/5247/actions> (last visited Feb. 11, 2019).

251. *Id.*

252. Paige Winfield Cunningham, *The Health 202: How Democrats Got a Version of 'Right to Try' They Like Even Less*, WASH. POST: POWERPOST (May 23, 2018), <https://www.washingtonpost.com/news/powerpost/376anada/the-health-202/2018/05/23/the-health-202-how-democrats-got-a-version-of-right-to-try-they-like-even-less>.

253. Rachel Roubein, *House Eyes Changes for 'Right to Try' Bill*, HILL (Feb. 8, 2018, 6:00 AM), <http://thehill.com/policy/healthcare/372858-house-eyes-changes-for-right-to-try-bill> (quoting Letter from the American Cancer Society Cancer Action Network et al., to U.S. Reps. Paul Ryan & Nancy Pelosi (Feb. 6, 2018), <https://www.asco.org/sites/new-www.asco.org/files/content-files/February-2018-Right-to-Try-Coalition-Letter.pdf>) (noting a group of almost forty patient advocacy groups and professional organizations sent a letter to House leaders that “warned the measure would ‘likely do more harm than good’”).

254. See 21 U.S.C. § 360bbb-0a (2018); *Actions Overview: S. 204 — 115th Congress*, CONGRESS.GOV, <https://www.congress.gov/bill/115th-congress/senate-bill/204/actions> (last visited Feb. 11, 2019).

255. White House Press Release, *supra* note 13.

IV. THE RIGHT TO TRY ACT OF 2017

A. THE LAW

The Right to Try Act creates “national standards and rules by which investigational drugs may be provided to terminally ill patients.”²⁵⁶ The federal law—like its predecessor state laws—is permissive and not mandatory. A manufacturer is not required and cannot be compelled to provide access to an investigational drug after receiving a right-to-try request pursuant to the federal Right to Try Act.²⁵⁷

1. Who is Eligible?

First, a patient may pursue a right-to-try request if they have a “life-threatening disease or condition.”²⁵⁸ Senator Johnson chose this disease threshold, rather than the “immediately life-threatening disease” standard previously used in the expanded access program “because [he thought that the ‘immediately life-threatening disease’ definition] would exclude patients with Duchenne muscular dystrophy, an illness [he] explicitly intended to be covered.”²⁵⁹ Second, the patient must have “exhausted approved treatment options” and be “unable to participate in a clinical trial involving the eligible investigational drug.”²⁶⁰ A physician—but not necessarily the requesting physician—must certify the patient cannot participate in a clinical trial.²⁶¹ The physician who certifies that a patient is unable to participate in the clinical trial must be in “good standing” and cannot receive compensation from the manufacturer in direct response to the certification.²⁶² Third, the patient must provide “written informed consent”—a term that is undefined under the law, rather than using the existing federal regulation defining informed consent.²⁶³

256. Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, Pub. L. No. 115–176, 132 Stat. 1372, 1372 (2018).

257. See generally 21 U.S.C. § 360bbb-0a (2018) (noting no such liability exists under the law).

258. *Id.* § 360bbb-0a(a)(1)(A). “Life-threatening” is defined to be “where the likelihood of death is high unless the course of the disease is interrupted” or where there is the potential for fatal outcomes. 21 C.F.R. § 312.81(a) (2018).

259. Press Release, Johnson to FDA, *supra* note 231.

260. 21 U.S.C. § 360bbb-0a(a)(1)(B) (2018).

261. *Id.*

262. *Id.* § 360bbb-0a(a)(1)(B)(i)–(ii). Of note, the Act does not limit other types of compensation (in other words, the certifying physician could theoretically have an equity interest in the drug company).

263. *Id.* § 360bbb-0a(a)(1)(C). This may have been intentional given that the federal regulation does not allow informed consent to include “any exculpatory language through which the subject . . . is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release . . . the sponsor [that is, manufacturer], the institution, or its agents from liability for negligence.”

2. When Would an Investigational Drug Qualify?

To qualify for right to try, an investigational drug must satisfy four requirements. First, it must have completed a phase I clinical trial.²⁶⁴ The Act does not specify whether the investigational drug must have completed a phase I clinical trial in the requested indication. The Act also does not preclude requests for investigational drugs that have only been tested in healthy volunteers. Second, the drug must not be approved for any other use.²⁶⁵ Third, the manufacturer must either (1) have already filed a marketing application for the investigational drug with the FDA, or (2) be investigating the drug in a clinical trial that is “intended to form the primary basis of a claim of effectiveness in support of approval” and is the subject of an active IND.²⁶⁶ This language is broad because, as Senator Johnson explains, the Act was “not intended to enable the FDA to exclude any clinical trial as a basis for precluding access to treatments under right to try.”²⁶⁷ Fourth, the drug must be in active development (that is, not discontinued) and not subject to a clinical hold.²⁶⁸

An investigational drug that meets these requirements is then exempt from certain statutory and regulatory requirements²⁶⁹ as long as the providing company also complies with sections 312.6 (labeling of investigational new drugs), 312.7 (promoting investigational drugs), and

21 C.F.R. § 50.20 (2018); *see also id.* § 50.25 (describing the basic elements of informed consent); *Id.* § 312.305(c)(4) (cross-referencing 21 C.F.R. pt. 50 as the applicable informed consent standard for the expanded access program).

264. 21 U.S.C. § 360bbb-0a(a)(2)(A). The Act uses the definition of phase I trial from section 312.21 of Title 21, Code of Federal Regulation. *Id.* § 360bbb-0a(a)(3); *see also* 21 C.F.R. § 312.21(a) (2018).

These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug’s pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 studies.

21 C.F.R. § 312.21(a).

265. 21 U.S.C.S. § 360bbb-0a(a)(2)(B).

266. *Id.* § 360bbb-0a(a)(2)(C).

267. Press Release, Johnson to FDA, *supra* note 231.

268. 21 U.S.C. § 360bbb-0a(a)(2)(D) (2018). “A clinical hold is an order issued by FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation.” 21 C.F.R. § 312.42(a).

269. *See* 21 U.S.C. § 360bbb-0a(b) (2018) (citing 21 U.S.C. § 352(f) (stating directions for use and warnings on labels); *id.* § 353(b)(4) (misbranded drugs); *id.* § 355(a)(i) (necessity of effective approval of application; exemptions of drug research); 42 U.S.C. § 262(a) (biologics license); 312 C.F.R. § 50 (protection of human subjects); *id.* § 56 (IRBs)). Of note, the Act, however, does not exempt a company from all statutory and regulatory requirements pertaining to INDs. Holly Fernandez Lynch et al., *Opinion, Promoting Patient Interests in Implementing the Federal Right to Try Act*, 320 JAMA 869, 870 (2018) (noting ongoing reporting obligations).

312.8 (charging for investigational new drugs) of the Code of Federal Regulations.²⁷⁰

3. What are the Reporting Obligations?

a. Companies' Reporting Obligations

The Right to Try Act requires a company to file a yearly report of right-to-try use with Health and Human Services (“HHS”). This yearly report to HHS must include “the number of doses supplied, the number of patients treated, [and] the uses for which the drug was made available”; the manufacturer must also report “any known serious adverse events.”²⁷¹

b. FDA's Reporting Obligations

The Right to Try Act also requires the publication of a yearly report summarizing right-to-try use on the FDA's website. This yearly report must disclose how often the FDA determines a clinical outcome to be critical to deciding safety, how often a manufacturer asks the FDA to consider such outcomes, and how often the FDA does not consider clinical outcomes when reviewing the investigational drug's marketing application.²⁷²

4. When Can the FDA Use Clinical Outcomes?

The Right to Try Act bars the FDA from considering a “clinical outcome” related to a patient's use of an investigational drug “to delay or adversely affect the review or approval” of that drug—except in two situations.²⁷³ The FDA is allowed to use a clinical outcome if it is (1) critical to the assessment of the investigational drug's safety, and (2) the company that provided the investigational drug can also ask for a clinical outcome to be considered.²⁷⁴ The Act does not define “critical.”

* * *

270. *Id.*

271. *Id.* § 360bbb-0a(d)(1).

272. *Id.* § 360bbb-0a(d)(2).

273. *Id.* § 360bbb-0a(c)(1).

274. *Id.* § 360bbb-0a(c)(1)(a)–(b). If the FDA decides it needs to use outcome data, it must give written notice to the company explaining why it was necessary for public health. *Id.* § 360bbb-0a(c)(2). This decision can only be made by “the director of the agency center that is charged with the premarket review of the eligible investigational drug.” *Id.*

TABLE 2. Comparison of Right to Try Criteria to Individual Patient Expanded Access Criteria

	<i>Right to Try</i>	<i>Expanded Access</i>
Patient Eligibility		
<i>Disease</i>	Life-threatening	Serious or immediately life-threatening
<i>Treatment Options</i>	Exhausted approved therapies	No comparable or satisfactory alternative therapy
<i>Clinical Trial Eligibility</i>	Not eligible as certified by physician	Not eligible
<i>Informed Consent</i>	Yes, but not defined	Yes, as defined in 21 C.F.R. pt. 50
IRB Review	...	Full <i>or</i> IRB chair / another designated member available
Drug Qualification	Completed phase I trial; Not approved; Filed marketing application <i>or</i> under investigation in a clinical trial to form primary basis of effectiveness claim in support of approval <i>and</i> active IND development must be ongoing and not discontinued	Investigational drug; Potential benefit justifies risks; Cannot interfere with clinical development
Therapy Duration	...	One course of treatment <i>or</i> specified length
Manufacturer Compliance	Voluntary	Voluntary
Reporting Obligations		
<i>Manufacturer</i>	Submit annual summary to HHS, including number of doses given, indications, and known serious adverse events	...

TABLE 2. Comparison of Right to Try Criteria to Individual Patient Expanded Access Criteria

	<i>Right to Try</i>	<i>Expanded Access</i>
<i>Physician</i>	...	Submit written results summary after treatment concludes, including adverse events <i>and</i> report serious and unexpected adverse events if evidence suggests causal relationship between adverse reaction and drug
<i>FDA</i>	Must publish number of drugs for which clinical outcomes were used in annual report available on FDA's website	...
FDA's Use of Clinical Outcomes	Cannot use clinical outcome to delay or adversely affect review or approval <i>unless</i> FDA center director decides it is <i>critical</i> to a safety determination <i>or</i> manufacturer requests its use	Evaluate adverse events within the context of the drug's expanded access use
Cost / Insurance Coverage	Direct costs <i>and</i> insurance not required to cover	Direct costs <i>and</i> insurance not required to cover
Liability	Cannot be liable for any act or omission unless they act reckless, act with willful or gross negligence, or commit an international tort	...

B. INDUSTRY'S POTENTIAL PATH MOVING FORWARD

This Section proceeds as follows. Section IV.B.1 explains why regardless of future FDA guidance, most companies are unlikely to adopt a two-pathway approach or even a single-pathway approach using just right to try, favoring continued use of the expanded access program instead. Section IV.B.2 argues that the status quo, however, is insufficient and that companies need to address some of the criticisms raised during the right-to-try movement by (1) revising their existing expanded access policies, and (2) improving clinical trial access.

1. Even with the Right to Try Act, Most Companies Will Continue to Use Expanded Access

All along, right-to-try advocates have contended that the Right to Try Act's provisions limiting liability and limiting the FDA's use of outcome data would incentivize manufacturers to utilize this new pre-approval pathway.²⁷⁵ Yet, as this Note explains below, these two provisions are not enough for most companies to utilize the Right to Try Act.²⁷⁶

Lack of Support from Key Stakeholders. The Right to Try Act lacks support from industry, advocacy groups, physician organizations, and the FDA. Companies, including Janssen and Bristol-Myers Squibb, have already stated that right-to-try requests will be funneled through the expanded access pathway.²⁷⁷ Janssen announced prior to the enactment of the federal Right to

275. Sammy Caiola, *Federal Right to Try Law Could Mean More Access—and Risk—for California Patients*, CAPITAL PUB. RADIO (May 31, 2018), <http://www.capradio.org/articles/2018/05/31/federal-right-to-try-law-could-mean-more-access-and-risk-for-california-patients>. The Right to Try Act does not “modify or otherwise affect the right of any person to bring a private action under any State or Federal product liability, tort, consumer protection, or warranty law.” 21 U.S.C. § 360bbb-0a (2018) (Limitation of Liability).

276. See Reddy, *supra* note 6; Arlene Weintraub, *Biotech Executives Fret Over Hassles and Uncertainties of ‘Right to Try’*, FORBES (Jun 13, 2018), <https://www.forbes.com/sites/arleneweintraub/2018/06/13/biotech-executives-fret-over-hassles-and-uncertainties-of-right-to-try/#6df52d69bc78>.

277. See *Janssen Policy: Evaluating and Responding to Pre-Approval Access Requests for Investigational Medicines*, JANSSEN [hereinafter *Janssen Policy*], <http://www.janssen.com/sites/www.janssen.com/files/janssenpolicyevaluatingrespondingpreapprovalrequests022018.pdf>; *Pfizer’s Position on Federal Right to Try Legislation*, PFIZER (May 2018), <https://www.pfizer.com/files/research/PolicyPositionRighttoTryFederalLegislationMay2018.pdf>; GlaxoSmithKline, *U.S. Public Policy Position Paper: Right-to-Try Legislation*, GLAXOSMITHKLINE (Mar. 2015), <https://us.gsk.com/media/1444389/ppright-to-trylegislation.pdf>; *Early Patient Access to Investigational Medicine*, BRISTOL-MYERS SQUIBB [hereinafter *Bristol-Myers’ Position*], <https://www.bms.com/healthcare-providers/early-patient-access-to-investigational-medicine.html> (last visited Feb. 11, 2019); see also Michelle Cortez, *Dying Patients Face Reality Check on Right to Try*, BLOOMBERG (June 8, 2018, 7:53 AM), <https://www.bloomberg.com/news/articles/2018-06-08/dying-patients-seeking-drugs-face-reality-check-on-right-to-try> (discussing how manufacturers do not plan to change their “current approach” even after the enactment of the Right to Try Act).

Try Act that it would not “evaluate right-to-try requests because [the state] laws don’t allow for FDA input, which is ‘critical for ensuring patient safety.’”²⁷⁸ Patient advocacy groups and physician organizations have not significantly changed their position on the Right to Try Act since its adoption.²⁷⁹ The FDA has also since voiced its continued preference for use of the expanded access program in November 2018,²⁸⁰ and announced in December 2018 a new program, “Project Facilitate,” which aims to further alleviate the criticisms of the expanded access program. Project Facilitate will establish a department within the FDA that (1) will field calls from physicians requesting expanded access on behalf of a patient and patients seeking single-patient expanded access for themselves; (2) complete Form FDA 3926, and if necessary forward the completed form to a patient’s treating physician for sign-off if the initial request was made by the patient; (3) forward the request to an IRB; and (4) ultimately submit the request to the company developing the requested drug, which must make a determination “within a specified time period . . . yet [to be] determined” by the FDA.²⁸¹ With industry generally reticent to act without agency

278. Dan Diamond, *Johnson & Johnson Won’t Consider Patients’ Right-to-Try Requests*, POLITICO (Jan. 17, 2018, 10:00 AM), <https://www.politico.com/newsletters/politico-pulse/2018/01/17/hhs-readying-new-rule-to-expand-conscience-protections-075342>; see also *Janssen Policy*, *supra* note 277.

279. See Thaddeus Mason Pope, *Why Oncologists Should Decline to Participate in the Right to Try Act*, ASCO POST (Aug. 10, 2018), <http://www.ascopost.com/issues/august-10-2018/declining-to-participate-in-the-right-to-try-act> (“Because the extra risks posed by the Right to Try Act are not offset by any countervailing benefit, it would be unethical for oncologists to use it to gain access to an experimental drug for their patients.”).

280. See Statement, U.S. Food & Drug Admin., Statement from FDA Commissioner Scott Gottlieb, M.D., on New Efforts to Strengthen FDA’s Expanded Access Program (Nov. 8, 2018), <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm625397.htm>.

281. Usdin, *supra* note 101. The goal of this program is two-fold: (1) “to remove impediments that prevent physicians and patients from seeking access to investigational drugs and [(2)] to communicate FDA’s support for manufacturers providing access.” *Id.* The agency anticipates rolling out a pilot version for oncology requests in 2019. *Id.*

This modification to the expanded access program goes well beyond the modifications discussed in Section III.B. The aptly named program creates a new tension within the expanded access program: the FDA is now not only a key decisionmaker, but also, as the program is aptly named, a facilitator, and possibly the key facilitator. This modification raises new questions that, although beyond the scope of this Note, are worth noting. First, to what extent will a patient-initiated request impair the treating physician’s decisionmaking responsibility? Will FDA staff consult with the requesting patient’s physician to ensure he or she weighed the risks associated with use of the investigational drug against the risks associated with the disease (and discussed those risks with the patient) prior to filling out Form FDA 3926 and sending to the physician for signature? Second, will an FDA-facilitated request ensure a fair and separate IRB review process? Will the FDA be responsible for costs associated with the IRB or will those costs continue to be covered by the patient? Third, how will the FDA ensure companies comply with a response deadline? Will the FDA’s to-be-determined manufacturer review period result in more

guidance,²⁸² the November 2018 announcement and the forthcoming Project Facilitate arguably send strong signals to keep using the expanded access program.

Insufficient Incentives. The Right to Try Act's provisions limiting a company's liability and limiting the FDA's use of outcome data are insufficient incentives. First, the Right to Try Act does limit a company's potential liability but does not protect a manufacturer against any and all liability claims. As attorney James M. Beck notes, the Act still allows claims of reckless or willful misconduct, gross negligence, or intentional tort.²⁸³ The Right to Try Act also does not foreclose claims under state or federal product liability, tort, consumer protection, or warranty law.²⁸⁴ A company would also be trading more liability protection for less FDA input when it is not clear further liability protection is even necessary. As others have pointed out, there are no examples of patients suing manufacturers of investigational drugs for "treatment-related harm[s]" stemming from expanded-access use.²⁸⁵ Therefore, companies—at least within the context of expanded access—should have minimal concern over potential tort claims.

Second, although the Right to Try Act limits the FDA's use of outcome data to when it is "critical" to determining safety, in practice the FDA rarely uses expanded access data when reviewing an investigational drug unless

companies denying requests to avoid simply missing that deadline?

282. See, e.g., Rich Thomaselli, *FDA's Social-Media 'Guidelines' Befuddle Big Pharma*, ADAGE (Dec. 30, 2011), <https://adage.com/article/digital/fda-s-social-media-guidelines-befuddle-big-pharma/231855> (suggesting the lack of FDA guidance regarding social media has restrained biopharmaceutical companies' use of expanded access).

283. James M. Beck, *Federal Right to Try Legislation—Is It Any Better?*, DRUG & DEVICE L. (Sept. 5, 2017), <https://www.druganddeviceblog.com/2017/09/federal-right-to-try-legislation-is-it-any-better.html>.

That's not much protection at all, given how readily the other side throws around such allegations, and how infrequently judges throw them out. In subsection 1, "Reckless/willful" is a standard for punitive damages, which routinely survive dismissal in [multidistrict litigation] and other actions around the country. "Gross negligence" is a standard even less than that—merely an aggravated form of negligence that doesn't require any finding of intent at all. Intentional torts include fraud, which is currently included in just about any product liability complaint. Battery, which encompasses informed consent in many states, is also an intentional tort.

Id.

284. Though some states' right-to-try laws could preclude these types of claims. *E.g.*, CAL. HEALTH & SAFETY CODE § 111548.5 (West, Westlaw through 2018 Sess.).

285. Jonathan J. Darrow et al., *Practical, Legal, and Ethical Issues in Expanded Access to Investigational Drugs*, 327 NEW ENG. J. MED. 279, 282 (2015) ("Litigation in this arena, however, has been limited to obtaining access rather than seeking redress of treatment-related harm."); see also Lynch et al., *supra* note 269, at 870 (suggesting that FDA input and IRB oversight might be "an important indication of reasonableness" in a hypothetical expanded access-product liability case).

there is evidence to suggest a causal relationship.²⁸⁶ Even though the FDA's use of outcomes is often a concern for manufacturers, the FDA has assured companies it rarely uses expanded access data, so it is unclear how the Right to Try Act's provision further limits the FDA's use. Furthermore, as the Act does not define "critical," without some guidance from the FDA it is unclear whether this is the same standard as used in expanded access, a more relaxed standard, or a heightened standard given that the FDA is not involved in reviewing the right-to-try request and determining proper usage, such as dosage. Finally, even if the FDA is limited in its ability to assess reported events, manufacturers may still be concerned about whether any adverse events associated with right-to-try use would impact regulatory approval in other countries.²⁸⁷

Third, the Right to Try Act does not contain a significant financial incentive for industry. The Act requires companies to comply with the existing regulation, which limits cost recovery to direct costs, except under specific circumstances.²⁸⁸ A two-pathway approach would require companies to allocate additional money, personnel, and drug supply to another program that is outside the drug development process. With the cost of developing a new drug estimated to be around \$2.6 billion,²⁸⁹ it seems unlikely that manufacturers would be willing to expend any additional resources to only recoup direct costs.²⁹⁰ A publicly traded company, like Pfizer or Janssen, might have the necessary financial resources and employees but will still answer to shareholders and still have concerns about maintaining adequate supply of the drug for its clinical trials.²⁹¹ A small, private company under pressure from investors is likely to have even less motivation to redirect limited resources to a two-pathway pre-approval program, or even a single-pathway program without some financial

286. See *supra* Section III.B.

287. See, e.g., *ClinRegs: Canada*, NAT'L INST. HEALTH, <https://clinregs.niaid.nih.gov/country/385anada> (last updated Feb. 8, 2018) ("During a clinical trial, the sponsor is required to inform [Health Canada] of any serious, unexpected [adverse drug reaction] that has occurred inside or outside Canada.").

288. 21 C.F.R. § 312.8 (2018) (charging for investigational drugs under an IND); U.S. FOOD & DRUG ADMIN., CHARGING FOR INVESTIGATIONAL DRUG UNDER AN IND—QUESTIONS AND ANSWERS: GUIDANCE FOR INDUSTRY 6–7 (2016), <https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351264.pdf>.

289. See DiMasi et al., *supra* note 50, at 20; Herper, *supra* note 50.

290. 21 U.S.C. § 360bbb-0a(b) (2018) (citing 21 C.F.R. § 312.8 (2018) (charging for investigational drugs under an IND)).

291. See *infra* Appendix (listing companies citing adequate supply); see also Darrow et al., *supra* note 285, at 280–81 (describing the "administrative burden" for companies when preparing an intermediate-size patient expanded access protocol).

upside.²⁹² Take, for example, BrainStorm Therapeutics, which announced plans to offer its therapy through right to try and would have charged patients seeking the right to try its drug potentially \$300,000. The company's now-retracted plan likely did not comply with federal regulation given that it was positioned as a "semicommercial enterprise with modest profits."²⁹³

Unanswered Implementation Questions. The Right to Try Act is meant to be a parallel pathway to expanded access and not a replacement, but it would be difficult for a company to implement a pre-approval access program in which both of these programs co-exist. The Right to Try Act does not provide companies considering utilizing right to try as a parallel pathway guidance to the threshold issue: when it should use right to try and when it should use expanded access. The FDA is working to develop guidance,²⁹⁴ but for now it has said that companies are in the best position to make that determination.²⁹⁵ While this Note identifies two potential options, each is not without their own drawbacks and complexities. A company could (1) use right to try when an investigational drug will be used by a single patient and use expanded access when an investigational drug will be used by a larger patient population, or (2) use right to try under certain pre-defined circumstances (for example, pediatric patients or patients with exceptional safety risks) and use expanded access in all other circumstances.

The first option—use of right to try in the single-patient setting—would be administratively easier. A company would not need to develop new policies delineating between the two pathways for individual patients. That said, this approach does have potential challenges. First, individuals with certain types of serious diseases would not qualify for the right-to-try pathway, therefore limiting their pre-approval access options until the drug

292. CLINICAL LEADER, *supra* note 171; see also Paige E. Finkelstein, *Expanded Access to Investigational Drugs: What Physicians and the Public Need to Know About FDA and Corporate Processes*, 17 AM. MED. ASS'N J. ETHICS 1142, 1143–44 (2015). See generally Kenneth I. Moch, *Ethical Crossroads: Expanded Access, Patient Advocacy, and the #SaveJosh Social Media Campaign*, 1 MEDACCESS 1 (2017) (describing one company's response to a targeted expanded access social media campaign).

293. Cortez, *Cost Dying Patients*, *supra* note 51.

294. Zachary Brennan, *FDA Prepares to Implement 'Right-to-Try' Law*, REG. FOCUS (May 31, 2018), <https://www.raps.org/news-and-articles/news-articles/2018/5/fda-prepares-to-implement-right-to-try-law> ("[The FDA] is convening an internal group to assess how to effectively and efficiently implement the new law. [The FDA] will report on [their] implementation steps regularly." (quoting an emailed statement from the FDA)).

295. *Id.* ("[I]f [FDA staff] receive inquiries about the legislation from patients or physicians about a specific product, [they] refer them to the sponsor of the investigational drug If sponsors contact [FDA staff] regarding their obligations under this law, [the FDA] suggest[s] that [staff] refer them to the statute." (quotation omitted)).

has sufficient evidence to support expanded access for intermediate-size or widespread treatment.²⁹⁶ Take, for example, the conditions narcolepsy or rheumatoid arthritis, which the FDA has said would independently qualify as a serious disease; these conditions would not be considered “life-threatening” because both are considered chronic diseases and are alone not fatal.²⁹⁷ Therefore, adoption of this approach would likely be dependent on a company’s investigational drug pipeline. A company with a single drug in development might be less concerned about this issue, but a company with a large disease pipeline that targets multiple different disease areas might be.

Second, it is not clear what the patient limit should be for right to try (that is, at what point should a company stop providing pre-approval access through right to try and transition over to expanded access for intermediate-size and widespread treatment). The Right to Try Act does not provide any guidance. A company should not be able to provide five, ten, or fifteen patients at a single hospital with an investigational drug through the right to try pathway. That starts looking more like an intermediate-size expanded access protocol²⁹⁸ and arguably should have FDA oversight. Without specific right-to-try guidance, a manufacturer would need to rely on expanded access guidance as a benchmark for when a company should transition from the right-to-try pathway to intermediate-size or widespread use through expanded access, but even then the existing FDA guidance does not address other concerns regarding the potential applicability of the Right to Try Act’s provisions limiting liability and use of outcome data once a certain patient threshold is crossed.

The second option—use of right to try under certain pre-defined settings—would be administratively more complicated, given that it would

296. See *supra* Table 1 (describing the additional criteria the FDA needs to determine whether intermediate-size or widespread expanded access use is appropriate).

297. Jennifer Freeman, *RA Life Expectancy: Can I Live a Long Life with Rheumatoid Arthritis?*, RHEUMATOID ARTHRITIS SUPPORT NETWORK (Sept. 17, 2018), <https://www.rheumatoidarthritis.org/ra/prognosis/life-expectancy> (characterizing rheumatoid arthritis as a chronic, but progressive disease); *Narcolepsy Fact Sheet*, NAT’L INST. OF NEUROLOGICAL DISORDERS & STROKE, <https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Narcolepsy-Fact-Sheet> (describing narcolepsy as a chronic neurological condition) (last visited Feb. 11, 2019).

298. The FDA has not established an exact numeric threshold that would trigger intermediate-size use, but explains that it will recommend when “it is generally most efficient to consolidate expanded access in a single intermediate-size patient population IND or protocol.” EXPANDED ACCESS: GUIDANCE FOR INDUSTRY, *supra* note 145, at 14. The FDA has also not established a threshold for when intermediate-size expanded access as opposed to widespread treatment expanded access should be used, instead considering two criteria: (1) “whether the drug is under development for marketing for the expanded access use,” and (2) “the size of the patient population.” *Id.* at 15.

require companies to determine those pre-defined circumstances and ensure that the criteria for those standards is clear and easy to apply. That said, some companies might consider this approach in order to allow some patients who might otherwise not be eligible for expanded access to receive the drug through right to try, given the Act's provisions limiting liability and use of outcome data. Two such settings that a company might reasonably consider are (1) patients who have exceptional safety risks²⁹⁹ and (2) patients who are children.³⁰⁰ The former group is frequently ineligible for a clinical trial and likely to be denied expanded access use because of manufacturers' concerns about potential liability or adverse events impacting clinical development.³⁰¹ The latter group—often the face of the right-to-try movement³⁰²—is also frequently ineligible for industry-sponsored clinical trials and may be denied expanded access use because of manufacturers' concerns about inadequate clinical data to determine an adequate dosage in the pediatric setting, potential liability, or adverse events impacting clinical development.³⁰³

This second approach is also not without its drawbacks. First, the pre-defined settings would need to be unambiguous. Though pediatric patients can be more clearly defined by age, the term “exceptional safety risks” is not susceptible to one definition, so companies allowing pre-approval access in this setting would need to establish a specific standard and make sure it is clearly communicated internally and externally. Second, with pediatric patients³⁰⁴ and patients who are terminally ill,³⁰⁵ there are also ethical

299. See, e.g., *How We Operate: Compassionate Use*, SHIRE, <https://www.shire.com/who-we-are/how-we-operate/policies-and-positions/compassionate-use> (last updated Apr. 2015) (excluding “patients with exceptional safety risks that have not been sufficiently studied” from expanded access use).

300. See Florence T. Bourgeois et al., *Pediatric Versus Adult Drug Trials for Conditions with High Pediatric Disease Burden*, 130 PEDIATRICS 285, 286 (2012) (children often treated with drugs only approved for adult use); Tirrell, *supra* note 5 (companies declining to grant pediatric expanded access request due to insufficient pediatric data).

301. PUBLIC WORKSHOP: EVALUATING INCLUSION AND EXCLUSION CRITERIA, *supra* note 203, at 3.

302. See RIGHTTOTRY, <http://righttotry.org> (last visited Feb. 11, 2019); Vice President Mike Pence, March 13 Tweet, *supra* note 12.

303. See Bourgeois et al., *supra* note 300, at 286; Tirrell, *supra* note 5; PUBLIC WORKSHOP: EVALUATING INCLUSION AND EXCLUSION CRITERIA, *supra* note 203, at 4–5.

304. Pathama D. Joseph et al., *Clinical Trials in Children*, 79 BRITISH J. CLINICAL PHARMACOLOGY 357, 360–61 (2013) (describing complex nature of informed consent in the pediatric setting).

305. A study published in the *Journal of the American Medical Association* (“JAMA”) found that not only do “cancer patients tend to overestimate their prognoses,” but that the overestimation impacts treatment decisions. Jane C. Weeks et al., *Relationship Between Cancer Patients' Predictions of Prognosis and Their Treatment Preferences*, 279 JAMA 1709, 1712–13 (1998); see also Andrew S. Epstein et al., *Discussions of Life Expectancy and Changes in Illness Understanding in Patients with Advanced Cancer*, 34 J. CLINICAL ONCOLOGY 2398, 2398–2401 (2016) (“Results of this study demonstrate how poorly patients with advanced cancer understand their prognoses and how effective

considerations requiring companies to adopt more rigorous informed consent requirements and procedures. Take pediatric patients, for example, cases in which “[p]arents or other surrogates technically provide ‘informed permission’ for diagnosis and treatment, with the assent of the child whenever appropriate.”³⁰⁶ Third, companies would also still need to refer back to the state right-to-try laws to ensure their pre-defined settings are compliant. Oregon, for example, limits the right to try pathway to individuals who are at least eighteen years old.³⁰⁷ This could increase the complexities of implementation. Fourth, the drawbacks relating to the first option likely would also impact the second option.

The practical complexities of operating a two-pathway approach, stemming from presently unanswered legal questions regarding the Right to Try Act and concerns that might arise from utilizing Right to Try in specific patient settings, make companies unlikely to use right to try even if the FDA provides guidance.

State Right-to-Try Laws. The applicability of state right-to-try laws is also still uncertain.³⁰⁸ While the Right to Try Act creates a national standard,³⁰⁹ it does not explicitly preempt these state laws.³¹⁰ Senator Ron Johnson has previously stated that the Right to Try Act was meant to be the “federal counterpart” to the state right-to-try laws.³¹¹ With forty-one state-

recent prognostic discussions are to improve illness understanding by patients.”).

306. Am. Acad. Of Pediatrics, *Informed Consent in Decision-Making in Pediatric Practice*, 138 PEDIATRICS 2 (2018), <http://pediatrics.aappublications.org/content/pediatrics/early/2016/07/21/peds.2016-1484.full.pdf>.

307. OR. REV. STAT. § 127 (2017), https://www.oregonlegislature.gov/bills_laws/ors/ors127.html.

308. Kate Gallin Heffernan et al., *Federal “Right to Try”: Don’t Disregard Your State Laws Just Yet! How Federal Preemption (or Lack Thereof) Could Influence the Use of Federal “Right to Try”*, VERRILL DANA LLP (2018), <http://www.verrilldana.com/federal-right-to-try-dont-disregard-your-state-laws-just-yet>.

309. Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, Pub. L. No. 115–176, 132 Stat. 1372, 1372 (2018).

310. U.S. CONST. art. VI, cl. 2 (“This Constitution, and the laws of the United States which shall be made in pursuance thereof . . . shall be the supreme law of the land.”); see also Phoebe Mounts et al., *A Closer Look at New Federal ‘Right to Try’ Law*, LAW360 (June 1, 2018, 12:17 PM), <https://www.morganlewis.com/-/media/files/news/2018/law360-a-closer-look-at-new-federal-right-to-try-law-01jun18.ashx>; Heffernan et al., *supra* note 308 (suggesting enactment of the Right to Try Act revives the preemption issue because the Act is “less in conflict with its state counterparts” and “state laws could reasonably be found by a court to supplement and explicate the way in which this activity (the provision of investigational drugs outside of FDA’s purview) can occur in a given jurisdiction, rather than serving to frustrate Congress’ intent in making the ‘right to try’ pathway available”).

311. *Exploring a Right to Try for Terminally Ill Patients: Hearing Before the S. Comm. on Homeland Sec. & Gov’t Affairs*, 114th Cong. 2 (2016) (statement of Sen. Ron Johnson). The Act also authorizes pre-approval access “in accordance with State law.” Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, Pub. L. No. 115–176, 132 Stat. 1372,

level right-to-try laws, implementation and compliance would be complicated. A company would likely need to comply with *at least some of* the provisions of the state right-to-try laws in addition to the Right to Try Act's provisions.

Take, for example, the California state statute's criteria for patient eligibility, which requires a person to have: (1) "an immediately life-threatening disease or condition"; (2) "considered all other treatment options currently approved"; (3) "not been accepted to participate in the nearest clinical trial to his or her home . . . within one week of completion of the clinical trial application process, or, in the treating physician's medical judgment, it is unreasonable for the patient to participate in that clinical trial"; (4) "received a recommendation from his or her primary physician and a consulting physician"; (5) "given written informed consent"; (6) "documentation . . . attesting that the patient has met the requirements . . ." ³¹²

The first requirement limiting patient eligibility is narrower than the Right to Try Act.³¹³ The second requirement is arguably broader, because it would allow a patient to rely on the pathway after considering, but not exhausting, all treatment options. The first part of the third requirement could possibly supplement the Right to Try Act's clinical trial requirement if it was interpreted as requiring proof of non-acceptance, but it is likely more accurately interpreted as allowing a patient to make a request within one week of not receiving a response, which is broader than the Right to Try Act. The second part of that requirement is clearly broader, however, than the federal law, as the Right to Try Act requires a physician to certify that a patient cannot participate in a clinical trial, and not just that it would be unreasonable for a patient to participate in a clinical trial; the California law uses a different standard. The fourth requirement supplements the Right to Try Act because it requires confirmation from a second physician.³¹⁴ The fifth requirement also supplements the federal law because, whereas the federal law leaves "informed consent" undefined, California defines "informed consent" in another part of the statute.³¹⁵ The sixth requirement

1372 (2018).

312. CAL. HEALTH & SAFETY CODE § 111548.1(b)(1)–(6) (West, Westlaw through 2018 Sess.).

313. Compare *id.* § 111548.1(d) ("Immediately life-threatening disease or condition" means a stage of disease in which there is a reasonable likelihood that death will occur within a matter of months.), with 21 U.S.C. § 360bbb-0a(a)(1)(A) (2018) (requiring "life-threatening disease or condition").

314. See *supra* Section IV.A (describing Right to Try Act provisions).

315. CAL. HEALTH & SAFETY CODE § 111548.1(h) (West, Westlaw through 2018 Sess.) (right to try informed consent requirements); *id.* § 24173(a)–(e) (general informed consent requirements).

mirrors the federal law.³¹⁶

Although a company could theoretically challenge state right to try laws as preempted by the federal provision, this is not an issue that an individual company, or companies collectively, are likely to challenge, particularly given the high costs of litigation and limited financial incentive of success on the merits.³¹⁷ This issue could also impact patient's actual interest³¹⁸ and healthcare providers' willingness to offer such treatments.³¹⁹

External Regulatory Challenges. The adoption of the Right to Try Act by industry seems less likely given that companies already face "challenges particularly related to . . . managing divergent requirements and guidance from ex-US health authorities" when implementing expanded access.³²⁰ The potential effect of right-to-try use on product development or regulatory review in other countries is unclear. And, if companies are already overly tasked from other countries' requirements, they are not going to add another pathway to that mix.

Confidential Information. A final reason the Right to Try Act will not gain industry support is that, as practitioners James Valentine and David Clissold explain, some of the Right to Try Act's drug eligibility requirements may require companies to "disclose details of their development program that might otherwise be confidential, commercial information."³²¹ This potential disclosure requirement is not an issue with expanded access because the FDA has access to this proprietary information through the drug's IND file and can utilize it when evaluating an expanded access request

316. See *supra* Section IV.A (describing Right to Try Act provisions).

317. See Press Release, Pharm. Research & Mfg. of Am. & Biotech. Innovation Org., PhRMA and BIO Initiate Litigation to Challenge Unconstitutional Provisions of Nevada's SB 539 (Sept. 1, 2017), <https://www.phrma.org/phrma-bio-release> (initiating litigation over a Nevada law, which the groups argued "attempt[s] to set de facto price controls" on diabetes medicines).

318. See *supra* notes 194–95 and accompanying text.

319. See Bateman-House, *Findings*, *supra* note 184.

[T]here is no guidance for physicians about which law to follow in cases of conflicts. For example, if a patient lives in South Dakota but seeks care in North Dakota, which state law ought to be observed? If a hospital is located in Arkansas but is part of a network based in Delaware, which state law ought to be observed? If the patient and doctor are in Tennessee but the experimental product they wish to try can be administered only in Texas, which state law ought to be observed?

Id.

320. EXPANDED ACCESS PROGRAM REPORT, *supra* note 160, at 3.

321. James E. Valentine & David B. Clissold, *Burden of "Right to Try" Implementation on Sponsors (for Now); Risk of Unexpected SAEs Negatively Impacting Development and Approval Still Remains*, HYMAN, PHELPS & MCNAMARA PC: FDA L. BLOG (June 8, 2018), <http://www.fdalawblog.net/2018/06/burden-of-right-to-try-implementation-on-sponsors-for-now-risk-of-unexpected-saes-negatively-impacting-development-and-approval-still-remains>.

and making recommendations regarding use and dosage.³²² With the FDA's ability to review proprietary drug information, the expanded access program offers two benefits over the right-to-try pathway—(1) it limits a company's potential need to disclose confidential commercial development information and (2) it ensures patients who may not be undergoing treatment from a physician also acting as a clinical trial investigator can still request access to an investigational drug.³²³

These reasons make adoption of a two-pathway approach or abandonment of expanded access in favor of right to try unlikely. However, maintaining the status quo is not feasible—nor is it appropriate. Companies have already started receiving calls from patients seeking the right to try with some of those calls even escalating to threats when people are referred back to the expanded access program.³²⁴ This could further escalate to widespread social media campaigns and media coverage if companies do not explicitly address right to try within their existing pre-approval access policies. With the public's negative perception of the pharmaceutical industry,³²⁵ companies need to address at least some of the criticisms raised during the right-to-try debate that were not rectified through adoption of the Right to Try Act.

2. Charting Industry's Path Forward

a. Companies Should Revise Existing Expanded Access Guidelines

Right-to-Try Position Statement. Companies should update both their expanded access guidelines to include language that clearly addresses the Right to Try Act and their plans to only offer pre-approval access through

322. Expanded Access to Investigational Drugs for Treatment Use, 74 Fed. Reg. 40,900, 40,924 (Aug. 13, 2009) (codified at 21 C.F.R. pts. 312, 316).

323. Cortez, *Cost Dying Patients*, *supra* note 51. BrainStorm planned to limit provider access to those physicians “who participated in the drug's clinical trials,” and therefore would be experienced with the drug and, presumably, its appropriate dosage and potential side effects. *Id.* This plan might be one way to combat widespread disclosure, but it would arguably limit the availability of right to try to academic centers and other major hospitals where clinical trials are conducted as opposed to increasing access across the United States—the whole point of the Right to Try Act.

324. Weintraub, *supra* note 276 (“The new law doesn't require drug makers to comply with Right to Try requests, but that doesn't make the burden of dealing with phone calls and e-mails from patients demanding access to experimental products any less burdensome.”).

325. See EDELMAN, EDELMAN TRUST BAROMETER—HEALTHCARE: GLOBAL 26–27 (2018) (presenting an online survey in twenty-eight markets with 1,150 respondents per market); Laura Entis, *Inside Pharma's Trust Problem*, MM&M (June 26, 2018), <https://www.mmm-online.com/home/channel/commercial/inside-pharmas-trust-problem> (citing high drug prices, misconceptions that companies are withholding the cure for financial gain, and misleading direct-to-consumer advertising as reasons for this distrust).

expanded access. Some companies have already done this. Take, for example, the statement Bristol-Myers Squibb features prominently on the section of its website addressing pre-approval access:

We believe our current approach to early patient access . . . is consistent with the objectives of the Right to Try Act. Requests for early patient access to Bristol-Myers Squibb investigational medicines should continue to be made through the treating physician and by visiting Bristol-Myers Squibb Early Patient Access Requests Portal.³²⁶

To avoid potential criticisms from right-to-try advocates and patients, companies need to take additional steps outlined below.

Company Pre-Approval Access Reporting. Companies should publish annual reports on their websites regarding their expanded access programs. Although companies are granting expanded access requests,³²⁷ this information is often not publicly available. The reports should include detailed information, such as the number of requests received (and of those the number of requests approved), the most common reasons for a denial (for example, ability to enroll in a clinical trial or insufficient clinical data to support the requested use), and the number of patients referred to clinical trials (and of those, the number that chose to enroll).³²⁸ If companies are unwilling to publish this data on their own websites, then an alternative approach would be for BIO and PhRMA to commission a report summarizing this data. If the report is published by BIO and PhRMA, companies might be more comfortable providing additional data, such as the number of requests received by investigational drug (or class of drug) and the number of requests received by disease (or category of disease). Either approach—self-reporting or industry-wide reporting—could increase transparency regarding the gap between the number of requests received by companies and the number of requests received by the FDA.

Patient Eligibility—Clinical Trial Ineligibility. Companies need to better explain what factors render a patient unable to participate in clinical

326. *Bristol-Myers' Position*, *supra* note 277; *see also Janssen Policy*, *supra* note 277 (“We are committed to helping patients with serious illnesses and their families request access to our investigational medicines. We support these requests through our established review and evaluation processes, which includes independent review by the FDA.”).

327. EXPANDED ACCESS PROGRAM REPORT, *supra* note 160, at 21 (“40% to 95% [are] the manufacturer approval rates for [expanded access] requests.”).

328. *See* Rep. Michael McCaul, *Expanded Access to 21st Century Cures Act*, <https://mccaul.house.gov/sites/mccaul.house.gov/files/Expanding%20Access%20to%2021st%20Century%20Cures.pdf> (last visited Feb. 11, 2019) (proposing the Cures Act include a provision requiring manufacturers to track and report requests for expanded access to the FDA).

trials beyond just not qualifying. The only factor sometimes listed is geographic limitations, and companies sometimes list this as only an example of a factor that will generally not support expanded access use. This creates two distinct problems. First, without additional information, physicians and patients are left guessing what other factors render a patient unable to participate in a clinical trial. This could discourage a physician from submitting an otherwise valid request. Second, the FDA will consider geographic limitations when reviewing a request even when the company does not, making the agency's guidance at odds with some companies' policies. This is confusing. For those companies generally unwilling to consider geographic limitations as a factor impacting a patient's ability to participate, companies could add additional criteria such as transportation and financial limitations. The FDA has identified both as common obstacles to clinical trial enrollment.³²⁹

*Patient Eligibility—Pediatrics.*³³⁰ Companies often either do not address pediatric expanded access use³³¹ or will not consider pediatric expanded access use without sufficient pediatric data.³³² The former approach is short-sighted from a public relations perspective, especially with the enactment of the Right to Try Act and its focus on pediatric access. In 2014, Bristol-Myers Squibb cited lack of pediatric data when asked about a specific patient's denial by CNBC, but even four years after that media firestorm, the company still does not address pediatric expanded access use in its published guidelines.³³³ A physician might recommend expanded access for a child only to learn after submitting a request that the company will not provide pre-approval access without sufficient pediatric data. Thus, companies should strive to increase transparency. The latter approach also needs to be reconsidered. With so many pediatric patients currently being treated using FDA-approved drugs that only underwent clinical testing in

329. PUBLIC WORKSHOP: EVALUATING INCLUSION AND EXCLUSION CRITERIA, *supra* note 203, at 6; Caroline McNeil, *Broadening the Evidence Base for Older Patients: FDA-ASCO Workshop Explores Emerging Strategies*, ASCO POST (Dec. 25, 2017), <http://www.ascopost.com/issues/december-25-2017/broadening-the-evidence-base-for-older-patients-fda-asco-workshop-explores-emerging-strategies> (“50% of U.S. oncologists are concentrated in eight states.”). Some patients' jobs might also limit their ability to travel to a clinical trial site on a regular basis while other patients' insurance may not cover the portions of the clinical trial not paid for by the trial sponsor. See Caroline Chen & Riley Wong, *Black Patients Miss Out on Promising Cancer Drugs*, PROPUBLICA (Sept. 19, 2018, 5:00 AM), <https://www.propublica.org/article/black-patients-miss-out-on-promising-cancer-drugs>.

330. See *supra* notes 6, 177 and accompanying text (discussing specific cases of companies denying pediatric patient expanded access requests).

331. Tirrell, *supra* note 5; see *infra* Appendix.

332. *Allergan Pre-Approval Access Program*, *supra* note 125.

333. Tirrell, *supra* note 5; see *infra* Appendix.

adults,³³⁴ the justification that pediatric data is needed can be difficult to reconcile, especially given how few industry-sponsored pediatric trials there are.³³⁵ There is also evidence, at least with oncology drugs, that “[d]rug exposure in adolescents (age 12 to 18 years) and adults is similar, supporting the enrollment of adolescents in adult trials that involve the same disease and/or therapeutic target.”³³⁶ Therefore, companies with explicit pediatric expanded access criteria should reconsider whether it would be appropriate to loosen or eliminate this requirement for adolescents.

Qualifying Drugs. A manufacturer’s determination of when an investigational drug has sufficient data can sometimes differ from that of the treating physician and patient.³³⁷ Companies should consider publishing a list of drugs (updated on a regular basis) for which they will consider expanded access requests. This is a practice already adopted by some companies.³³⁸

External Review Committee. Companies should consider adopting Janssen’s approach of utilizing an outside review board in collaboration with its internal decisionmakers.³³⁹ Janssen piloted the New York University program, Compassionate Use Advisory Committee (“CompAC”), in 2015 with one investigational drug.³⁴⁰ Janssen has since rolled out the program to other disease areas.³⁴¹ The CompAC approach is as follows: (1) the treating physician submits expanded access request to Janssen; (2) company physicians and medical personnel review requests to determine whether any are medically inappropriate or eligible for clinical trials and expanded-access programs; (3) CompAC reviews the other requests providing an “independent recommendation” to Janssen; (4) the treating physician can

334. See Bourgeois et al., *supra* note 300.

335. *Id.* at 287.

336. Kim et al., *supra* note 49, at 3740.

337. Reddy, *supra* note 6.

338. *Investigational Drugs Available*, BRISTOL-MYERS SQUIBB, <https://www.bms.com/healthcare-providers/early-patient-access-to-investigational-medicine/investigational-drugs-available.html> (last visited Feb. 11, 2019); *Investigational Medicines for Compassionate Use Requests*, JANSSEN, <https://www.janssen.com/compassionate-use-pre-approval-access/investigational-medicines-for-compassionate-use-requests> (last updated Feb. 11, 2019).

339. *Janssen Policy*, *supra* note 277, at 361.

340. *CompAC: The Compassionate Use Advisory Committees*, N.Y.U. LANGONE HEALTH, <https://med.nyu.edu/pophealth/divisions/medical-ethics/compassionate-use-advisory-committee> (last visited Feb. 11, 2019) (describing the role of CompAC and the composition of the committee).

341. *Id.*

appeal a CompAC decision.³⁴² An independent review committee could reduce public misconceptions that companies' default response to an expanded access request is "no," especially given media's widespread coverage of those denials. Likewise, the committee may be helpful when evaluating cases involving pediatric patients or patients with exceptional safety risks. The built-in appeal process could reduce the public appeals initiated through social media. Furthermore, just as there are independent IRBs available for physicians whose institutions do not have internal committees,³⁴³ smaller companies with limited financial and personnel resources to devote to expanded access requests could consider partnering with other companies to develop an independent, external review committee to aid in assessing expanded access requests.

Cost-Recovery Policy. Companies need to adopt more transparent cost recovery guidelines even if their policies mandate not charging patients because of concerns that doing so could impact a "higher sale price"³⁴⁴ in the future or because insurance will not reimburse even direct costs.³⁴⁵ A few companies do post cost-recovery policies,³⁴⁶ but of the companies surveyed in this Note, none had this information available. The rising cost of healthcare in the United States is on the public's mind; it was the top issue in the 2018 mid-term elections.³⁴⁷ Furthermore, HHS recently announced "a proposed rule to require pharma to include list prices in direct-to-consumer ads" for approved drugs.³⁴⁸ This increasing scrutiny makes it even more

342. Caplan & Ray, *supra* note 131, at 979–80. This approach emphasizes fairness, attempting to ensure that requests are not granted to only those individuals who are social media savvy or well-connected. *Id.*

343. *About the Expanded Access Navigator*, *supra* note 215 (providing a "roadmap" for IRBs).

344. Alexander Gaffney, *Regulatory Explainer: FDA's Expanded Access (Compassionate Use) Program*, REG. FOCUS (Feb. 4, 2015), [https://www.raps.org/regulatory-focus%E2%84%A2/news-articles/2014/2/regulatory-explainer-fda-s-expanded-access-\(compassionate-use\)-program](https://www.raps.org/regulatory-focus%E2%84%A2/news-articles/2014/2/regulatory-explainer-fda-s-expanded-access-(compassionate-use)-program).

345. Letter from Marc B. Wilenzick, Pfizer Senior Counsel on behalf of Pfizer, Comment Letter on Proposed Rule Charging for Investigational Drugs 7 (Feb. 14, 2007), https://www.pfizer.com/sites/default/files/research/research_clinical_trials/Charging_for_Investigational_Drugs.pdf.

346. Jung et al., *supra* note 113, at 1018.

While the 21st Century Cures Act did not require manufacturers to include pricing information in their expanded access policies, seven addressed financial aspects of accessing investigational medicines. Five indicated that they provide investigational medicines to patients at no cost, and among these five, one also stated that the manufacturer may reimburse fees and expenses associated with the use of the drug for expanded access. The other two manufacturers described pricing as depending on insurance and other factors.

Id.

347. Ashley Kirzinger et al., *KFF Election Tracking Poll: Health Care in the 2018 Midterms*, KAISER FAMILY FOUND. (Oct. 18, 2018), <https://www.kff.org/health-reform/poll-finding/kff-election-tracking-poll-health-care-in-the-2018-midterms>.

348. Dan Diamond, *Drug Prices in Ads Are Coming—If HHS Gets Its Way*, POLITICO PULSE (Oct. 15, 2018, 10:00 AM), <https://www.politico.com/newsletters/politico-pulse/2018/10/15/drug-prices-in->

important for companies to publish clear cost-recovery policies for their expanded access programs.

Expanded Access Navigator. Companies should submit a Navigator Directory listing when they initiate a phase II or phase III study for an investigational drug. Companies' websites should also refer physicians and patients to the Expanded Access Navigator. Neither of these recommendations are currently required by the Cures Act.

b. Companies Need to Improve Access to Clinical Trials

Companies will often cite concern about maintaining adequate supply of an investigational drug for their clinical trials as a factor in their expanded access criteria. This is arguably a genuine concern given that a manufacturer will develop only enough supply for its clinical trials, but not more until it receives FDA approval.³⁴⁹ At the same time, however, companies often struggle to fully enroll their clinical trials.³⁵⁰ Trials often have strict inclusion and exclusion criteria, which can affect some patient populations more so than others.³⁵¹ Furthermore, clinical trials are often conducted in regions with large academic institutions and major medical centers,³⁵² which can limit certain patients' ability to participate and negatively affect some patient populations disproportionately from others.³⁵³

Inclusion and Exclusion Criteria. As discussed in Section II.B, companies generally prefer standardized study groups, but companies should reconsider eligibility criteria because “[b]roadening the eligibility criteria for

ads-are-coming-if-hhs-gets-its-way-373552. PhRMA has proposed its own plan in which “[a]ll TV ads that mention a medicine by name should direct patients to information about cost, ‘such as a company-developed website.’” *Feds, Big Pharma Issue Competing Price Transparency Plans*, MODERN HEALTHCARE (Oct. 20, 2018), <https://www.modernhealthcare.com/article/20181020/NEWS/181019859>.

349. See *infra* Appendix (adequate supply); Fraser, *supra* note 185 (“[Genentech] was already in the process of trying to dramatically ramp up its production of Herceptin, encountering roadblocks in machinery, engineering and chemistry along the way.”).

350. See *supra* notes 46–47 and accompanying text.

351. Kim et al., *supra* note 49, at 3740 (studies often exclude pediatric patients); Chen & Wong, *supra* note 329 (noting criteria often excludes patients with more than chronic condition, which can disproportionately affect African Americans); Judith Graham, *Seniors Miss out on Clinical Trials*, KAISER HEALTH NEWS (June 29, 2017), <https://khn.org/news/seniors-miss-out-on-clinical-trials/> (“[O]nly 40 percent of patients participating in cancer clinical trials were 65 and older” despite “more than 60 percent of cancer patients [being] older adults.”).

352. See PHARMA. RESEARCH & MFR. OF AM., BIOPHARMACEUTICAL INDUSTRY-SPONSORED CLINICAL TRIALS: IMPACT ON STATE ECONOMIES, at I (2015) (“The five states with the highest number of active clinical trial sites were California (3,111), Florida (2,571), Texas (2,799), New York (2,476), and Pennsylvania (1,972).”).

353. See *supra* note 329 and accompanying text.

clinical trials [would] provide the opportunity for more people to participate in research studies,” and “it [would] make the trial results more reflective of the people that will ultimately use the drug.”³⁵⁴ While specific to oncology, the American Society of Clinical Oncology (“ASCO”) and Friends of Cancer Research, identified five common exclusion factors (brain metastases, age, HIV infection, organ dysfunction, and prior or concurrent cancer diagnoses) and proposed recommended clinical trial protocols that would facilitate inclusion of patients with these factors in clinical trials.³⁵⁵ Their recommendations address both early-phase trial design (for example, proposing study groups limited to “specific patient population” to “inform the decision as to whether and how to include (or not) the patient population in later phase trials”) and later-phase trials (for example, “expand[ing] eligibility criteria to include a specific patient population,” but “restricting primary analysis to defined patient population”).³⁵⁶ A *JAMA Oncology* study, published in January 2019, estimates that at least “6,317 additional patients would be allowed to join trials each year” if these recommendations were adopted.³⁵⁷ Companies should work with the FDA, ASCO, and Friends of Cancer Research to determine how to incorporate these recommendations into their existing clinical trials, not only to ease patient access to the clinical trial process, but also to ensure clinical trial data reflects real-world patients.

Diversity in Clinical Trials. Some companies have initiatives aimed at improving diversity in participation,³⁵⁸ but others are more resistive.³⁵⁹ With most clinical trial participants white, more companies need to adopt

354. *ASCO and Friends*, *supra* note 47; *see also* Bateman-House & Robinson, *supra* note 231, at 322 (proposing Congress should explore measures that would encourage greater potential access to investigational drugs through clinical research).

355. Kim et al., *supra* note 49.

356. *Id.* at 3742.

357. Press Release, SWOG Cancer Research Network, Cancer Comorbidities Reduce Trial Enrollment (Jan. 10, 2019), <https://www.swog.org/news-events/news/2019/01/10/cancer-comorbidities-reduce-trial-enrollment>. The lead author of the *JAMA Oncology* study Joseph Unger explained,

[i]f you look at the numbers, they tell you that the ASCO/Friends/FDA guidelines were well focused, as they alone would account for more than half of the potential gains from updating eligibility criteria in trials. . . . This would have the short-term impact of helping patients by giving them access to new treatments and have a long-term impact on the discovery of new treatments, speeding the time it takes to run trials and get new treatments to the public.

Id.

358. *Compare Diversity in Lilly-Sponsored Clinical Trials in North America*, ELI LILLY, <https://www.lilly.com/diversity-in-lilly-sponsored-clinical-trials-in-north-america> (“[E]very study conducted with more than 25 clinical trial sites must select at least two sites meeting Lilly’s diversity criteria.”) (last visited Feb. 11, 2019), *with Advancing Inclusive Research*, GENENTECH, <https://www.gene.com/patients/advancing-inclusive-research> (assessing its site selection process and developing new “inclusive research” standards) (last visited Feb. 11, 2019).

359. Chen & Wong, *supra* note 329 (noting biotech firm CEO citing concerns that regulation aimed at improving diversity would delay development efforts).

measures addressing diversity in clinical trials that go beyond just patient education. In 2015, the FDA approved a drug for the treatment of multiple myeloma, a blood cancer that disproportionately affects blacks, “yet of the 722 participants [enrolled in its phase III study] only 13—or 1.8 percent—were black.”³⁶⁰ Efforts to improve potential pre-approval access through the clinical trial process need to address this underrepresentation of minorities. Companies, rather than resisting those efforts, should work with the FDA, patient groups, and professional organizations to develop legislation that would incentivize widespread participation. For example, companies could propose legislation, modeled off of state laws encouraging diversity and inclusion in certain industries,³⁶¹ that would give tax credits and clinical trial grants to companies³⁶²—utilizing the FDA’s various expedited approval pathways—that submit diversity proposals detailing how they plan to ensure clinical trial enrollment is representative of a disease’s U.S. incidence rates by race, age, and gender even if specific risk factors don’t require it and then meet certain minimum thresholds based on those incidence rates.³⁶³

CONCLUSION

The Right to Try Act passed with great fanfare and proclamations of hope by President Trump and others. Yet industry—as a whole—is unlikely to adopt this parallel pathway.³⁶⁴ This will likely further increase frustration and confusion amongst the public regarding pre-approval access,³⁶⁵

360. *See id.*

361. Chreasea Dickerson, *Incentives Watch: Illinois Diversity and Inclusion Tax Credit Initiatives*, BLOOMBERG BNA: SALT TALK BLOG (Sept. 12, 2017), <https://www.bna.com/incentives-watch-illinois-b57982087723> (discussing state efforts to include diversity and inclusion provisions in film production tax credits). The adoption of diversity inclusion plans could require companies to reevaluate their inclusion and exclusion criteria.

362. The FDA already gives tax credits, trial grants, and exemptions from the Prescription Drug User Fee Act to incentivize development of drugs for rare diseases. *Designating an Orphan Drug Product: Drugs and Biological Products*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/forindustry/developingproductsforrareconditions/howtoapplyfororphanproductdesignation/default.htm> (last updated July 26, 2018). For more information about the Prescription Drug User Fee Act, see *Prescription Drug User Fee Amendments*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee> (last updated Feb. 8, 2019).

363. *See* Chen & Wong, *supra* note 329.

364. *But see* Michelle Cortez, *Brain Cancer Patient Is First to Get Untested Treatment Under Trump-Backed Law*, BLOOMBERG (Jan. 10, 2019, 6:16 AM), <https://www.bloomberg.com/news/articles/2019-01-10/brain-cancer-patient-gets-unproven-therapy-first-under-new-law> (reporting that a European-based biotechnology company is “the first publicly known” company to provide an investigational drug through the Right to Try Act).

365. *E.g.*, Munz, *supra* note 191 (discussing a patient moving to a state with a right-to-try law, but who is unable to secure access); Weintraub, *supra* note 276 (noting that one relative’s calls seeking right to try for a family member escalated to threats).

especially since the Right to Try Act was marketed as a “right to try” when in reality it is simply a “right to ask”—a right the public has had all along through the expanded access program.³⁶⁶ With this added risk, companies should and need to move beyond the status quo, adopting measures aimed at increasing transparency and awareness of their expanded access programs and pursuing initiatives aimed at improving access to clinical trials.

This proposal is not without its limitations. First, it relies on companies choosing to adopt these changes. Companies already do not fully comply the Cures Act expanded access requirements. These proposed changes may be more broadly implemented if BIO and PhRMA revise their existing expanded access guidelines to incorporate some of these proposals as many companies now model their guidelines off of the either BIO or PhRMA’s guidelines. Another option is for Congress to amend the Cures Act to not only to give the FDA power to assess civil monetary penalties when a company fails to comply with the Cures Act expanded access requirements, but also to further require companies to submit an annual summary of their expanded access programs to the FDA, thereby extending the Right to Try Act’s reporting requirement to the expanded access program. These amendments will not, however, have any weight unless the FDA has enforcement capability.³⁶⁷ Any civil money penalties collected for non-compliance could be used to support “Project Facilitate” and other expanded access awareness initiatives such as the Expanded Access Navigator, FDA-sponsored webinars, or targeted educational programming in regions underutilizing expanded access.

Second, changes aimed at increasing manufacturer transparency and clarifying companies’ existing policies admittedly do not directly improve manufacturer participation. That said, increased manufacturer transparency may reveal greater manufacturer participation than one would anticipate based on the media’s coverage of companies denying expanded access requests. Furthermore, clarification of companies’ existing policies may ease physicians’ and patients’ overall frustration with the expanded access program and encourage more widespread utilization of the program.

Third, the second part of this proposal relies on companies to adopt

366. Rita Rubin, *Experts Critical of America’s Right-to-Try Drug Laws*, LANCET (Oct. 3, 2015), [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(15\)00393-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(15)00393-1/fulltext).

367. The FDA can currently assess civil monetary penalties against companies that fail to submit registration or clinical trial results to ClinicalTrials.gov. 42 U.S.C. § 282(j) (2018). Congress should also amend the Cures Act to give the agency a similar enforcement mechanism when a company fails to publish its expanded access guidelines and related cost recovery policies. *Id.*; see also Bateman-House, *Examining Patient Access*, *supra* note 210.

clinical trial measures that improve overall access through diversity and inclusion initiatives and less-restrictive eligibility criteria or to advocate for legislation that would help facilitate these efforts. With some companies potentially resistive due to ongoing concerns that increased diversity or less-restrictive eligibility criteria could delay drug development or cost millions of dollars, it may be difficult to secure wide-scale adoption without Congressional action aimed at not only improving patient access to investigational drugs through the clinical trial process, but also ensuring that clinical trials produce the data necessary to allow the FDA “to separate the relative handful of discoveries which prove to be true advances in therapy from a legion of false leads and unverifiable clinical impressions,”³⁶⁸ and also to “maximize generalizability of results” to patients in the real world.³⁶⁹

368. JUNOD, *supra* note 15 (quoting William Thomas Beaver, who drafted the controlled clinical trial regulation promulgated after the enactment of the Kefauver--Harris Amendment). The adoption of diversity and inclusion plans would likely require companies to reevaluate their inclusion and exclusion criteria. See *ASCO and Friends*, *supra* note 47 (“Broadening the eligibility criteria for clinical trials will provide the opportunity for more people to participate in research studies. Not only will this improve access, it will make the trial results more reflective of the people that will ultimately use the drug.”).

369. Kim et al., *supra* note 49, at 3737.

APPENDIX

APPENDIX TABLE. Companies' Expanded Access Eligibility Criteria

	<i>Decisionmaker</i>	<i>Serious / Immediately Life- Threatening Disease</i>	<i>Active Clinical Development</i>
Pfizer ^a	Medical professionals familiar with investigational drug's data	Yes <i>and</i> patient must have received standard treatment without success and no other treatment is available	Yes
Novartis ^b	Medical team	Yes <i>and</i> patient must have received standard treatment without success and no other treatment is available	Yes
Genentech, a member of the Roche Group ^c	Clinical team	Yes <i>and</i> patient must have received standard treatment without success and no other treatment is available	Yes
Sanofi ^d	...	Yes	Yes
Merck ^e	...	Yes	Yes <i>and</i> with good grasp of indication <i>and</i> a plan to file marketing application

APPENDIX

APPENDIX TABLE. Companies' Expanded Access Eligibility Criteria

<i>Ineligible for Clinical Trial</i>	<i>Potential Benefit Outweighs Potential Risk</i>	<i>Use Cannot Interfere with Clinical Development</i>	<i>Other Criteria</i>
Yes <i>and</i> includes geographic limitation to participation	Yes	Yes <i>and</i> adequate supply a consideration	Other relevant criteria established by company's medical professionals working on development
Yes	Yes	Yes	Other relevant criteria established by company's medical professionals working on development
Yes <i>but</i> excludes geographic limitation to participation	Yes <i>and</i> requires sufficient clinical data to determine appropriate drug dose	Yes <i>and</i> adequate supply a consideration	...
Yes	Yes	Yes <i>and</i> adequate supply a consideration	...
Yes	Yes	Yes <i>and</i> adequate supply a consideration	...

	<i>Decisionmaker</i>	<i>Serious / Immediately Life- Threatening Disease</i>	<i>Active Clinical Development</i>
Janssen ^f	Clinical personnel / physicians; Compassionate Use Advisory Committee ("CompAC") also evaluates and provides suggestion	Yes <i>and</i> patient must have received standard treatment without success and no other treatment is available	Yes
GlaxoSmith-Kline ^g	...	Yes <i>and</i> patient must have no other treatment available	Yes <i>and</i> plan to file marketing application and commercialize drug
Gilead Sciences ^h	Medical professionals familiar with investigational drug's data	Yes <i>and</i> patient must have no other treatment available	Yes
Abbvie ⁱ	Medical team within research and development function	Yes <i>and</i> patient must have no other treatment available	Yes
Amgen ^j	Medical experts	Yes <i>and</i> patient must have no other treatment available	Yes <i>and</i> active development in the indication

<i>Ineligible for Clinical Trial</i>	<i>Potential Benefit Outweighs Potential Risk</i>	<i>Use Cannot Interfere with Clinical Development</i>	<i>Other Criteria</i>
Yes	Yes	Yes <i>and</i> adequate supply a consideration	...
...	Yes	Yes	...
Yes	Yes
Yes	Yes	Yes	...
Yes	Yes	Yes <i>and</i> adequate supply a consideration	...

	<i>Decisionmaker</i>	<i>Serious / Immediately Life- Threatening Disease</i>	<i>Active Clinical Development</i>
AstraZeneca ^k	Medical team	Yes <i>and</i> patient must have no other treatment available <i>and</i> the ability to regularly travel to treating site for monitoring and follow up	Yes <i>and</i> reasonable likelihood of filing marketing application
Bristol-Myers Squibb ^l	...	Yes <i>and</i> patient must have no other treatment available	Yes <i>and</i> plans to file marketing application and commercialize
Teva Pharma ^m	Cross-functional team evaluates and gives suggestion; Chief Medical Officer and Head of Global Medical Affairs approves	Yes <i>and</i> patient must have no other treatment available	Yes <i>and</i> either approval in at least one country <i>or</i> if not approved, active pursuit of approval with due diligence in at least one country (unless indicated for rare disease)
Bayer ⁿ	...	Yes <i>and</i> patient must have received standard treatment without success and no other treatment is available	Yes
Eli Lilly ^o	...	Yes	Yes

<i>Ineligible for Clinical Trial</i>	<i>Potential Benefit Outweighs Potential Risk</i>	<i>Use Cannot Interfere with Clinical Development</i>	<i>Other Criteria</i>
Yes <i>and</i> includes medical or other reasons	Yes	Yes <i>and</i> adequate supply a consideration	...
Yes	Yes	Yes <i>and</i> adequate supply a consideration	...
Yes <i>and</i> includes geographic limitation to participation	Yes	Yes <i>and</i> adequate supply a consideration	...
Yes <i>and</i> includes geographic limitation to participation	Yes
Yes	Yes	Yes	...

	<i>Decisionmaker</i>	<i>Serious / Immediately Life- Threatening Disease</i>	<i>Active Clinical Development</i>
Novo Nordisk ^p	...	Yes <i>and</i> patient must have received standard treatment without success and no other treatment is available	Yes
Allergan ^q	Medical experts	Yes <i>and</i> patient must have received approved treatment either without success or not well tolerated and no other treatment is available	Yes <i>and</i> active development in the indication
Takeda ^r	...	Yes	Yes
Celgene ^s	...	Yes <i>and</i> patient must have no other treatment available.	Yes
Astellas ^t	Medical and clinical teams	Yes <i>and</i> patient must have no other treatment available	Yes

<i>Ineligible for Clinical Trial</i>	<i>Potential Benefit Outweighs Potential Risk</i>	<i>Use Cannot Interfere with Clinical Development</i>	<i>Other Criteria</i>
Yes	Yes
	Yes <i>and</i> must have sufficient clinical data to determine appropriate drug dose <i>For pediatric requests</i> , must be sufficient clinical data to determine appropriate drug dose in pediatric patients	Yes	...
Yes	Yes
Yes	Yes
Yes	Yes <i>and</i> must have sufficient clinical data to determine the appropriate drug dose	Yes	...

-
- a. *Pfizer Policy*, *supra* note 100; *Pfizer's Position on Preapproval Access to Investigational Drugs*, PFIZER (May 2018), https://www.pfizer.com/files/research/Policy_paper_Preapproval_Access_to_Investigational_Drugs_May2018.pdf.
- b. *Managed Access Programs*, NOVARTIS, <https://www.novartis.com/our-focus/healthcare-professionals/managed-access-programs> (last visited Feb. 11, 2019).
- c. *Genentech Policy*, *supra* note 100.
- d. *Compassionate Use of Sanofi Investigational Products*, SANOFI, <https://www.sanofi.com/en/science-and-innovation/clinical-trials-and-results/compassionate-use-expanded-access> (last visited Feb. 11, 2019).
- e. *Access to Investigational Medicines*, MERCK, <https://www.merck.com/about/views-and-positions/access-to-medicines/home.html> (last visited Feb. 11, 2019).
- f. *Janssen Policy*, *supra* note 277.
- g. GLAXOSMITHKLINE, GSK PUBLIC POLICY POSITIONS: COMPASSIONATE USE 1–2 (2017), <https://www.gsk.com/media/3368/compassionate-use.pdf>.
- h. *Expanded Access: Individual Access to Investigational Medicines Intended to Treat Serious Diseases*, GILEAD, <http://www.gilead.com/research/expanded-access> (last visited Feb. 11, 2019).
- i. *Pre-Approval Access to Investigational Drugs Policy*, ABBVIE, <https://www.abbvie.com/our-company/access-to-investigational-drugs-policy.html> (last visited Feb. 11, 2019).
- j. *Access to Investigational Medicines*, AMGEN, <https://www.amgen.com/responsibility/access-to-medicine/access-to-investigational-medicines> (last visited Feb. 11, 2019).
- k. *Policy on Early Access to Investigational Medicines*, ASTRAZENECA, <https://www.astrazeneca.com/content/dam/az/PDF/2017/AstraZeneca%20Policy%20on%20Early%20Access%20to%20Investigational%20Medicines%20September%202017.pdf> (last visited Feb. 11, 2019).
- l. *Early Patient Access to Investigational Medicine*, BRISTOL-MYERS SQUIBB, <https://www.bms.com/healthcare-providers/early-patient-access-to-investigational-medicine.html> (last visited Feb. 11, 2019).
- m. TEVA PHARM., *supra* note 121, at 1–8.
- n. *How to Request Access to Investigational Medicines*, BAYER, <http://pharma.bayer.com/en/commitment-responsibility/ethics-and-transparency/ethics-in-r-and-d/access-to-investigational-medicinal-products> (last visited Feb. 11, 2019).
- o. *Expanded Access*, LILLY, <https://www.lilly.com/discovery/clinical-trials/expanded-access> (last visited Feb. 11, 2019).
- p. *Expanded Access*, NOVO NORDISK, <http://www.novonordisk-us.com/whoweare/about-novonordisk/expanded-access.html> (last visited Feb. 11, 2019).
- q. *Allergan Pre-Approval Access Program*, *supra* note 125.
- r. *Expanded Access to Investigational Drugs*, TAKEDA ONCOLOGY, <http://www.takedaoncology.com/medicines/access-to-investigational-drugs> (last visited Feb. 11, 2019).
- s. *Clinical Trials*, CELGENE, <https://www.celgene.com/research-development/clinical-trials> (last visited Feb. 11, 2019).
- t. *Astellas Position*, *supra* note 124.