REGENERATIVE MEDICINE AND THE RIGHT TO TRY

Christine Coughlin, Nancy M.P. King, and Melissa McKinney†

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† © 2018 Christine Nero Coughlin, Professor of Legal Writing, Wake Forest University School of Law, Wake Forest University Center for Bioethics, Health & Society; Nancy M.P. King, Professor, Department of Social Sciences and Health Policy, Wake Forest School of Medicine, & Co-Director of the Wake Forest University Center for Bioethics, Health, and Society; Melissa McKinney, Wake Forest University School of Law, J.D. Expected 2020. The authors would like to acknowledge and thank Dr. Mark Furth, who participated in the symposium panel from which the idea for this essay originated. We would also like to acknowledge and thank Josh Revilla, Wake Forest School of Law, for his excellent research assistance.
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I. INTRODUCTION

Charlie Gard appeared healthy at the time of his birth on August 4, 2016.¹ Two months later, he was hospitalized in intensive care at Great Ormond Street Hospital (GOSH) in London, where he was diagnosed with infantile onset encephalomyopathic mitochondrial DNA depletion syndrome (MDDS), which was caused by a mutation in his RRM2B gene.² MDDS is typically diagnosed during a child’s infancy, and Charlie’s condition worsened rapidly.³ He became paralyzed and dependent on respiratory support and suffered increasing damage to his brain.⁴ Charlie’s mother began to do research online about his condition, and soon his parents sought to take him to the United States to pursue an experimental nucleoside treatment, which had apparently produced some benefit in MDDS infants with a mutation in a different gene—the TK2 gene.⁵ Through a GoFundMe campaign, Charlie’s parents raised sufficient funds to travel to the United States.⁶

Charlie and his parents were granted permanent United States residency status by Congress in July 2017, so he could be brought to the United States for the experimental treatment. The offering physician-researcher claimed the experimental treatment had a ten percent chance of improving Charlie’s condition.⁷ However, a protracted legal battle in the United Kingdom and the European Court of Human Rights resulted in a determination that palliative care and withdrawal of life-prolonging treatment were in Charlie’s best interests.⁸ His parents

³ See id.; see also Ayman W. El-Hattab & Fernando Scaglia, Mitochondrial DNA Depletion Syndromes: Review and Updates of Genetic Basis, Manifestations, and Therapeutic Options, 10 J. AM. SOC’Y EXPERIMENTAL NEUROTHERAPEUTICS 186, 189 (2013).
⁵ Hammond-Browning, supra note 2, at 463; see also Sharon Begley, Trump Tweeted About a Dying Boy. Here’s What You Need to Know About His Rare Disease, STAT NEWS (July 3, 2017), https://www.statnews.com/2017/07/03/trump-tweet-dying-boy/.

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agreed on July 24, 2017, and Charlie died four days later.9

Rapid advances in biotechnology research, the widespread proliferation of optimistic scientific and medical information, and the demand for access to investigational treatments via media and social media10 have combined to create a perfect storm of data, advocacy, and speculation about pharmacological and biological remedies for not only rare genetic disorders like Charlie’s, but also for common complex disorders with multiple contributory factors.11 Regenerative medicine12 research has become one of the focal points of growing public belief that breakthrough treatments are just around the corner but are being withheld from desperately ill patients by an over-regulatory bureaucracy.13 At the same time, novel pharmaceutical and

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9 Hammond-Browning, supra note 2, at 467. The case of Charlie Gard raises a large number of questions about science, medicine, and the history and sociocultural role of medical research and its regulation, and about the ethical issues on which medical and health policy decisions are based. There is a considerable literature discussing Charlie’s story from a range of perspectives, only some of which we address herein.

10 See, e.g., Tim K. Mackey & Virginia Schoenfeld, Going Social to Access Experimental and Potentially Life-Saving Treatment: An Assessment of the Policy and Online Patient Advocacy Environment for Expanded Access, BMC Med., Feb. 2016, at 1, 1–5 (explaining that social media has altered the way in which health information is gathered and shared, especially through patients’ use of online petitions and campaigns attempting to gain access to unproven medical treatments they believe may save their lives).


12 According to the National Institutes of Health, “Regenerative medicine is the process of creating living, functional tissues to repair or replace tissue or organ function lost due to age, disease, damage, or congenital defects. This field holds the promise of regenerating damaged tissues and organs in the body by stimulating previously irreparable organs to heal themselves. Regenerative medicine also empowers scientists to grow tissues and organs in the laboratory and safely implant them when the body cannot heal itself.” Regenerative Medicine, NAT’L INST. HEALTH, https://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=62 (last visited Aug. 22, 2018). See, e.g., Nancy M.P. King & Jacob Perrin, Ethical Issues in Stem Cell Research and Therapy, STEM CELL RES. & THERAPY, July, 2014, at 1, 2–6 [hereinafter King & Perrin]; see also discussion infra Section V.

biotechnological treatments are being rapidly approved and made available, albeit at breathtaking cost.\textsuperscript{14} Are we in a new era that holds the potential to defeat death, especially for the innocent, vulnerable Charlies of the world? Or have we moved so far toward relaxing protective regulations that we have begun to enable fraud, exploitation, and injustice toward the sickest among us?

Charlie Gard’s parents sought access to an intervention that had barely been studied and apparently had little likelihood of benefiting him, but they nonetheless viewed it as worth trying.\textsuperscript{15} Under what circumstances should as-yet-unproven potential treatments be made available, especially when the intervention sought falls into the category of regenerative medicine? Has death—always profoundly difficult to face, especially when it seems untimely—become wholly unacceptable in light of science?

While the system of medical research, diagnosis, and treatment was originally built on drugs and surgery, medicine became substantially more complicated in the late 20th century by the introduction of genetic- and biologically-based diagnoses and treatments.\textsuperscript{16} By the time Charlie Gard was born, the idea of “precision medicine”\textsuperscript{17}—which is focused on targeted diagnoses and precisely tailored treatments based on individual patients’ genetic profiles\textsuperscript{18}—had attracted much media attention, but both popular understanding and medical progress have lagged behind the public’s imagination.\textsuperscript{19} Although Charlie’s parents believed that the experimental genetic treatment they sought could help him, it was designed to address a different genetic mutation; thus, any effect on Charlie was highly unlikely.\textsuperscript{20} Similarly, most regenerative...
medicine interventions—virtually all of which are still experimental—are highly individualized. How this “one-off” quality is likely to affect both cost and access is not yet appreciated by patients, families, and the public.

This essay therefore addresses the promise and the pitfalls of modern medical progress by examining the “right to try” movement and its historical and conceptual underpinnings, and then by considering whether the right to try has any reasonable application to regenerative medicine interventions. Part I of the essay provides a brief historical overview of the FDA’s regulation of medical products—focusing on drugs and biologics—as an attempt to balance protection with the imperative of ensuring reasonable access to those products for patients. This part further examines a range of initiatives, from the FDA and other legislative and regulatory bodies, that have speeded product approval and expanded product availability, thus potentially altering the balance between protection and access.

Part II then explores the history of the right to try movement, and the current status of right to try legislation, including consideration of how the sympathetic patient narratives spread on social and public media have garnered widespread political support. Part III critiques the right to try legislation by examining the attendant pressures and potential burdens on manufacturers, consumers, physicians, and society with respect to access, costs, safety, and health care disparities. Part IV then returns to regenerative medicine, further considering its relationship to the right to try movement, the individual focus of precision medicine, and our desire to rescue so-called “identified lives.” This part also considers potential conflicts that may arise between the right to try legislation and the Patient Protection and Affordable Care Act (“Affordable Care Act”), the 21st Century Cures Act, and the overall goal of protecting the public’s health.

This essay concludes with reflections on the continuing challenges of balancing protection and access in human research, the future of the right to try, and future policy directions.

23 See infra Part I.
24 Id.
25 See infra Part II.
26 See infra Part III.
27 See infra Part IV.
28 See infra Part VI.

continued . . .
II. THE FOOD AND DRUG ADMINISTRATION REGULATION

A. Historical Background

The Food and Drug Administration (FDA), charged with the enforcement of the regulation of the drug production process, oversees the protection of the public from unsafe or mislabeled goods. The FDA derives its authority from various federal statutes passed throughout the twentieth century.

The Pure Food and Drug Act of 1906, which was signed into law by President Theodore Roosevelt to prevent the movement of adulterated food and poisonous patent medications, created the administrative background for what ultimately became the FDA. Congress then enacted the Food, Drug, and Cosmetic Act of 1938 following public outrage when a lethal batch of sulfanilamide, an early antibiotic, caused the deaths of more than 100 children. This marked the beginning of the modern era of drug regulation.

In 1962, motivated by revelations that Thalidomide, a drug marketed to alleviate morning sickness in pregnant women, resulted in severe birth defects, Congress passed the Kefauver-Harris

29 See Caitlyn Martin, Questioning the “Right” in State Right to Try Laws: Assessing the Legality and Effectiveness of These Laws, 77 OHIO ST. L.J. 159, 165 (2016).
33 See Martin, supra note 29, at 165; see also Rebecca Eisenberg, The Role of the FDA in Innovation Policy, 13 MICH. TELECOMM. & TECH. L. REV. 345, 345 n.1 (2007) (citing PHILIP J. HILTS, PROTECTING AMERICA’S HEALTH: THE FDA, BUSINESS, AND ONE HUNDRED YEARS OF REGULATION 89, 93 (2003)).
34 See Chanapa Tantibanchachai, The Embryo Project Encyclopedia: Recording and Contextualizing the Science of Embryos, Development and Reproduction (Aug. 1, 2014), https://embryo.asu.edu/pages/us-regulatory-response-thalidomide-1950-2000; see also Martin, supra note 29, at 166 n.42. Dr. Frances Oldham Kelsey, a former family physician who worked for the FDA, worked to prevent Thalidomide from becoming licensed in the United States. She is considered by many to be an “American heroine for her role in the thalidomide case, celebrated not only for her vigilance, which spared the United States from widespread birth deformities, but also continued...
Amendments, which shifted the burden to drug manufacturers to prove that their drugs were safe for public consumption. One important consequence of these amendments was the development of a more complex, lengthy, and regulated clinical trial process, with the goal of protecting public health and patients from unknown and unintended consequences by making drugs safer, and ultimately requiring more proof of effectiveness.

At the same time, however, the FDA oversight and new drug approval processes work hand-in-hand with the patent system to encourage research and development of new drugs and therapies. The market exclusivity provided by FDA approval and patent protection helps encourage the development and sale of new medical products, which improves patients’ access by making more treatments available. Thus, the system of research and development seeks to maintain an appropriate balance between two potentially competing goals: protecting the public from unsafe treatments and increasing the public’s access to treatments. The tension between the goals of protection and access has continued to increase as medical technology advances and the economic pressures on all system stakeholders grow more intense and complex.


37 See What We Do, FDA, https://www.fda.gov/AboutFDA/WhatWeDo/default.htm (last updated Mar. 28, 2018).

38 Id.; See generally Eisenberg, supra note 33, at 347–84 (examining the relationship between drug development and regulation and patents).

39 See Eisenberg, supra note 33, at 361.

40 See Eisenberg, supra note 33, at 364.

41 The complexity and expense of the FDA’s regulatory scheme has created loopholes that manufacturers can exploit to reduce the costs to them of establishing a foothold in the medical market. Many examples exist, such as orphan drug designations, breakthrough therapy designations, and narrowly focused new drug applications to gain approval for drugs and biologies for narrow applications, with the expectation that off-label uses will expand markets without the requirements of

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B. The Process and Phases of Clinical Trials

An important component of the FDA’s ability to advance its goals of protection and access by improving both safety and efficacy is the generation of data about investigational drugs and biologics through the highly regulated clinical trial process. This data includes the effects of the investigational drugs or biologics, both positive and negative, the mechanisms by which they function in the body, and their potential interactions with other medications.42 By way of brief background, after developing an investigational drug or biologic in the laboratory, manufacturers must submit an Investigational New Drug (IND) application, containing initial “preclinical” research to show that the drug is ready for human trials.43 The FDA then conducts a preliminary review to determine that human research subjects will not incur unreasonable risks.44 After the IND is approved, , an institutional review board (IRB) also reviews the application.45 Next, the drug or biologic undergoes clinical testing, a stepwise phased process that may cost a manufacturer over a billion dollars and take more than a decade to complete.46

The traditional clinical trial phases for drug development are usually numbered 1–3.47 In Phase 1, a small group of 20 to 80 healthy participants receives the drug, allowing researchers to experiment with dosage and study side effects. 48 During Phase 2, the drug is administered to a larger number of participants with the disease or condition of interest to evaluate the drug’s effectiveness when given at

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the maximum tolerated dose determined in Phase 1.\(^{49}\) This phase may last several months to two years.\(^{50}\) Phase 3 trials expand to include up to thousands of participants in order to evaluate the drug’s safety and effectiveness on a wider scale.\(^{51}\) However, although the traditional phases are still applicable at times, translational clinical trials developing drugs and biologics often follow a more complex pathway today.\(^{52}\) Phase 1 studies are far more often conducted on patients with the disease or condition of interest than on healthy volunteers.\(^{53}\) Phases may be skipped or combined, and phase designations are not even always applied to trials.\(^{54}\) Nontraditional clinical research pathways are especially likely to be designed for biologics, including cell- and gene-based products and regenerative medicine interventions.\(^{55}\)

If a drug or intervention survives the clinical trial portion of the process, the pharmaceutical company submits a New Drug Application (NDA) for review, so the product can be marketed in the U.S.\(^{56}\) However, the FDA continues to monitor drugs even after the initial approval process to ensure the continued safety of the public.\(^{57}\) This is

\(^{49}\) Id.

\(^{50}\) Step 3: Clinical Research, FDA, https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405622.htm#Clinical_Research_Phase_Studies (last updated Jan. 4, 2018) [hereinafter Step 3 Clinical Research]. The FDA estimates that 33% of investigational drugs proceed to the next phase of testing. Id.

\(^{51}\) See id.

The FDA reports that Phase 3 testing generally lasts one to four years, with approximately 25-30% of investigational drugs being approved. See id. Other studies report a much lower number of drugs that successfully obtain market approval. See, e.g., CHI HEMM WONG ET AL., ESTIMATION OF CLINICAL TRIALS SUCCESS RATES AND RELATED PARAMETERS 5–13 (2018), https://doi.org/10.1093/biostatistics/kxx069.


\(^{53}\) Step 3: Clinical Research, supra note 50. See, e.g., Amit Mahipal & Danny Nguyen, Risks and Benefits of Phase 1 Clinical Trial Participation, 21 CANCER CONTROL 193, 196 (2014) (explaining that phase 1 studies are often a patient’s “last ditch effort,” consequently many patients in phase 1 trials have short life expectancies).


\(^{55}\) See Nancy M.P. King & Odile Cohen-Haguenauer, En Route to Ethical Recommendations for Gene Transfer Clinical Trials, 16 MOLECULAR THERAPY 432, 436 (2008).

\(^{56}\) See FDA Drug Review Process, supra note 47.

\(^{57}\) Sandefur, supra note 46, at 517.

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known as Phase 4, or post-marketing surveillance trials, where manufacturers must: (1) undertake studies comparing their products with other products on the market; (2) monitor the new product’s long-term effectiveness and impact on patients; and (3) determine cost-effectiveness. Based on the information gathered, a product may be taken off the market or restrictions may be placed on its use.

Many investigational drugs and biologics never succeed in reaching the market. The majority fail to meet criteria for approval or are otherwise abandoned during clinical trials because of negative clinical outcomes, failure to demonstrate efficacy or safety, flawed study design, or costs that exceed the sponsor’s expectations.

Recruiting sufficient numbers of research subjects into clinical trials is essential in order to gather the data needed to demonstrate safety and efficacy. The human subjects enrolled in any clinical trial must satisfy eligibility requirements that are chosen to meet two goals: first, they must be able to provide the necessary data regarding the drug or biologic; and second, it must be possible to minimize harm to them from trial participation. It can be challenging to meet both of these goals in a clinical trial. Some patients may be too sick or their condition too advanced to participate in the trial—participation could further compromise their health and/or their advanced illness may make it too

59 See id.
61 In addition, stopping a clinical trial for cost reasons raises numerous ethical issues, because the failure to gather sufficient usable data wastes resources and exposes already-enrolled subjects to risks of harm without comparable benefit to society. The Geron trial of an oligodendrocyte product in spinal cord injury provides a recent example. See, e.g., Christopher Thomas Scott & David Magnus, Wrongful Termination: Lessons from the Geron Clinical Trial, 3 STEM CELLS TRANSLATIONAL MED. 1398, 1399–1400 (2014).
62 See e.g. Gina Kolata, For Scientists Racing to Cure Alzheimer’s, The Math is Getting Ugly, N.Y. TIMES (July 23, 2018), https://www.nytimes.com/2018/07/23/health/alzheimers-treatments-trials.html (discussing the complexity of recruiting human subjects, and using as an example, the search to find a requisite number of participants to test an Alzheimer’s drug. To recruit patient participants into over 100 Alzheimer’s studies, which collectively looked for 25,000 participants, 37.5 million patients in the right age group needed to be informed in order to ultimately net the necessary 25,000 participants.).
63 See King & Perrin, supra note 12, at 436.
64 Id. at 436–37.

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difficult to distinguish the effects of the intervention being studied from the effects of their condition or concomitant medications.65

In contrast, some patients may not be sick enough to learn from or may still have standard treatments available to them, so it would not be fair to ask them to participate in research.66 Other potential subjects may have a disease, condition, or genetic marker that differs from what is being tested at the time, or may have comorbidities that make evaluation of the product’s effect on the condition of interest too difficult.67 Prior or concurrent treatment can also disqualify potential participants.68 While such eligibility requirements may seem unreasonable at first, these restrictions help generate scientifically sound data while protecting subjects because they limit the complications that can arise from drug interactions, comorbidity, and advanced disease complexity.69 They do, however, prevent some patients who would like to be research subjects from enrolling in the clinical trials they may want to join.70

Conversely, eligible patients may be unwilling to participate in clinical trials for a variety of reasons.71 Some may refuse to enroll because of the need to undergo additional medical tests or to spend more time in the hospital or clinic.72 Others are simply not aware of the clinical trial or live too far away from where it will be conducted.73 Finally, some may not wish to risk receiving a placebo, or even receiving standard treatment instead of the experimental intervention, because of a deep-seated belief that what is new must be better—even when what is new is unproven and could be ineffective or even harmful.74

65 See e.g., id. at 435.
66 Id.
67 See, e.g., Ruth Ann Marrie et al., The Challenge of Comorbidity in Clinical Trials for Multiple Sclerosis, 86 NEUROLOGY 1, 2 (2016).
68 Martin, supra note 29, at 171.
69 Mark Greener, Drug Safety on Trial, 6 EMBO REPORTS 202, 203 (2005).
70 Information about the product’s effects on the broadest range of patients is collected in Phase 4 studies and from other sources of what the FDA calls “real world evidence.” See Real World Evidence, FDA, https://www.fda.gov/ScienceResearch/SpecialTopics/RealWorldEvidence/default.htm (last visited Aug. 2, 2018); see also Rachel E. Sherman et al., Real World Evidence—What is it and What Can it Tell Us?, 375 NEW ENG. J. MED. 2293, 2293–96 (2016).
71 Martin, supra note 29, at 171.
73 Martin, supra note 29, at 171.
74 This optimistic view is one aspect of the therapeutic misconception. See Sam Horng & Christine Grady, Misunderstanding in Clinical Research: Distinguishing continued . . .
C. FDA Regulation of Cells, Tissues, and Cellular or Tissue Products

In 1954, the first successful human organ transplant of a kidney took place.75 Within a decade, other kinds of organs, such as liver, heart, and pancreas, were successfully transplanted.76 Transplants became a more common treatment option as medical advances occurred in the prevention and treatment of organ rejection and as techniques for the collection, storage, and transplantation of human organs and tissues continued to improve.77

However, despite initial screening tests and procedures to monitor donor tissues and organs for diseases, after numerous transplant recipients were found to have contracted HIV infection or Creutzfeld-Jackob disease, a degenerative and fatal brain disease, from donor organs.78 In response, the FDA promulgated regulations specifically geared to cells, tissues, and cellular or tissue products used for transplantation and re-transplantation purposes.79

In 1997, the FDA issued its final rule on screening and testing donor tissues, providing further clarification on screening, record keeping, and inspection procedures.80 The FDA further determined that cells, tissues, and cellular-based or tissue-based products, that are likely to need more oversight to ensure safety and patient protection because of the way they


76 Id.

77 Id.; See also Martha A. Wells, Overview of FDA Regulation of Human Cellular and Tissue-Based Products, 52 FOOD & DRUG L. J. 401, 401 (1997).
79 Id.
80 See Human Tissue Intended for Transplant, 21 C.F.R. §1270 (July 29, 1997).
are prepared or used in the recipient’s body, must satisfy the stringent standards for premarket and marketing approval described above.\textsuperscript{81}

Overall, the regulatory burden to show safety and efficacy, regardless of the type of drug or biologic being tested, promotes public health goals but takes time and incurs costs.\textsuperscript{82} The length and demands of the process often frustrate patients with a serious disease who believe they could benefit from an as-yet-unapproved product and would prefer more rapid access.\textsuperscript{83} In addition, some diseases are so rare or progress so rapidly to end-stage severity that they are essentially untreatable, and patients with these conditions may not be well-served by the standard system of clinical trials.\textsuperscript{84} Such patients often argue that they have the autonomy to incur the risks of harm posed by early access to unproven interventions, and that if no effective standard treatment is available, they have nothing to lose by trying unapproved treatments.\textsuperscript{85}

\textsuperscript{81} Investigational New Drug Application, 21 C.F.R. § 312.2(a) (2009). Manufacturers of biologic products must additionally show that the biologic is “safe, pure, and potent,” which includes providing information about the facility, the manufacturing process, operating procedures, and equipment used in the product’s manufacture. 42 U.S.C. §§ 262(a)(1), (2)(C)(I)(I) (2012); Licensing, 21 C.F.R. § 601.2(a) (1985). The current status of the biologic regulation process is discussed in more detail in Part V, Regenerative Medicine. See infra Part V.

\textsuperscript{82} Eisenberg, supra note 33, at 346–47.

\textsuperscript{83} See, e.g., Sam Adriance, Fighting for the “Right To Try” Unapproved Drugs, YALE L. J. FORUM 148, 150 (2014) (providing an illustration about how a family fought for a fatally ill patient to try an unapproved drug, but was unsuccessful and the patient died without ever having the opportunity to test the drug).

\textsuperscript{84} See generally Carolyn Y. Johnson, The Truth About ‘Breakthrough’ Drugs, WASH. POST (July 17, 2018), https://www.washingtonpost.com/news/to-your-health/wp/2018/07/17/the-truth-about-breakthrough-drugs/?utm_term=.c58709ca35c4 (explaining that certain drugs with breakthrough status which are meant to treat serious diseases may receive expedited approval procedures rather than be subjected to standard clinical trials). Other cells, tissues, and cellular or tissue products that are only minimally manipulated and intended for homologous use and that meet certain other criteria are subject to less stringent regulations. Human Cells, Tissues, and Cellular and Tissue-Based Products, 21 C.F.R. § 1271.10 (2004). See Duranske, supra note 30, at 641. See also infra pp. 26–27.

\textsuperscript{85} These patients and their advocates argue that refusing them access to unproven interventions is paternalistic and therefore morally wrong. However, as some research ethics scholars and policymakers have observed, the imperative to conduct research in a manner that enables the collection of useful data is a matter of research ethics and responsible science rather than paternalism; moreover, it is very rare to truly have nothing to lose. See generally Steven Joffe & Franklin Miller, Bench to Bedside: Mapping the Moral Terrain of Clinical Research, 38 HASTINGS CTR. REP. 30 (2008); Darrow et al., supra note 36, at 283–84; George Annas, Questing for Grails: Duplicity, Betrayal, and Self-Deception in Post Modern Medical Research, 12 J. CONTEMP. HEALTH L. POL’Y 297 (1996); Gina Kolata, When the Dying Enroll in Studies: A Debate Over False Hopes, N.Y. TIMES (Jan. 29, continued . . .
In response, the FDA began to allow physicians and patients to informally petition for access to unapproved drugs still in clinical trials. These practices were formalized during the HIV/AIDS epidemic, when many terminally ill patients and their advocates argued that they should be allowed to incur the risks inherent in not yet fully approved experimental drugs rather than waiting years for more definitive results through the lengthy clinical trial process. To attempt to alleviate these pressures, the FDA created—and continues to this day to expand—alternative “parallel” pathways to accelerate market approval or provide access to drugs prior to approval.

D. Expedited Approval Programs

The FDA’s Accelerated Approval programs grant expedited FDA approval for drugs if the manufacturer proves that the investigational drug can treat a serious and previously untreatable medical condition. There are four different types of accelerated programs: (1) “Fast Track” is a process to speed the review of drugs that treat serious conditions and fill unmet needs; (2) “Breakthrough Therapy” is a designation linked to a process that expedites the development and review of drugs.

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87 Dresser 2, supra note 72, at 1636; Expanded Access (sometimes called “Compassionate Use”), FDA, https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm (citing Steven Epstein, Impure Science: AIDS, Activism, and the Politics of Knowledge (1996)). HIV activists were the first to suggest that too-rapid approvals could tilt the protection-access balance too far in one direction. Ezekiel Emanuel & Christine Grady, Four Paradigms of Clinical Research and Oversight, 16 CAMBRIDGE Q. HEALTHCARE ETHICS 90–92 (2006).


90 § 356(d).
that may provide substantial improvement over available therapy;91 (3) “Accelerated Approval” allows approval based on a surrogate endpoint for drugs that treat serious conditions with an unmet medical need;92 and (4) “Priority Review”93 is a designation that means the FDA will take action within six months.94

All in all, these expedited approval programs essentially enable a drug manufacturer to conduct fewer clinical trials with fewer participants, submit results of its clinical trials sooner based on certain intermediate or surrogate endpoints (e.g., a cancer drug’s ability to reduce tumor size, instead of assessing its ability to prolong survival in a longer trial), and/or apply for market approval earlier in the process.95 If later studies produce unfavorable results, approval may be withdrawn.96 These ways of accelerating product approval were helpful to some patients, but were not regarded as fast enough for others because they still required completion of the clinical trial process.97

E. Expanded Access Pathway

In addition to creating pathways to accelerate approval, the FDA created a formal pathway in 1987 to allow patients, with the help of their physicians, to gain access to unapproved drugs still in clinical trials.98

91 § 356(a) (defining a breakthrough drug as one that is “intended alone or in combination with one or more other drugs to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development”). See also Johnson, supra note 83.

92 § 356(c).


94 Id.


96 See FDA Drug Review Process, supra note 47.


98 See FDA Drug Review Process, supra note 47.
This Expanded Access Pathway was then revised in 200999 to provide three specific avenues for individual patients and groups of patients to use an experimental product outside of the clinical trial process.100 The individual pathway, by far the most commonly used, eased access upon request, especially in emergencies and for the most seriously ill patients.101 Completing the necessary application, however, imposed significant administrative burdens on physicians and manufacturers.102

Following the Abigail Alliance litigation (detailed below), the passage of right to try laws in several states, and partisan disagreement over the FDA’s role during the 2014 Ebola crisis, the FDA reformed its Expanded Access Pathway again in 2015 to reduce the administrative burden.103 Before the reforms, completing and processing the paperwork for an expanded access application took over 100 hours.104 Now, using an updated Form FDA 3926, a patient’s physician can complete the two-page form in less than an hour.105 Treatment may begin thirty days after the FDA receives the application, or earlier if the FDA permits.106 Patients must show that they have no other viable medical treatment options and do not qualify for any clinical trials.107 There must be research supporting the investigational product’s effectiveness at treating the patient’s illness,108 and it must be demonstrated that expanded use does not interfere with current clinical trials.109

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101 Expanded Access Q&A, supra note 99 (adding a number of pathways based on the size of the population seeking access, the availability of an IND, and the presence of emergencies). See Mackey & Schoenfeld, supra note 10, at 19.
102 Darrow et al., supra note 36, at 282.
103 Mackey & Schoenfeld, supra note 10, at 3.
104 See Martin, supra note 29, at 162.
105 Expanded Access Q&A, supra note 99, at 9 (discussing that Form FDA 3926 was created specifically to streamline the individual patient IND submission process. All other categories of Expanded Access still require the submission of Form 1571).
106 Id.
107 Darrow et al., supra note 36, at 282.
109 Expanded Access (Compassionate Use), supra note 86. For example, in the 1990s, HDC-ABMT, a rigorous regimen of high dose chemotherapy followed by autologous bone marrow transplant, showed initial promise in early clinical trials for the treatment of breast cancer. After intensive political lobbying, threats of litigation and media involvement, insurance plans agreed to cover the procedure, and more

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Expanded access applications still must be approved by the FDA and an IRB. Patients must also give their informed consent to receiving the unproven intervention, after being advised about the product’s risks of harm and unknown effects. Informed consent is particularly important to help counter the vulnerability of desperate patients, but IRB review and approval of the application and consent form can take more time than anticipated or desired. The FDA may, however, permit treatment without waiting for IRB approval in emergency situations, so long as the IRB is notified of the emergency use within five days.

In addition, the FDA still requires sponsoring physicians to submit reports detailing the patient’s use and results at the conclusion of treatment. Any evidence of adverse effects stemming from the product must be reported, a requirement some manufacturers consider problematic because seriously ill individuals who seek expanded access and do not qualify for clinical trials have complex and advanced diseases and comorbidities. Adverse events are more frequent and difficult to categorize in these patients, and thus could negatively affect a manufacturer’s ability to obtain market approval or could subject the manufacturer to adverse publicity.

In 2017, the FDA received 1,741 IND submissions and approved 1,730 of those—an approval rate of ninety-nine percent. Despite these overwhelming approval rates, manufacturers may still deny expanded access to patients, and the FDA cannot compel manufacturers to make unapproved products available.
reluctant for a number of reasons.\textsuperscript{119} For example, they need to prioritize the use of investigational products in ongoing clinical trials in order to obtain marketing approval, especially when supplies are scarce.\textsuperscript{120} They also need to ensure that granting expanded access will not jeopardize their ability to enroll patients as subjects in ongoing trials and will not expose them to any liability.\textsuperscript{121} They also need to recoup the costs of providing expanded access.\textsuperscript{122}

Moreover, the FDA cannot control drug costs.\textsuperscript{123} In contrast to trial participants, who usually receive expensive investigational interventions at no charge, manufactures usually expect patients who receive investigational products through expanded access to pay for them.\textsuperscript{124} Expanded access patients may also be responsible for any additional costs of administration and monitoring, along with the cost of the product.\textsuperscript{125} Private insurance companies, Medicare, and Medicaid all conduct independent review of expanded access expenses and rarely, if ever, approve these costs.\textsuperscript{126}

Even with expedited approval, expanded access, and increasing emphasis on alternative trial designs, critics argue that the FDA’s continuing reliance on a clinical translation process that culminates in the classic Phase 3 randomized controlled trial is still too “one size fits all” and should be updated.\textsuperscript{127} They point out that the FDA’s regulatory

\textsuperscript{119} Winniford, \textit{supra} note 43, 218; Darrow et al., \textit{supra} note 36, at 281–82.

\textsuperscript{120} \textit{Id.}

\textsuperscript{121} \textit{Id.}

\textsuperscript{122} \textit{Id.}


\textsuperscript{124} \textit{Id.}

\textsuperscript{125} \textit{Expanded Access: Information for Patients, supra note 110.}

\textsuperscript{126} \textit{Charging for Investigational Drugs Q&A, supra note 122, at 3.}


\textit{continued . . .}
system may prompt Americans to turn to other countries for treatment. They also argue that the FDA’s involvement is harmful to patients because too many still succumb to their diseases while access to investigational drugs and biologics is delayed in the name of patient safety. In doing so, critics highlight the struggle of real patients succumbing to disease while waiting for final approval of potentially effective new treatments, these are the arguments that gave rise to the right to try movement.

### III. The Right to Try Movement

Despite the expedited approval and Expanded Access Pathways, the call for open access to investigational drugs outside of the FDA regulatory realm grew into a social movement. These calls to action have resulted in the passage of right to try laws in approximately forty states and at the federal level.

#### A. Abigail Alliance for Better Access to Developmental Drugs

Diagnosed with cancer in 2000, Abigail Burroughs underwent months of ineffective treatments before seeking out experimental options. Her doctor suggested treating her cancer with either Iressa or Erbitux, although neither had been approved by the FDA at the time. Due to her prognosis, Abigail was not eligible for the clinical trials then underway, and her direct requests to pharmaceutical

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129 David T. Harris, “My Right to Try”: The Dangers of Unregulated Stem Cell Clinics, 8 CELL & TISSUE TRANSPLANTATION & THERAPY 1 (2016) (noting an increase in overseas medical tourism and clinics offering unsubstantiated stem cell therapies).


132 Adriance, *supra* note 82, at 150.

companies for access to the drug were denied.\textsuperscript{134} Her family and friends embarked on a media campaign to pressure Congress to provide Abigail with access to the experimental drug, but their efforts ultimately failed.\textsuperscript{135} Having exhausted her options, Abigail passed away in 2001.\textsuperscript{136}

After Abigail’s death, her father founded the Abigail Alliance for Better Access to Developmental Drugs, an organization dedicated to reducing the access barriers to non-FDA approved drugs for terminally ill patients who have exhausted all other alternatives.\textsuperscript{137} Although the FDA had not been directly involved in the denial of Abigail’s request for either of the drugs her doctor recommended, the Alliance targeted their campaign at reform of FDA procedures and policies.\textsuperscript{138} The FDA was unresponsive to the Alliance’s petition, so in 2003, the Alliance sued the FDA to invalidate its regulations governing the accessibility of experimental products, claiming that terminally ill patients have a fundamental right of access to drugs or biologics that have successfully completed Phase 1 trials.\textsuperscript{139}

The lawsuit was initially dismissed by the district court,\textsuperscript{140} but the Alliance successfully appealed.\textsuperscript{141} In applying the Supreme Court’s substantive due process framework of analysis, the D.C. Circuit Court recognized the Alliance’s claim,\textsuperscript{142} holding that “the right to access potentially life-sustaining medicine” warranted protection under the

\textsuperscript{134} Id. At the time of the requests, one of the companies provided Erbitux only to patients with colon cancer. Abigail, having been diagnosed with head and neck cancer, did not qualify for this study. The other company denied access because Abigail did not meet the inclusion criteria of its clinical trials.

\textsuperscript{135} Adriance, supra note 82, at 150.

\textsuperscript{136} Id.

\textsuperscript{137} Id.; see also Winniford, supra note 43, at 208–09.

\textsuperscript{138} Dresser 2, supra note 72, at 1637; Martin, supra note 29, at 172.

\textsuperscript{139} Complaint at 10–11, Abigail All. for Better Access to Dev. Drugs v. Von Eschenbach, 445 F.3d 470 (D.C. Cir. 2006); Martin, supra note 29, at 172-173. This suit was not the first challenge to the FDA’s policies regarding the terminally ill’s access to experimental drugs. In Rutherford v. United States, 442 U.S. 544, 556 (1979), the U.S. Supreme Court held that the safety and efficacy standards for experimental drugs did not change for terminally ill patients; thus, the FDA did not have to provide drugs that had not been proven safe for the general public to terminally ill patients.


\textsuperscript{141} Abigail All. for Better Access to Dev. Drugs v. McClellan, 495 F.3d 695, 697 (D.C. Cir. 2007) (en banc).

\textsuperscript{142} Abigail All. for Better Access to Dev. Drugs v. Von Eschenbach, 445 F.3d 470, 472 (D.C. Cir. 2006). For an in-depth analysis of the District Court’s decision and the controlling constitutional authority the court used to make its decision, see Winniford, supra note 43, at 209-12.

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Due Process Clause. The D.C. Circuit remanded the case to the district court to determine whether the FDA’s policies violated this right. The holding did not remain in place for long, as the D.C. Circuit reheard the case en banc and held that a fundamental right did not exist for terminally ill patients to gain access to experimental products. This court’s ruling has remained the final decision on the issue, as the Supreme Court denied certiorari.

While public awareness from the Abigail Alliance case did lead some large drug manufacturers to create their own expanded access programs (EAPs), separate from the FDA’s Expanded Access program, to help patients who wished to obtain unproven medications through the FDA’s program, demand still far exceeded supply.

Advocates, still frustrated by what they perceived as over-regulation by the FDA, turned to state legislatures for policy reform.

B. State Legislation

Patient advocates focused their reform efforts on creating state legislation to circumvent the FDA’s regulations entirely. The Goldwater Institute, a libertarian think tank, has been a prominent supporter of efforts to circumvent the FDA’s regulatory procedures. In 2012, after partnering with the Cancer Treatment Centers of America, a for-profit hospital chain, the Goldwater Institute joined the movement by coining the phrase “right to try” and advocating for an alternative pathway to access experimental drugs and devices without acquiring

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143 Abigail All., 445 F.3d at 484–485.
144 Id. at 472, 486.
145 Abigail All., 495 F.3d 695.
146 Winniford, supra note 43, at 214.
148 Realistically, only large manufacturers tend to have the funds and administrative support necessary to implement a manufacturer sponsored EAP. Id.

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permission from the FDA.\(^{152}\) They argued that patients and their physicians should be able to ask manufacturers directly, without any FDA oversight, for drugs and biologics that have completed Phase 1 clinical trials and are actively being tested in Phase 2 or 3 trials.\(^ {153}\) Goldwater drafted model legislation with these goals in mind.\(^ {154}\) In order to be eligible, patients must: (1) have a terminal disease; (2) have exhausted all FDA-available options including clinical trials; (3) consult with a physician who recommends the experimental drug; and (4) provide informed consent in writing to use the experimental drug, which must have completed Phase 1 testing.\(^ {155}\) The model legislation also provided limited liability protection for physicians, prohibiting licensure revocation based on the recommendation of or treatment with an experimental product.\(^ {156}\)

Sympathetic responses to the compelling stories of individuals with terminal diseases helped the movement gain widespread support in state legislatures.\(^ {157}\) Beginning with Colorado in 2014, approximately forty states passed similar right to try legislation.\(^ {158}\) Professor Rebecca Dresser explains why the laws were so appealing to state legislators: “Patients tell stories of desperate but unsuccessful efforts to obtain investigational drugs. Families describe loved ones who died without having a chance to try the drugs they were seeking. To lawmakers and the public hearing those stories, it would be cruel to vote against a right to try law.”\(^ {159}\)

Although these laws are popular and responsible in part for the

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\(^{154}\) Id.


\(^{156}\) Corieri, *supra* note 152, at 3.

\(^{157}\) See id. at 7–8.

\(^{158}\) Right to Try in Your State, RIGHT TO TRY, http://righttotry.org/in-your-state/ (last visited July 1, 2018). The remaining states have all introduced legislation, with the exception of Hawaii, which has already vetoed Right to Try.

\(^{159}\) Dresser, *supra* note 74, at 10.

*continued...*
FDA’s ongoing reforms of its Expanded Access Pathway, state right to try laws have proven somewhat ineffective. Their failure is attributable, in part, to concerns that they were arguably preempted by federal law, could result in a federal backlash for manufacturers, and did not, after all, ensure access.\(^{160}\) Right to try supporters began to argue that a federally approved pathway was the only way to eliminate the risk of federal preemption, correct confusing and burdensome variations across the states, reassure manufactures that expanding access would not put FDA approval of their products at risk, and lessen the FDA’s stronghold on the drug approval process.\(^{161}\)

C. Federal Legislation

In 2016, Senator Ron Johnson introduced the Trickett Wendler Right to Try Act of 2016.\(^{162}\) The bill called for the same changes as the state versions: eliminating FDA oversight, allowing terminally ill patients and their physicians to ask drug companies directly for access to drugs that have completed Phase 1 trials, and offering liability protection for “a producer, manufacturer, distributor, prescriber, dispenser, possessor, or user of an experimental drug.”\(^{163}\) The new bill also presented a direct amendment to the FDA’s authority by prohibiting the FDA from using outcomes “to delay or otherwise adversely impact review or approval of such experimental drug, biological product, or device.”\(^{164}\) This provision was intended to...


\(^{161}\) Howard, *supra* note 155, at 223. See also 164 CONG. REC. H3460 (daily ed. May 22, 2018) (reading Johnson’s letter of legislative intent into the record). Senator Johnson wrote a letter to Commissioner Gottlieb, the head of the FDA, clarifying his intent behind the legislation and its relationship to the FDA. He stated that the law’s purpose is to “diminish the power of the FDA over people’s lives” in response to Commissioner Gottlieb’s remarks on implementing the new Right to Try legislation. Johnson’s statement further emphasizes that the new pathway will be out of the reach of FDA regulation. *Id.*; But see Jonathan Friedlaender, *The Proposed Federal ‘Right-to-Try’ Law Is Not the Answer for Critically Ill Patients*, HEALTH AFFAIRS BLOG (Sept. 27, 2016), https://www.healthaffairs.org/do/10.1377/hblog20160927.056819/full/.

\(^{162}\) S. 2912, 114th Cong. (2016). In addition, in 2015, two representatives introduced a bare bones version of right to try legislation that authorized experimental drug use with state law. H.R. 3012, 114th Cong. (2015). This bill did not incorporate most of the Goldwater Institute’s model legislation, but it did pass the House.

\(^{163}\) S. 2912, 144th Cong. (2016).

\(^{164}\) S. 2912, 144th Cong. §2(b)(2).
reassure manufacturers that providing access would not jeopardize their chances of receiving FDA approval.\textsuperscript{165}

Ultimately, S. 2912 failed, as did subsequent bills from both the House and the Senate.\textsuperscript{166} Debates about safety, the appropriate role for the FDA, and the best balance of patient protections with access expansion delayed policymakers.\textsuperscript{167} Lawmakers continued to refine the legislation with little success, until President Trump mentioned the right to try in his 2018 State of the Union address,\textsuperscript{168} which renewed the urge to pass federal measures.\textsuperscript{169}

President Trump signed the “Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017” into law on May 30, 2018.\textsuperscript{170} Named for four attractive and compelling individuals who all had or have terminal diagnoses,\textsuperscript{171} the Act retained the provision prohibiting the use of reported outcomes in the FDA approval process.\textsuperscript{172} The significant curtailment of FDA oversight in this bill sparked opposition by some health care providers, scientists, and bioethics scholars, who began to identify ethical and safety concerns.\textsuperscript{173} Patient eligibility has also been broadened; the Act defines

\begin{itemize}
\item \textsuperscript{165} Right To Try: Hearing On S. 2912 Before the S. Comm. On Homeland Security and Governmental Affairs, 114th Cong. 21 (2016) (statement of Ms. Goodman).
\item \textsuperscript{166} S. 2912, 144th Cong.
\item \textsuperscript{167} 164 \textsc{Cong. Rec.} H997 (daily ed. Feb 6, 2017); 163 \textsc{Cong. Rec.} H8381 (daily ed. Nov. 1, 2017).
\item \textsuperscript{168} Donald J. Trump, State of the Union Address (Jan. 30, 2018).
\item \textsuperscript{169} Sarah Karlin-Smith, \textit{What’s next for right-to-try?}, \textsc{POLITICO} (Mar. 26, 2018) https://www.politico.com/newsletters/prescription-pulse/2018/03/26/whats-next-for-right-to-try-150036.
\item \textsuperscript{171} All of the named persons of the Act were active proponents for Right to Try laws in their states. Their stories were shared as part of the movement to encourage federal action. Senator Johnson began advocating for Right to Try in his state after meeting Trickett Wendler, a constituent of Wisconsin who died from ALS in 2015. Joe Mongiello and Matthew Bellina also have ALS and have spoken out in favor of federal measures. Jordan McLinn, who has Duchenne muscular dystrophy, became a spokesperson for the movement in Indiana. \textit{See generally} 163 \textsc{Cong. Rec.} S4788 (daily ed. Aug. 3, 2017) (statement of Sen. Johnson).
\item \textsuperscript{173} Several patient advocacy groups, including the American Cancer Society, submitted letters to Congress in protest of the various versions of the bill. They cite the lack of safety as the main issue for opposition. \textit{See} 164 \textsc{Cong. Rec.} H1744 (daily ed. Mar. 21, 2018); 164 \textsc{Cong. Rec.} H4357 (daily ed. May 22, 2018) (listing all of the undersigning advocacy groups); Ike Swetlitz, \textit{Physicians, Ethicists Urge Congress Not to Pass “Right-to-Try Legislation}, \textsc{STAT} (Feb. 1, 2018), https://www.statnews.com/2018/02/01/physicians-ethicists-congress-right-to-try/.
\end{itemize}
a life-threatening condition as one “where the likelihood of death is high unless the course of the disease is interrupted” or one that is “potentially fatal.”¹⁷⁴ The Act also retains liability protection for manufacturers, physicians, and other providers, for both permitting and denying access.¹⁷⁵

Like the state legislation, the legislation named for Trickett Wendler, Frank Mongiello, Jordan McLinn,¹⁷⁶ and Matthew Bellina had bipartisan support even while many scientists, regulators, and ethicists opposed it.¹⁷⁷ Thus, while the FDA’s Expanded Access Pathway remains intact for now, patients in every state have a uniform alternative pathway that is outside the FDA’s authority.¹⁷⁸


¹⁷⁷ See supra note 173 and accompanying text; See Alison Bateman-House, Arthur Caplan & Kelly McBride Folkers, “Right to Try” Is Merely “Thoughts and Prayers” for the Terminally Ill, SLATE (Mar. 21, 2018), https://slate.com/technology/2018/03/the-house-will-pass-right-to-try-this-week-it-shouldnt.html; However, some supporters concede that widespread impact is not necessarily the goal, admitting that even if the law does not help millions, as long as it helps some, then it is effective; See Linda Qui, Trump Oversells New ‘Right to Try’ Law, N.Y. TIMES (May 30, 2018), https://www.nytimes.com/2018/05/30/us/politics/fact-check-trump-right-to-try-law-.html.

¹⁷⁸ See generally Qui, supra note 177 (“But the effect of similar laws [to the continued . . .
IV. CONCERNS ABOUT RIGHT TO TRY LEGISLATION

Right to try laws are designed to help a cohort of seriously ill patients gain early access to investigational drugs and biologics that they believe will extend their lives. However, most of the benefits afforded to such patients from even the most effective new treatments are modest at best: life prolongation and/or symptom attenuation that can be measured only in months, not years. Moreover, reducing access barriers by avoiding FDA oversight raises safety concerns. The legislation thus significantly alters the balance between protection and access that has characterized the regulation of drugs and biologics by FDA since its beginnings, and it raises important questions about the fair distribution of costs, burdens, risks of harm, and access to unproven interventions.

A. The Legislation Does Not Mandate That Access Be Provided

Some critics of the right to try opine that the legislation should be called “the Right to Ask,” as it only allows a patient, physician, and manufacturer to bypass FDA oversight if both the physician and the manufacturer agree that the patient should receive the investigational product. The legislation does not compel a physician to assist a patient or require that a manufacturer provide access.

In order to support a request, physicians need to weigh the potential benefits to the patient against the risks of harm that could occur. This is difficult to do when there is a lack of information about the drug or

‘Right to Try’ law] in some states has been muted.”).
179 See Hellman, supra note 173.
180 Id.
181 Id.
184 Id.
185 Id.

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biologic, its side effects, or interactions.\textsuperscript{187} Simply because it exists, the legislation may put increased pressure on physicians to comply with patients’ requests, even if they may not agree that trying the investigational drug or biologic is the best course of action or in the patient’s best interest.

Even if a physician agrees to ask, manufacturers may be unwilling to permit access, due to persisting administrative responsibilities, concerns about limited medication supplies, fears about slowing clinical trial enrollment, negative press arising from potential adverse effects of using unproven products in uncontrolled settings, and other prudential worries that the pharmaceutical industry faces with or without right to try protections.\textsuperscript{188}

\textbf{B. The Legislation May Increase Economic Burdens on Patients and Manufacturers}

The right to try legislation allows drug manufacturers to recover the cost of providing patients with unproven drugs and biologics.\textsuperscript{189} Manufacturers incur significant expense when distributing unproven medications outside the clinical trial process.\textsuperscript{190} Under right to try laws, manufacturers are free to charge patients directly for access to the medications they seek, or to pass the costs on in other ways.\textsuperscript{191} And the costs keep increasing.\textsuperscript{192} For example, novel biopharmaceuticals generally come with astronomical price tags.\textsuperscript{193} Many cost more than \$100,000 per year for repeated and usually lifelong administration.\textsuperscript{194} One-time treatments are rare, and complete cures are even more rare; instead, many new medications only slow disease progression or restore partial function.\textsuperscript{195} Many of these new treatments are most effective

\textsuperscript{187} Id.
\textsuperscript{188} See supra notes 119–26 and accompanying text. While it is true that manufacturer-sponsored EAPs are increasing in popularity for large pharmaceutical companies, many small manufacturers or start-ups do not have the resources or organizational structure to develop EAPs. See Friedlaender, supra note 161. See also Bateman-House et al., supra note 177.
\textsuperscript{189} Corieri, supra note 152, at 3.
\textsuperscript{190} Id. at 9–10.
\textsuperscript{191} Id. at 3.
\textsuperscript{192} Martin, supra note 29, at 176.
\textsuperscript{194} Id.
\textsuperscript{195} For example, a new biologic that is the first FDA-approved treatment for spinal muscular atrophy requires repeated injections but can only slow the

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when combined with other therapies, which can drive costs much higher.\textsuperscript{196} If a manufacturer requests payment from patients for expanded access, only the wealthy may be able to pay, as most patients simply cannot afford such a hefty price tag.\textsuperscript{197} Further, right to try legislation does not compel insurance providers to cover the cost of expanded access to experimental products.\textsuperscript{198} It does nothing to address the reality described above: both public and private payers reasonably question the cost-effectiveness of payment for unproven interventions, whether in clinical trials or through expanded access.\textsuperscript{199} Patients, families, and advocacy groups have long battled insurers to expand reimbursement, and the right to try has not altered that ongoing debate.\textsuperscript{200}

Many of the larger manufacturers of drugs and biologics have established indigent drug availability programs to facilitate patients’ access to approved medications.\textsuperscript{201} Such programs may provide price discounts, support patients’ appeals to health insurers, or help patients apply for state and federal aid.\textsuperscript{202} Whether these programs should be extended to cover expanded access raises questions about the fair distribution of burdens and benefits when resources are limited. As previously mentioned, some manufacturers have also established their own EAPs in order to separately consider how to apportion access to unproven medications.\textsuperscript{203}

\textsuperscript{196}See Nancy M.P. King & Christine Bishop, New Treatments for Serious Conditions: Ethical Implications, 24 GENE THERAPY 534–38 (2017); see also infra note 202 and accompanying text.
\textsuperscript{197}See Corieri, supra note 152, at 7.
\textsuperscript{198}See Mineo, supra note 160, at 9.
\textsuperscript{199}See Corieri, supra note 152, at 3.
\textsuperscript{202}Id.
\textsuperscript{203}See, e.g., Joanne Weldstreicher, Johnson & Johnson Expands Access to Investigational Medications Through Its CompAC Program, JOHNSON & JOHNSON (Sept. 28, 2016), https://www.jnj.com/latest-news/johnson-and-johnson-expands-access-to-investigational-medications-through-its-compac-program. While it is true that manufacturer-sponsored EAPs are increasing in popularity for large

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Expanded access decisions are both difficult and costly for the pharmaceutical industry. Developing new medications is increasingly expensive. Figures in the billions of dollars are routinely quoted by the manufacturers of drugs and biologics. The accuracy of such figures is routinely disputed, and the unrelenting climb in medication charges is a point of significant contention in health care. Nonetheless, it is indisputable that providing access to unproven medications outside of clinical trials is expensive for manufacturers who may regard it as impeding their ability to move medications efficiently to market and thereby fulfill their fiduciary duty to shareholders.

Although charging patients for expanded access products may help manufacturers recoup the costs of providing access, it may also publicize the manufacturing cost before the medication becomes available for general use. Even though the right to try law specifically permits charging patients, doing so may expose manufacturers to the risk of appearing merciless toward dying individuals.

Most significantly, right to try laws may sacrifice patient safety in exchange for the false hope provided by the prospect of doing everything possible to live longer. This sacrifice undermines the FDA’s overall purpose to protect the public. Right to try laws enable patients to attempt to gain access to unproven therapies that have not completed the rigorous testing that the FDA requires, which leaves patients vulnerable to potentially significant harms. Patients may waste resources on unproven treatments that are ineffective, instead of pursuing potentially effective therapies that are less spectacular. They may continue to seek unproven alternatives instead of accepting the

pharmaceutical companies, many small manufacturers or start-ups do not have the resources or organizational structure to develop EAPs. Friedlaender, supra note 161.

Corieri, supra note 152, at 6.

Id.

Id.

Corieri, supra note 152, at 6, 15.

Friedlaender, supra note 161.

Kearns & Bateman-House, supra note 200, at 173; Spencer, supra note 200, at 48–49. Some states, however, bar manufacturers from recovering costs, which probably discourages companies from providing expanded access. See Howard, supra note 155, at 294 (describing the Texas Right to Try Act).


Duranske, supra note 30, at 650.

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many forms of supportive care that can improve quality of life near the end of life. Unproven interventions could worsen or complicate patients’ conditions, both shortening and significantly impairing the quality of their remaining time. Although the federal right to try legislation may convince some patients that they no longer need to seek treatment options outside the United States, medical tourism into the United States has, in fact, increased, thus leading to more patients putting themselves at risk to try experimental therapies.

Removing the requirement that an IRB review and approve an expanded access application has eliminated an important patient safety measure. Although the terminally ill unquestionably deserve to make choices about their own healthcare, they also deserve to be offered only those interventions that can reasonably be provided in a sufficiently safe and effective manner. A system that allows unfettered access to experimental interventions without adequate patient protections is likely to increase the possibility of painful side effects or even hasten death.

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212 Id. (stating a patient “has inadequate information to determine whether a drug or biologic is safe and effective even after receiving it”); Sipp et al., supra note 128, at 3.
213 Duranske, supra note 30, at 652–53 (discussing the opportunity cost as well as physical harm); Sipp et al., supra note 128, at 3 (stating ineffective therapies “come at the cost of alternative effective therapies and other activities that could improve their quality of life”).
214 President Donald J. Trump, State of the Union Address (Jan. 30, 2018).
215 Harris, supra note 129, at 1.
216 Howard, supra note 155, at 291 (stating IRB approval is not required under the law).
217 Dr. Ebrahim Delpassand’s work highlights the concern that the right to try laws’ alternative pathway permits experimental use without the protection of safety protocols. The Goldwater Institute promotes his work as a success story, claiming that he treated between 100 and 200 patients under the Texas right to try law after the FDA denied his request to expand his existing clinical trial. The FDA’s rejection, however, was based on the discovery that he had violated several safety conditions while conducting his trial, after an investigation based on complaints from patient-subjects in the trial, an aspect of the narrative has not been acknowledged by media or right to try supporters. See Alex Barasch, The Lie Behind the Right to Try, SLATE (Feb. 8, 2018, 10:29 AM), https://slate.com/technology/2018/02/right-to-try-legislation-is-redundant-and-possibly-harmful.html (detailing various therapies that proved ineffective at treating diseases and sometimes even deadly despite passing Phase 1 testing); see also U.S. House Passes Right to Try Law, GOLDWATER INST. (Mar. 22, 2018), https://goldwaterinstitute.org/article/u-s-house-passes-right-to-try-law/; Mackey & Schoenfeld, supra note 10, at 7–8 (discussing the need for transparency regarding access options).
218 See Barasch, supra note 217.
C. FDA Oversight Generates Valuable Information

Despite its burdens, the clinical trials process promotes and protects the generation of valuable data that advance scientists’ understanding of disease and treatment.\(^{219}\) Limiting the collection and use of data gathered from expanded access to unproven drugs and biologics may prevent or slow the development of significant knowledge about some products still in development—knowledge that could prevent harm to patients. This data helps advance scientists’ understanding of traditional and regenerative medicine as a whole, not just the specific drug or therapy being tested.\(^{220}\) Concern also exists that the right to try law’s curtailment of FDA oversight of expanded access is only a first step toward further minimizing the FDA’s authority and thus jeopardizing the future of medical research and development in the U.S.\(^ {221}\)

Moreover, success or failure in recruiting patients into clinical trials directly affects a manufacturer’s ability to generate and collect scientifically sound data.\(^ {222}\) Right to try legislation may further detract from clinical trial participant enrollment, which already suffers from a scarcity of eligible patients.\(^ {223}\) Lower numbers of participants enrolled in studies results in less information flowing through the clinical trial process, which slows the development of therapies with proven track records and the ability to demonstrate both failure as well as success; the long delay in completion of HDC-ABMT trials in the 1990s illustrates the problem.\(^ {224}\)

D. Right to Try Laws May Increase Existing Health Care Disparities

The right to try movement highlights the health care disparity created by giving priority to individuals who are able to gain access to treatment through social media and media campaigns.\(^ {225}\) Terminally ill patients without the means to launch a successful medial campaign may never receive access to treatment, under the right to try law or otherwise.\(^ {226}\) Especially if the decision to provide access results from public pressure, both to provide access and to help pay for it, the appeal

\(^{219}\) Duranske, supra note 30, at 655.
\(^{220}\) Duranske, supra note 30, at 655.
\(^{221}\) Id. at 681–82.
\(^{222}\) Martin, supra note 29, at 183.
\(^{223}\) See Dresser 2, supra note 72, at 1644.
\(^{224}\) Maschke & Gusmano, supra note 95, at 930.
\(^{225}\) Dresser, supra note 74, at 10.
\(^{226}\) Van Groningen, supra note 183.
of rescuing identified lives exacerbates this disparity.227

This potentially places the right to try at odds with the Affordable Care Act’s mandate to reduce the number of uninsured by making basic health insurance available to most of those in need.228 The right to try movement’s goal of circumventing the FDA thus seems to reinforce attention to rescue medicine applied to identified lives at the expense of improving health care access for all and maintaining a reasonable balance between access and safety. As a result, right to try laws may exacerbate health care disparities; at best, the law simply does nothing to address them.229

The foregoing discussion gives broad consideration to the impact of the right to try movement on the translational pathway for development of drugs and biologics overall. Stories like Charlie Gard’s, however, raise new questions specifically about how the right to try might interface with the highly individualized patient focus promised by precision medicine, which is made possible by genetics and regenerative medicine. Thus, we turn to a brief discussion of the broad and fast-moving field of regenerative medicine research.230

V. REGENERATIVE MEDICINE

A. The Promise of Regenerative Medicine

The explosive growth of genetic knowledge in the 20th century has fueled 21st century optimism about the development of new treatments.231 Regenerative medicine is an innovative and rapidly growing medical research field focused on development of cell- and gene-based interventions.232 It makes use of all types of stem cells,

227 Id. For more on “identified lives,” see Section V.C.
228 See Paradise, supra note 41, at 691–92; Patient Protection and Affordable Care Act, 42 U.S.C. § 18001 (2010).
229 See Van Groningen, supra note 183. Several of the highly publicized patient narratives received attention due to their social media campaigns. Those who lack the resources or skills to launch an effective campaign may further be disadvantaged. For a recent study on the efficacy of using social media to gain access, see Mackey & Schoenfeld, supra note 10, at 5–7.
230 Given the broad and diverse nature of regenerative medicine, this discussion is not meant to provide a comprehensive scientific overview. Indeed that might not be possible, as this field advances rapidly. Rather, this section focuses on aspects of regenerative medicine that are most widely discussed in the media and that intersect with the right to try movement and related developments.
DNA and RNA, bioprinting, and a variety of other biotechnologies to repair, restore, or replace damaged tissues or organs or to augment the function of failing organs. Regenerative medicine products and interventions are often designed to be highly patient-specific, employing autologous stem cells taken directly from the research subject or patient to create tissues or organs that minimize the individual’s immune response to transplanted material. This focus on interventions using autologous or closely matched cells, tissues, and organs virtually eliminates the need for the powerful immunosuppressive drugs that are both quite dangerous and essential to prevent rejection of donated tissues and organs in standard allogeneic transplantation practice.

Regenerative medicine thus has potentially broad applications, but the development of precisely tailored interventions is time-consuming, labor-intensive, and costly. These costs are unlikely to decrease significantly once a regenerative medicine product or intervention is approved as a treatment. Organ and tissue regeneration will therefore presumably be more costly and less accessible than standard transplantation of organs and tissues.

All types of stem cells play a vital role in regenerative medicine research. Some stem cells are “highly multipotent,” with the capacity

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233 Id.

234 Nat’l. Inst. of Health., supra note 231.

235 Keys et. al; supra note 232; see also Duranske, supra note 30, at 632–33; Nancy M.P. King, Christine Nero Coughlin & Mark E. Furth, Ethical Issues in Regenerative Medicine, 9 Wake Forest Intell. Prop. L.J. 215 (2009) [hereinafter King et al., Ethical Issues].

236 See King & Perrin, supra note 12, at 87; Nancy M.P. King, Ethics in Regenerative Medicine and Transplantation, in REGENERATIVE MEDICINE TECHNOLOGIES AS APPLIED TO ORGAN TRANSPLANTATION (Giuseppe Orlando, ed., Elsevier, 2013).


238 Id.


to develop into a wide range of cell and tissue types. Others have more limited capacity and are able to differentiate into only a few cell types. Even “determined” stem cells, which can become only one type of cell, are significant for much important research, and have long been used in some standard treatments.

Scientists obtain stem cells from a variety of sources and create and manipulate them using a variety of methods. One of the first sources, human embryos left over from assisted reproduction and donated for research, provides stem cells that can become all types of cells, but their use is controversial, and they are also prone to developing tumors. Amniotic fluid, placental and umbilical cord blood, and even urine can provide multipotent stem cells, which have more limited ability to differentiate into different cell types. “Determined” (also called “adult”) stem cells can also be produced by most organs and tissues in the body, including blood, bone marrow, and the liver; these have very limited ability to differentiate, but are still useful in repair and regeneration of the organs from which they are extracted. Finally, non-stem cells can be “induced” to differentiate into pluripotent stem cells through genetic reprogramming. These induced pluripotent stem cells can be quite versatile but may also produce tumors.

Research with stem cells has many potential therapeutic

(2011) [hereinafter King et al., Pluripotent Stem Cells].

241 King et al., Pluripotent Stem Cells, supra note 240.
243 See Keys et al., supra note 232. Autologous transplantation of hematopoietic (blood-forming) stem cells taken from a patient’s blood or bone marrow is a highly effective standard treatment used to restore a cancer patient’s immune system after high-dose chemotherapy has destroyed it in an effort to eradicate the cancer. Regenerative Medicine Innovation Project, NATIONAL INSTITUTES OF HEALTH, https://www.nih.gov/rmi (last visited July 16, 2018). Because this is such a well-recognized treatment use of stem cells, patients and the public can mistakenly conclude that all regenerative medicine interventions are proven treatments, when in truth, nearly all remain experimental, with only a few exceptions. Duranske, supra note 30, at 651–55; Angelo S. Mao & David J. Mooney, Regenerative Medicine: Current Therapies and Future Directions, 112 PNAS 14452-59 (2015).
244 Id. at 3.
245 Id. at 5.
246 Id.
247 See Keys et al., supra note 232.
248 Keys et al., supra note 232, at 7.
249 Id. at 5; King et al., Pluripotent Stem Cells, supra note 240, at 719; King & Perrin, supra note 12, at 87; King et al., Ethical Issues, supra note 235, at 218.
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applications.\textsuperscript{250} Hundreds, if not thousands, of research studies on the use of stem cells to treat different forms of cancer, autoimmune disorders, and diseases like diabetes are ongoing.\textsuperscript{251} Determined stem cells are also used extensively in tissue engineering research.\textsuperscript{252} For example, stem cells taken from muscle are being studied in wound repair research to grow muscle tissue that can be transplanted into injuries and defects.\textsuperscript{253} The ability to bioengineer tissue to repair or supplement failing organs and regenerate whole organs has also proved somewhat promising.\textsuperscript{254} For example, blood vessels and damaged portions of essentially hollow or tubular organs like tracheas and urethras\textsuperscript{255} can be grown in a laboratory, prepared for the stresses of the body by being further developed in a bioreactor, “seeded” with determined stem cells from the patient-subject, and then implanted in the body, which then completes the process of lining the lab-grown tissue with the patient-subject’s own cells.\textsuperscript{256} This process has had some success in the relatively few research studies using human subjects that are currently underway.\textsuperscript{257}

\textsuperscript{250} Duranske, supra note 30, at 636.
\textsuperscript{252} Hannah B. Baker, John P. McQuilling, Nancy M.P. King, Ethical Considerations in Tissue Engineering Research: Case Studies in Translation, 99 METHODS 135-44 (2016), http://dx.doi.org/10.1016/j.meth.2015.08.010. One of the few FDA-approved regenerative medicine products is made from determined stem cells taken from cartilage, processed, and reinfused to repair injuries or defects to existing cartilage. Durankse, supra note 30, at 636; Mao & Mooney, supra note 243, at 14452.
\textsuperscript{253} See Baker et al., supra note 252, at 135–44.
\textsuperscript{254} Id. at 140.
\textsuperscript{256} Id.
\textsuperscript{257} With respect to seeding bioartificial structures with stem cells taken from patient-subjects and implanting them successfully, Dr. Anthony Atala’s work is perhaps the farthest along. He has successfully augmented the underdeveloped bladders of patient-subjects with spina bifida by engineering additions to the subjects’ bladders. He created appropriately sized and fitted biodegradable scaffolds from collagen, seeded them with patient-subjects’ own determined bladder stem cells, and attached the regenerated bladders to the patient-subjects’ existing bladders to increase their bladder capacity. Spina bifida patients have no neuromuscular function in their bladders, so to urinate they must self-catheterize. The experimental procedure has allowed all of the patient-subjects in this long, ongoing trial to continued . . .
Whole organ regeneration is being pursued in two distinct lines of preclinical research. The first model takes whole organs from animals and washes them in a mild detergent solution to “decellularize” them, or remove all the cells that make up the organ and that would cause an immune response in an organ recipient while leaving behind the collagen matrix, which retains the shape and structure of the organ. This scaffold can be seeded with cells from the potential recipient and be surgically implanted when ready to function.

The second method for whole organ regeneration, 3D bioprinting, began when an ink-jet printer was adapted to use cells as ink. Refinement of the tools and methods for printing organs has been a lengthy process; it includes development of bioprinters able to print using more than one type of cell at once, when the cell types have different viscosities that fit their different roles and locations in the printed organ, as well as development of a library of “bioinks.” These 3D bioprinters can even be used to print the layers of the skin, and are being developed to repair even full-thickness burns in the operating room.
B. Promoting The Promise of Regenerative Medicine While Preventing Exploitation

Further development of regenerative medicine products and technologies is essential to the field’s treatment potential but will undoubtedly take more time and research effort. A great deal of essential knowledge remains elusive, and regenerative medicine products and interventions can be extremely complex. Thus, there is much basic research yet to do before most regenerative medicine can bear fruit for patients. Nonetheless, the field is developing so rapidly that there is an ongoing need to review and update legislation, regulations, and guidance documents to maintain an appropriate balance between protecting research subjects, patients, and the public and promoting access to effective regenerative medicine interventions to meet the needs of patients. The promise of individual treatment tailoring through autologous stem cell interventions has so captured public imagination that stem cell clinics can advertise pay-to-play clinical trials and attract willing patient-subjects from all around the world. Profit-oriented stem cell clinics can capitalize on public confusion and media hype about stem cells, offering unproven interventions or participation in questionable research to desperate implanted in a different place from the organs with which we are born.

264 See generally Varkey & Atala, supra note 261.
265 Id.
266 See generally About Regenerative Medicine, MAYO CLINIC, https://www.mayo.edu/research/centers-programs/center-regenerative-medicine/patient-care/about-regenerative-medicine (last visited Oct. 1, 2018) (“Though great progress has been made in medicine, current evidence-based and palliative treatments are increasingly unable to keep pace with patients’ needs, especially given our aging population.”).
267 Duranske, supra note 30, at 694–95.
268 See, e.g., Jeremy Snyder & Leigh Turner, Selling Stem Cell “Treatments” as Research: Prospective Customer Perspectives from Crowdfunding Campaigns, 13 REGENERATIVE MED. 375, 376 (2018) (“[T]o date researchers have paid little attention to how the tokens of scientific legitimacy associated with pay-to-participate stem cell studies have been understood and used by individuals seeking stem cell treatments for various indications.”); Leigh Turner, ClinicalTrials.gov, Stem Cells and “Pay-to-Play” Clinical Studies, 12 REGENERATIVE MED. 705, 706 (2017) (“[I]ndividuals enrolled in what are often called ‘pay-to-participate’ studies are charged thousands or tens of thousands of dollars . . . . For example, individuals who must travel to visit a clinical trial site often have to pay for airline tickets, local accommodations, meals and ground transportation.”); Leigh Turner & Paul Knoepfler, Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry, 19 CELL STEM CELL 154 (2016) (“[H]ealth researchers, policy-makers, patient advocacy groups, and reporters often use the phrase ‘stem cell tourism’ when addressing the subject of unapproved cell-based interventions . . . .”); see also Charging for Investigational Drugs Q&A, supra note 122 and accompanying text. continued . . .
Patients. Patients who enroll in these pay-to-play trials can be seriously harmed, as happened to two individuals seeking experimental treatment for macular degeneration in 2015.

The International Society for Stem Cell Research (ISSCR) has published, and regularly updates, comprehensive guidelines for stem cell research to help clinicians and patients distinguish among approved treatments, registered and appropriately designed and conducted clinical trials, and questionable and potentially dangerous practices. And both to prevent future tragedies like the macular degeneration trial and to help facilitate clinical translation, the FDA has recently published guidance and draft guidance documents specifically addressing challenges in regenerative medicine and gene transfer research.

Of particular note is a recently finalized guidance document explaining and detailing when human cells, tissues, and products derived from them qualify for exceptions from the FDA requirement of premarket review and approval. These exceptions are known as “minimal manipulation” and “homologous use.” Using numerous examples, this guidance document distinguishes products that have been minimally manipulated and are being used in ways that match their...

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269 See Snyder & Turner, supra note 268, at 381 (explaining that “crowdfunding campaigns regularly demonstrate[] confusion over and exaggeration of the role and impact of legitimate stem cell scientific research”).

270 See Ajay E. Kuriyan et al., Vision Loss After Intravitreal Injection of Autologous “Stem Cells” for AMD, 376 NEW ENG. J. MED. 1047 (2017).


273 See Peter Marks & Scott Gottlieb, Balancing Safety and Innovation for Cell-Based Regenerative Medicine, 378 NEW ENG. J. MED. 954 (2018) (providing a more detailed discussion of the relevant FDA guidance documents).


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original uses in the body from those that may pose greater risks to safety or efficacy, and therefore need more oversight because they are being prepared more extensively and will be used in new ways in the body.\textsuperscript{276}

To give a standard treatment example, the collection and basic purification of hematopoietic stem cells from the bone marrow or peripheral blood of a patient about to receive high dose chemotherapy, and the reinfusion of those stem cells to reconstitute the patient’s blood- and bone-forming cells and to restore the patient’s immune system, exemplify both minimal manipulation and homologous use.\textsuperscript{277} In contrast, in the trial that caused blindness in two patient-subjects, liposuction was used to extract adipose (fat) cells from individuals’ abdomens.\textsuperscript{278} The cells were extensively processed and then injected into the eyes as a “treatment” for age-related macular degeneration.\textsuperscript{279} Because the cells were more than minimally manipulated and were used for a non-homologous purpose (adipose cells play no role in vision), this intervention posed safety risks and raised significant efficacy questions.\textsuperscript{280} The intervention should have undergone FDA review, but did not.\textsuperscript{281}

Finally, the story of Dr. Paolo Macchiarini\textsuperscript{282} further demonstrates why regulatory oversight of regenerative medicine interventions is essential, especially because patient need is great and public expectations are high.\textsuperscript{283} Dr. Macchiarini was a superstar at the prestigious Karolinska Institute when he began publishing about his research on implanting new tracheas in patient-subjects whose tracheas were damaged or diseased.\textsuperscript{284} The charming and charismatic surgeon first used decellularized cadaver tracheas and then turned to plastic tracheal scaffolds, which he seeded with bone marrow stem cells from the patient-subject before implantation.\textsuperscript{285} His work was widely

\textsuperscript{276} See Regulatory Considerations, supra note 274 (acknowledging that Structural HCT/Ps, which are minimally manipulated, “generally raise different safety and efficacy concerns than do cells or nonstructural tissues”).

\textsuperscript{277} See id.

\textsuperscript{278} See id.

\textsuperscript{279} Kuriyan et al., supra note 270, at 1047–48; Peter W. Marks et al., Clarifying Stem-Cell Therapy’s Benefits and Risk, 376 NEW ENG. J. OF MED. 1007, 1008 (2017).

\textsuperscript{280} See Kuriyan et al., supra note 270, at 1050–51.

\textsuperscript{281} See id. at 1053.


\textsuperscript{283} See supra Part V(A).


\textsuperscript{285} Kremer, supra note 282.

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regarded as groundbreaking; however, in 2015, his earliest publications from 2011 were investigated and deemed problematic.\textsuperscript{287} The Karolinska Institute defended him until it took a deeper look and discovered that he had lied not only in his research but on his CV and in his non-work life, resulting in his firing from Karolinska in 2016.\textsuperscript{288} Calls for the retraction of multiple publications followed in 2017.\textsuperscript{289} In fact, Macchiarini’s vaunted surgical research had outcomes for patient-subjects that were often devastatingly bad.\textsuperscript{290} The attention and adulation that he received, the ease with which he was able to continue his research despite high levels of morbidity and mortality in his subject population, and the questions raised by colleagues and whistleblowers, were attributable in large part to the star-studded status of the new and promising field of regenerative medicine.\textsuperscript{291}

The familiarity of this type of sad story underscores the risks of harm and exploitation faced by vulnerable and desperate patients seeking to participate in cutting-edge clinical trials like those offered by regenerative medicine. It is surprisingly easy to injure patient-subjects in research that is viewed as groundbreaking;\textsuperscript{292} the lure of continual progress and all that follows from progress can readily overshadow the careful attention to good research that protects patient-subjects and produces good data. When the rules of research are relaxed in an effort to speed that progress, the likelihood of exploitation and harm can only increase.

Several other legislative, scientific, regulatory, and policy changes that have been undertaken in the past few years go hand in hand with


\textsuperscript{287} Elliott, supra note 284.

\textsuperscript{288} Id.


\textsuperscript{290} Kremer, supra note 282.

\textsuperscript{291} See generally id. The Karolinska Institute, which had invested its reputation in regenerative medicine by allying itself with Macchiarini, was disposed to view his research favorably as a sign of their success in the field.

\textsuperscript{292} See generally id. 

\textit{continued . . .}
the FDA’s efforts to protect the public while facilitating clinical translation. The All of Us precision medicine initiative, introduced by President Obama in his 2015 State of the Union address, is building on the legacy of the Human Genome Project with plans to sequence the whole genomes of as many volunteers as possible and link their genetic information to a wide range of phenotypic information relating to their health and their lives. The initiative’s goal is to increase the speed and reduce the cost of finding genes associated with disease and identifying patient-specific treatments—thus fulfilling the potential of precision medicine.

Likewise, Congress passed the 21st Century Cures Act to expedite medical research and development in a variety of ways, including by providing another FDA expedited approval pathway for “regenerative medicine advanced therapies” (RMATs), such as cell therapies, therapeutic tissue engineering products, and certain combination products used “for serious or life-threatening conditions” if preliminary evidence indicates that they have “the potential to address unmet needs.” RMATs are entitled to expedited development and review like those provided to drugs designated as Breakthrough Therapy, and it may be eligible for Priority Review or Accelerated Approval. Expedited approval under this pathway still...
includes post-approval requirements, but RMATs have a larger category of options to satisfy regulatory obligations, including “clinical evidence, clinical studies, patient registries, or other sources of real world evidence, such as electronic health records”\(^{303}\) and monitoring of treated patients.\(^{304}\) Finally, in an even earlier legislative speeding of clinical translation, the Affordable Care Act also created a “significant new abbreviated approval process for biological products.”\(^{305}\)

To continue to meet the dual objectives of protection and access, there must be ways to monitor regenerative medicine research, gather outcome data, and move from the bench to the bedside only when safety and efficacy have been adequately demonstrated. Maintaining the integrity of the scientific process is a duty of investigators, but as we have seen, it should not be left to investigators alone.\(^{306}\) When desperate patients and willing physicians seek access that can entirely circumvent regulatory oversight, it is difficult to envision how to keep any form of the clinical trial process intact and functioning well enough to gather generalizable data. Yet the highly individualized interventions being studied in regenerative medicine might easily lead patients, advocacy groups, and policymakers to undervalue generalizable knowledge, as they might fail to recognize how broadly applicable data can help one patient who needs a precisely targeted treatment.

C. A Right to Try Regenerative Medicine?

The individual-patient focus of almost all regenerative medicine research stands in contrast to the development of most other drugs and biologics. Designing a research intervention from each patient’s own cells seems like the ultimate in precision medicine, with the individual patient’s right to try an unproven product potentially appearing as the next logical step in modern health care.

The Charlie Gard case is, in our view, one of the first examples of a


\(^{304}\) See 21 U.S.C. § 356(g)(7)(C) (Supp. IV 2016); Duranske, \textit{supra} note 30, at 647.


\(^{306}\) See, e.g., \textit{Expanded Access Q&A, supra} note 99 and accompanying text; see also \textit{Expanded Access (Compassionate Use), supra} note 86 and accompanying text. continued...
desperate attempt to secure the right to try an unproven biotechnological intervention. It is also an example of how readily false hope can lead to over-optimism and misunderstanding about the promise of novel biotechnologies, especially when popular and social media amplify public attention. Charlie’s parents sought access to an intervention that was highly unlikely to benefit him, because it was not targeted to the mutation that affected him. But what if they had instead asked the researcher, and any company that worked with him, to produce an intervention targeted to Charlie’s mutation?

As we have seen, the legislative goals of the right to try movement were substantially furthered by sympathetic portrayals of terminally ill individuals like Charlie Gard and Abigail Burroughs. The public support these stories garner exemplifies how the experiences of “identified lives” raise awareness for the Charlies and Abigails of the world, but may fail to help those who are less attractive or simply less visible. The concept of identified lives explains why legislators, policymakers, and the public are more likely to advance and support legislation and policy initiatives addressed to problems raised in the name of identified victims. The Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act is a stark


308 See Hammond-Browning, supra note 9 and accompanying text.

309 See Bilefsky, supra note 307.

310 “Identified lives” are quite literally those to whom the public can assign names and faces. For more on this phenomenon and its effect on policy see Wendy E. Parmet, Valuing the Unidentified: The Potential of Public Health Law, 53 JURIMETRICS J. 255, 256-57, n.6 (2013) (citing Thomas C. Shelling, The Life You Save May Be Your Own, in PROBLEMS IN PUBLIC EXPENDITURE ANALYSIS 127, 129 (Samuel B. Chase ed., 1968), reprinted in THOMAS C. SCHELLING, CHOICE AND CONSEQUENCES 113, 115 (1984)) (“By focusing on identifiable victims, we often fail to appreciate risks that only arise at, and can best be addressed at, a population level.”).

311 See supra notes 1–6; see also Adriance, Complaint, supra notes 131–35.

312 Parmet, supra note 311, at 257.

continued . . .
example of this phenomenon.\textsuperscript{313}

Although sympathy for identified lives, such as those individuals named in the federal right to try law, is rooted in compassion, empathy, and respect, the concept has unintended consequences.\textsuperscript{314} At the individual level, in order to garner sympathy, identified lives must be attractive and deemed “innocent.” Abigail Burroughs did not cause her cancer; Charlie Gard was a helpless and adorable infant.\textsuperscript{315} Identified lives must be able to capture the attention, assistance, and sympathy of the medical establishment, payers, administrators, contributors to GoFundMe sites, and the general public.\textsuperscript{316} Other unidentified terminally ill patients without the means to launch a successful media campaign may never receive access to treatment, under the right to try law or otherwise.\textsuperscript{317} Especially if the decision to provide access—and the decision to help pay for access—result from public pressure, the appeal of identified lives exacerbates this disparity.\textsuperscript{318}

At the policy level, focusing on identified lives may divert disproportionate resources to rescue medicine efforts. The desire to rescue well-publicized but also genuinely vulnerable and desperate patients can turn the policy gaze away from the increasingly controversial goal of helping the public at large secure access to basic health care services, including prevention and treatment that could obviate the need for rescue.\textsuperscript{319} The identified lives narrative thus runs a more profound risk than differential rescue: it moves society away from addressing basic health care needs, and may even reframe those needs as meriting attention only when potential recipients are somehow

\textsuperscript{313} See generally supra text accompanying Right to Try Act of 2017, supra notes 172–73.

\textsuperscript{314} Parmet, supra note 311, at 258.

\textsuperscript{315} See generally discussion supra Sections I, III.A.

\textsuperscript{316} One early identified life was Jamie Fiske, an attractive toddler born in the 1980s with pediatric liver disease. Her father convinced Blue Cross/Blue Shield to cover liver transplants as part of standard health insurance. Clark Havighurst & Nancy M.P. King, Liver Transplantation in Massachusetts: Public Policymaking as Morality Play, 19 IND. LAW REV. 955–87 (1987). But when a Georgia newspaper attempted to gain public approval for an expansion of the state’s child health insurance assistance program by profiling what the paper thought would be a sympathetic family, the effort backfired spectacularly. Charity Scott, Belief in a Just World: A Case Study in Public Health Ethics, 38(1) HASTINGS CENTER REP. 16–19 (2008).

\textsuperscript{317} Van Groningen, supra note 183.

\textsuperscript{318} Id.; Parmet, supra note 311, at 257. While outside the scope of this paper, note that the narratives also largely reflect the experiences of white, middle-class men, women, and children whose access has been blocked for bureaucratic reasons. Media coverage and inclusion on those who do not have the means to afford access is sparse.

\textsuperscript{319} Parmet, supra note 311, at 258.

\textit{continued...}
“deserving.” This potentially places the right to try at odds with the basic public health goal of preventing illness and improving health, which the Affordable Care Act, Medicare, and Medicaid all seek to achieve by making basic health care affordable for most of those in need.320

The goal of right to try legislation is to provide individual patients with the right to request direct and rapid access to what they regard as potentially life-saving or life-prolonging interventions, as long as those interventions have survived testing in a small number of research subjects.321 This goal may simply be at odds with the goal of ensuring that enough data can be gathered to prove that a new drug or biologic is sufficiently safe and effective to be provided to patients as a treatment.

Furthermore, the right to try movement’s goal of rescuing individual patients by avoiding the clinical trial process altogether may contribute to the further erosion of overarching public health goals. Regenerative medicine research is an integral component—and beneficiary—of a large and complex system of scientific and medical research; its development of precisely targeted treatments for individual patients thus benefits society as a whole.322

Of course, the request to develop a targeted regenerative medicine therapy is not covered by any right to try law.323 But the expectation that science has the capacity to determine what might work for Charlie’s particular mutation, and find a treatment for him, lies at the heart of both the precision medicine initiative and the field of regenerative medicine. The potential for such a request is a natural extension of the individualized access championed by the right to try and the over-optimism that accompanies public discussion of regenerative medicine and the precision medicine initiative.324 These exaggerated expectations of potential benefit rarely materialize, and the inability to respond rapidly enough to the desire for ever-swifter responses may increase the distress of patients and families when their hopes cannot be fulfilled.

322 See generally supra text accompanying What is the Precision Medicine Initiative?, supra note 17; The Precision Medicine Initiative, supra note 18; and Ginsburg, supra note 19.
323 See generally supra text accompanying Van Groningen, supra notes 183–84.
324 For a discussion on those who oppose Right to Try based on their personal unsuccessful experiences with experimental drugs, see Dresser 2, supra note 72, at 1649–52.
VI. CONCLUDING REMARKS

While regenerative medicine holds significant promise for the future, scientific advances always take longer than we hope because progress must remain careful and deliberate to ensure that it is real and sustainable. 325 This means that both progress and its regulation are necessarily incremental; yet, as we have seen, incremental improvements in potential regenerative medicine products and their regulatory pathways may well appear insufficient to patients facing life-threatening illness. 326 The right to try movement has now succeeded in its quest for a federal right to try law minimizing FDA involvement in sales of investigational products outside the context of ongoing trials. 327 The legislation claims to advocate for a right to try experimental drugs, 328 but that right is already provided through many different pathways for expanded access and accelerated approval in existing FDA regulatory processes. 329 Without the FDA review provided by those pathways, patients who succeed in taking the right to try route could be more at risk of harm than optimal, without increased likelihood of either benefiting or contributing to generalizable knowledge about the drugs they try. 330

Advocates who support transparency and quicker access should consider pursuing reforms that address systemic issues beyond the FDA’s control, rather than undermining the FDA’s ability to monitor and assess safety and efficacy. Addressing those issues could improve existing processes further without pulling patients from the protection of FDA oversight.

For example, increasing fairness and transparency in research funding decisions, whether those decisions are made by industry, philanthropic organizations, or federal and state governments, may improve public discussion about research priorities and decrease the perception—and perhaps even the likelihood—of bias. 331 Working to ensure that research oversight bodies like IRBs exercise their authority with knowledge, flexibility, and wisdom, and with support adequate to the task, can also help move clinical research forward safely and speedily. 332

325 See supra Section V.B.
326 See supra Section II.
327 See supra Section III.C.
328 Id.
329 See supra Sections II.D, II.E.
330 See supra Section III.
332 For thoughtful discussions of these broader aspects of the oversight system continued . . .
Perhaps most fundamentally, looking beyond the “identified lives” served by the right to try, to preserve and improve the health of large numbers of “statistical lives,” could encourage a harder look at the access problem from a different vantage point. From this broader perspective, the question of access to experimental interventions could be regarded as the tail that is wagging the dog. The right to try should not enjoy a higher priority than better health care for all. That it has garnered so much attention may be attributable to society’s reluctance to accept that deaths we consider untimely cannot always be postponed.

Moving swiftly and freely from the bench to the bedside provides hope, and sometimes relief, to those with serious conditions, but it also promotes high prices and often poses very real risks of harming patients needlessly. Yet a more deliberate march toward clinical applications, though ensuring more predictable and sustainable knowledge gains at lower personal and social cost, seems to run counter to the profound American belief in the benefits of progress and the capacity of medical science to help us escape death. The trends represented by the right to try movement, on the one hand, and by promotion of careful scientific progress in and policy oversight of regenerative medicine, on the other, capture these contradictory mindsets well, but fail to offer guidance regarding best practices. In the long run, good science is best served by slow and steady work. It is too early to tell whether the right to try movement will produce more benefits than harms for patients, but there is no doubt that many patients, policymakers, and scientists will be watching closely.


333 See supra Section V.B.
334 Hans Jonas, Philosophical Reflections on Human Experimentation, 98 DAEDALUS 219, 245 (1969) (“Let us not forget that progress is an optional goal, not an unconditional commitment, and that its tempo in particular, compulsive as it may become, has nothing sacred about it. Let us also remember that a slower progress in the conquest of disease would not threaten society, grievous as it is to those who have to deplore that their particular disease be not yet conquered, but that society would indeed be threatened by the erosion of those moral values whose loss, possibly caused by too ruthless a pursuit of scientific progress, would make its most dazzling triumphs not worth having.”); see also JONATHAN KIMMELMAN, GENE TRANSFER AND THE ETHICS OF FIRST-IN-HUMAN RESEARCH: LOST IN TRANSLATION (Cambridge Univ. Press) (2009).