# ACTS:

# A GOOD START, BUT A FEDERAL ACT IS NECESSARY

Ellen A. Black*

## INTRODUCTION

Dr. Kent Brantley and Nancy Writebol, two American medical missionaries, traveled to Liberia on behalf of charitable organizations to help Liberians who were suffering from a massive outbreak of the Ebola virus.[1] In spite of their careful efforts to not catch the virus, both Brantley and Writebol became infected with Ebola, a virus with a fatality rate of up to ninety percent.[2] These Americans undoubtedly feared for their lives,

this dreadful disease.[3] However, prior to transportation from Liberia to Emory University Hospital in Atlanta, Georgia, the American missionaries received a dose of ZMapp, a drug composed of antibodies from Ebola-infected mice, in an effort to treat the missionaries.[4] Three weeks after

* Ellen A. Black is an Assistant Professor of Law at Belmont University College of Law. She wishes to thank her research assistants, Jamie Sawyer and Zachary Barker, for their valuable assistance with this article.

1. *See* Brady Dennis & Lenny Bernstein, *Two Americans Who Contracted Ebola in Africa Received an Experimental Serum*, WASH. POST (Aug. 4, 2014), http://www.washingtonpost.com/national/health-science/2014/08/04/dbc44a48-1c07-11e4-ae54-0cfe1f974f8a_story.html.

2. *See Ebola Virus Disease Fact Sheet*, WORLD HEALTH ORG. (Jan. 2016), http://www.who.int/mediacentre/factsheets/fs103/en/.

3. *See* Dr. Sanjay Gupta & Danielle Dellorto, *Experimental Drug Likely Saved Ebola Patients*, CNN (Aug. 5, 2014, 8:22 PM), http://www.cnn.com/2014/08/04/health/experimental-ebola-serum/ ( y thought he was going to die. It was the ninth day since the American missionary worker came down sick with Ebola in Liberia. His condition worsening by the minute, Brantl

4. *See id.*

being admitted to Emory, both missionaries were released and sent home, both totally cured of the Ebola virus.[5] The precise role that ZMapp played in curing the missionaries is unknown, but some medical experts agree that[6]

The drug ZMapp, which was administered to both missionaries, had

when it was administered.[7] Indeed, it had not been tested on humans prior

petition the FDA for quicker access to an unapproved drug, but the program has received increased criticism from its inception because it is too complicated and often takes far too much time for approval.[12]

time-consuming approval process and have quicker access to potentially life-[13]

These state acts allow a terminally ill patient the right to access an investigational drug that has completed initial safety testing, known as Phase I, but that has not been approved by the FDA.[14] The reasoning behind these acts is that terminally ill patients, like missionaries Brantley and Writebol, with the guidance and counsel of their physicians, should

The amount of time it takes a drug manufacturer to follow the above process to get a drug on the marketplace is extraordinarily long, ranging anywhere from 10 to 15 years, and the amount of money the drug manufacturer spends can easily exceed $1 billion.[26] Thus, drug manufacturers invest inordinate time and money in developing drugs that will ultimately safely and effectively treat patients. Yet in many instances, terminally ill patients, who may be unable to participate in clinical trials, need access to particular drugs that have not yet received approval from the FDA, in spite of the drugs demonstrating the possibility of curing the or improving their quality of life during their remaining days. For these patients, the FDA has an exception to the typical drug approval process that allows expanded access to investigational drugs.

*A. Compassionate Use*

To give terminally ill patients the possibility of accessing

typical drug approval

use or otherwise compromise the potential development of the expanded access use [28]

If a patient meets the above three criteria, then the drug company must decide the appropriate category of access for the patient.[29] Then an

IND or a protocol amendment to an existing IND.[30] The submission must also include a specific cover sheet referred to as Form FDA 1571 along with seven other pieces of information about the drug and its intended use.[31] There are three different categories of compassionate use for which a patient may be eligible: single patient; intermediate size; or treatment.[32]

1. Single Patient Access

For the single patient access category, patients may be eligible to receive an investigational drug for treatment by a

[33] For regular or emergency access, the

[34] In

add

[35] If these requirements are met, either a

28. 21 C.F.R. § 312.305(a).

29. *See infra* Part I.A.1-3.

30. *See* 21 C.F.R. § 312.305(b).

31. *See id.* Specifically, along with the cover sheet, the submission must include:

(1) The rationale for the intended use of the drug, including a list of available therapeutic options that would ordinarily be tried before resorting to the investigational drug or an explanation of why the use of the investigational drug is preferable to the use of available therapeutic options; (2) The criteria for patient selection or, for an individual patient, a description of the patient's disease or condition, including recent medical history and previous treatments of the disease or condition; (3) The method of administration of the drug, dose, and duration of therapy; (4) A description of the facility where the drug will be manufactured; (5) Chemistry, manufacturing, and controls information adequate to ensure the proper identification, quality, purity, and strength of the investigational drug; (6) Pharmacology and toxicology information adequate to conclude that the drug is reasonably safe at the dose and duration proposed for expanded access use (ordinarily, information that would be adequate to permit clinical testing of the drug in a population of the size

physician or sponsor[36] may submit the expanded access submission as previously discussed.[37]

Should a patient qualify for single patient access, the expanded access program contains specific safeguards in an effort to protect the patient from unknown dangers.[38] Specifically, the patient may only receive a single course of treatment of the investigational drug for an explicit duration unless the FDA approves otherwise.[39] If a patient uses an investigational drug for an extended duration, the FDA may require the sponsor to monitor the patient.[40] In addition, at the end of the treatment, the sponsor or physician must provide the FDA with the results of the treatment, including whether there were any adverse reactions to the investigational drug.[41]

and require immediate access to an investigational drug, in which case the compassionate use program allows these patients to obtain access without having to submit the written submission to the FDA.[42] Instead, the emergency access may be requested by electronic means, including telephone or facsimile, and the FDA may authorize the emergency access via telephone.[43] The physician or sponsor must describe how the expanded access meets the requirements of the compassionate use program and must

access submit a written submission as required by the program.[44]

2. Intermediate-Size Populations

The intermediate-size population category allows access to an

45

patients requests individual expanded access, the FDA may require the sponsor to consolidate the individual access requests to become an

36.
an individual or pharmaceutical company, governmental agency, academic institution, private
C.F.R. § 312.3.

37. *See* 21 C.F.R. § 312.310(b).
38. *See* 21 C.F.R. § 312.310(c).
39. *See id.*
40. *See id.*
41. *See id.*
42. *See* 21 C.F.R. § 312.310(d).
43. *See id.*
44. *See id.*
45. 21 C.F.R. § 312.315.

intermediate-size population.[46] The compassionate use program statute outlines three scenarios for which this type of access might be needed.[47] First, the drug may no longer be in the process of development because the disease or condition for which it was created is so rare and there were not enough patients to recruit for a clinical trial.[48] In other cases, the drug may be in the development stage, but the patients desiring access are not able to participate in the clinical trial for various reasons.

acces

not tracked or reported to the FDA.

3926, which requires only 8 types of information and 1 attachment.[68] According to the FDA, a physician can complete the new form in 45 minutes, compared to the 100 hours listed on the old form.[69]
revised application process for compassionate use appears to be a much-needed change for making the process less onerous for physicians and for getting patients quicker access. Even if the implementation of this
m,
it is very doubtful this sole change will completely resolve the problem of limited investigational drug access for terminally ill patients.

is the limited number of drug manufacturers who choose to participate in the program.[70] The FDA does not mandate that drug manufacturers provide expanded access to their investigational drugs, which from a free market standpoint correctly balances the need for voluntary innovation and quality research and development, but the result is significantly reduced participation.[71] And with so few drug manufacturers participating, the chance for terminally ill patients to access potentially lifesaving drugs is greatly diminished. So the issue becomes determining what inhibits drug manufacturer participation and whether it can be resolved.

There are several reasons why more drug manufacturers do not

ill patient is granted access to an investigational drug through the program and that patient experiences an adverse condition, it must be reported to the FDA.[72] The FDA can then consider that adverse condition when deciding whether to approve the drug for entry into the market.[73] Thus, drug

68. *See Individual Patient Expanded Access Applications: Form FDA 3926, Draft Guidance for Industry*, FDA (Feb. 2015), http://www.fda.gov/downloads/Drugs/GuidanceCompliance RegulatoryInformation/Guidances/UCM432717.pdf.

69. *Id.* App. at 8-9 (attaching new Form 3926 which states that the burden time for completing the form is 45 minutes).

70. Darrow, *supra* note 63, at 280-81.

71. *See generally id.*
compassionate use program due to practical difficulties).

72. 21 C.F.R. § 312.310(c)(2); *see also* Expanded Access to Investigational Drugs for

manufacturers are hesitant to participate in a voluntary program, when it the theory being that it is better for the individual terminally ill patient to sacrifice for the greater population.[74]

Another reason for drug manufacturers limited participation involves the time and resources that must be expended coupled with diminished financial rewards. First, as mentioned previously, to participate in the program, the drug sponsor (or the physician) must submit extensive paperwork.[75] A drug manufacturer may have very few employees, most of whom are solely dedicated to getting the drug to the marketplace, and may not have the manpower to complete the necessary application for expanded access. In addition, a drug manufacturer may not have a sufficient supply of the investigational drug to cover the hundreds or thousands of requests it may receive for early access.[76] Not to mention the significant costs that would be involved in supplying the investigational drug, when some patients would be unable to pay and insurance companies would likely not cover.[77]

external pressure, often times in the form of social media, enters the picture and a drug manufacturer receives immense pressure to supply the drug, the drug manufacturer may acquiesce and provide the drug even if it threatens the future success of the investigational drug.[78]

---

product labeling, we are unaware of any cases in which adverse event information obtained from expanded access use has resulted in denial of approval for a pro

74. *See* Seema Shah & Patricia Zettler, *From a Constitutional Right to a Policy of Exceptions: Abigail Alliance and the Future of Access to Experimental Therapy*, 10 YALE J. HEALTH POL Y L. & ETHICS 135, 184 (2010).

75. *See supra* note 66 and accompanying text.

76. *See* Rebecca Dresser, *The "Right to Try" Investigational Drugs: Science and Stories in the Access Debate*, 93 TEX. L. REV. 1631, 1646-47 (2015) (mentioning the high costs of e Thomas, *Company Creates Bioethics Panel on Trial Drugs*, N.Y. TIMES limited supply of such treatments, leading to anguished decisions over who should be given the

77. *See* Dresser, *supra* note 76, at 1646- [drug companies] to recover their costs, companies may be unable to manage the logistics involved in operating a treatment-

From the objective standpoint of the drug manufacturer, participation

obvious benefit. Commentators have suggested numerous ways to improve
o make it easier for
patients to participate in clinical trials by making the trials larger and more accessible to those located outside the testing region.[79] Another suggestion is to create a national institutional review board, which would not only

considered any and all other treatment options currently FDA approved.[107]

provide a recommendation or prescription for the investigational drug.[108] Lastly, the pa

[109]

The eligibility requirements previously discussed seek to protect the patient by ensuring all other medical options have been considered and that the patient is aware of the risks of pursuing the right to try path. However, the statutes also safeguard third parties, which include physicians,

investigational drugs. First, the act protects a physician from liability for any harm caused to a patient due to an investigational drug.[110] It also

M CODE § - -102 (Westlaw); Nev. Assemb. B. 164; N.D. S.B. 2259; Okla. H.B. 1074; S.D. CODIFIED LAWS § 34-51- ENN. CODE ANN § 63-6-302 (Westlaw); UTAH C A . § 58- -102 (Westlaw); A. CODE A

cannot use FDA regulations or any other reason to prevent an eligible patient from access under the right to try act.[117] This provision would apply to any state agent, which would include a large, broad group of people.

to the bump in approval ratings the acts will generate for those legislators.[123] They claim the acts will not result in terminally ill patients receiving better access. Rather, they claim the acts will do absolutely nothing and patients will gain no access; or, if terminally patients do gain access, the unapproved, untested drugs could cause more harm than good in

### *A. Critics Argue Right to Try Acts Are Preempted by Federal Law*

At the outset, critics argue that the right to try acts, although well-intentioned, will ultimately have no effect because they are preempted by federal law.[124] Specifically, the right to try acts allow terminally ill patients the right to access investigational drugs that have not received approval from the FDA to be sold to the public; rather, the investigational drugs have only completed Phase I Testing initial testing that shows the drug is safe.[125]
process, which requires a minimum of three phases of testing, and are also

permission from the FDA for a terminally ill patient to receive access to investigational drugs.[126] The right to try acts operate outside the constraints of the FDA. Instead, the acts place the decision-making among the patient, physician and drug manufacturer.[127] When conducting preemption analysis, it appears the critics have a valid argument that the right to try acts are preempted.

The Supremacy Clause of the United States Constitution provides the basis for preemption and states
United States

with a federal law, the federal law prevails and the state law is invalid to the extent it conflicts with the federal law.[129] The cornerstone of preemption jurisprudence is the purpose of Congress, coupled with the assumption that the historic police powers of the States were not to be superseded by federal laws unless that was the clear and manifest purpose of Congress.[130] While states have traditionally held the power to regulate matters of health and safety of the citizenry, the FDA has regulated the drug market for the last century as Congress has continued to expand the role of the FDA.[131]

There are two types of preemption: express or implied. With express preemption, Congress has clearly stated that the federal law supersedes the state law dealing with the same subject.[132] Yet with implied preemption, even though Congress has not explicitly addressed the issue of preemption, the state law is still preempted to the extent it conflicts with the federal law.[133] Implied preemption can occur in three different ways, referred to as obstacle, field, and conflict. Conflict preemption occurs if it would be impossible to comply with both the federal law and state law.[134] Field preemption applies if

system will be assumed to preclude enforcement of state law on the same [135] Obstacle preemption applies

an obstacle to the accomplishment and execution of the full purposes and objectives of Congress. [136]

When considering whether the right to try statutes are preempted by federal law, the analysis begins with determining whether there is express or implied preemption.[137] There is no express preemption for the regulation of unapproved drugs in the Federal Food, Drug, and Cosmetic Act, so the next step involves considering whether there is implied preemption.[138] At

129. *See* n v. De La Cuesta, 458 U.S. 141, 153 (1982).

130. Wyeth v. Levine, 555 U.S. 555, 565 (2009).

131. *See* Howard L. Dorfman et al., *Presumption of Innocence: FDA's Authority to Regulate the Specifics of Prescription Drug Labeling and the Preemption Debate*, 61 FOOD & DRUG L.J. authority to regulate certain aspects of the pharmaceutical industry and

should and do have authority to protect th

first glance, the right to try statutes are most likely impliedly preempted because it would be physically impossible to comply with both the state right to try statutes and the federal regulations, which would be considered conflict preemption.[139]

whether the U.S. Supreme Court would definitively find the state statute preempted is unknown, but should a drug manufacturer provide access to an investigational drug pursuant to a right to try act and outside the approval ofn

would be stifled and everyone would suffer from fewer drugs coming onto the market.

Although critics of the right to try acts consistently claim that drug manufacturer participation is not mandatory, which will result in

compassionate use program suffers from the same dilemma, i.e., drug manufacturers are not required to grant expanded access to patients, even if the FDA would approve the access.[148] Thus, both the right to try acts and

However, there are drug manufacturers who appear to genuinely desire to grant expanded access to patients under right to try acts, without the constraints of the FDA. For example, drug manufacturer Neuralstem has developed a highly promising drug to treat amyotropic lateral sclerosis

Garr, plans to make the treatment available now to the thousands of people who suffer from ALS.[149] He constantly hears from terminally ill patients who would like to receive treatment.[150] But the average life expectancy for an ALS sufferer is between two to five years after diagnosis, so Garr knows most of them will die before final FDA approval.[151]

Although drug manufacturers are not required to participate in either

least one drug company that is taking a novel approach to providing expanded access to patients. Johnson & Johnson, a large and influential drug maker, has created a bioethics panel that will review requests for access to a limited number of experimental drugs and decide how Johnson & Johnson should respond.[152] Overseeing this panel of doctors, ethicists, and patient advocates will be Dr. Arthur L. Caplan of New York University.[153]
that drug manufacturers may be increasingly more open to participating in expanded access programs.

148. *See supra* Part I.A.

14B

Critics accurately argue that the right to try acts do not mandate participation by any party. And although this voluntary participation requirement might limit the involvement of some patients, alternatively, required participation would likely result in harsher consequences, such as stifled drug innovation and increased insurance premiums.

### *C. Critics Argue Investigational Drugs Not Sufficiently Tested*

Another critique of the right to try acts is that they only require Phase I Testing before a patient may access the investigational drug.[161] A typical

testing before it may be offered on the marketplace.[162] As previously discussed, Phase I Testing is meant to test the safety of the drug, with the subsequent phases testing the safety and efficacy of the drug.[163] Critics argue that terminally ill patients who desperately seek an investigational drug will be given false hope that the investigational drug will cure them or improve their health condition; however, with the investigational drug having undergone such little testing, the likelihood of the drug meeting the [164]

lives, they may experience increased pain and suffering due to the side effects of the investigational drug side effects that were not shown during Phase I Testing.[165] These critics further argue that very few drugs that pass Phase I Testing ultimately receive FDA approval.[166] However, according to the Abigail Alliance, the nonprofit organization previously discussed that very drug

for cancer and other serious life-threatening illness that the Abigail Alliance for Better Access to Developmental Drugs pushed for earlier approval of in [their] fourteen year history is now approved by the FDA. Not one of the 30 drugs [they] pushed for earlier approval of failed to make it through the

161. Zettler & Greely, *supra*

162. *See supra* Part I.

163. *See supra* Part I.

164. Zettler & Greely, *supra*
they draw attention and resources away from efforts to develop effective treatments, engender confusion about the FDA pathway for compassionate use of medications, or create false hopes for

165. *See* Gorski, *supra* note 122 (empathizing that the only thing worse than dying of a terminal illness is dying of a terminal illness and suffering unnecessary complications as a result of an investigational or experimental drug).

166. *Id.*

A subset of this argument that critics have raised is how a pat
access pursuant to a right to try act could ultimately jeopardize whether the FDA approves the drug.[174] For example, if a terminally ill patient accesses an investigational drug pursuant to the right to try act and experiences an adverse reaction, th
approve the drug.[175] Once again, the drug manufacturer would be risking

offered to a broader population, to assist a smaller group of patients. Additionally, if drug companies participate in the right to try acts, they will expend time and resources away from clinical trials, which will also inhibit
[176]

These concerns of jeopardizing or delaying FDA approval of a drug to assist patients pursuant to right to try acts have some validity; however,

he could sit up, do his homework, and play board games with his family.[189] Although Josh sustained damage to his kidneys, just two weeks after receiving the oral form of brincidofovir, the adenovirus was gone.[190]

Patient Nick Auden was the catalyst for the passage of the right to try act in Colorado, although his ending is heartbreakingly different than Josh [191] In September 2011, Nick, the father of three children, was diagnosed with melanoma and told that he would probably die within a year.[192] Merck and Bristol-Myers Squibb had developed an immune-boosting anti-PD-
have helped his immune system shrink his cancerous tumors.[193] Initially, Nick did not qualify for a clinical trial because of his growing brain tumors, but eventually his brain tumors stabilized, thereby making him eligible for the clinical trial.[194]
again rendered him unable to participate in the clinical trial.[195]
doctors informed him that this was the end of the road and gave him six to nine months to live.[196]
through an individual compassionate use trial; however, neither Merck nor Bristol-Myers Squibb allowed outside clinical trials citing safety considerations as the reason for denying access.[197]
massive media campaign and began gathering signatures for a petition to the drug companies to allow him to receive the drugs, but unfortunately, Nick never received the treatment and passed away on November 22,

189. Elizabeth Cohen, *Drug Brings Remarkable Improvement for Boy*, CNN (Mar. 24, 2014, 11:36 AM), http://www.cnn.com/2014/03/21/health/cohen-josh-hardy/.

190. Elizabeth Cohen, *Once Near Death, Boy Is 'Getting Stronger Every Day,'* CNN (May 7, 2014 2:34 PM), http://www.cnn.com/2014/6(4ua9(0)-6(1)7(4)-6o(,)11(4)-3(e)7(a)-6(l)-3(t)-3(h)7(/)10(c(h).)11(r)-3( )-140(

2013.[198] In March 2014, Merck announced that it would allow expanded access to the medication through compassionate use in the United States to -threatening illnesses for [199]

Admittedly these patient stories are tragic and moving, but critics stringently disagree about using such stories to advance right to try acts that ensuring that drugs are both safe and effective and that could ultimately cause these patients more harm than good.[200] These critics claim that using such heart wrenching stories clouds the true issue, which is not quicker access for terminally ill patients but,

effective drugs more quickly available to the general population, not just a small subset.[201] Instead, the passage of right to try acts does nothing to solve the real issue and instead deceitfully gives false hope to terminally ill patients.[202]

## IV. IMPROVEMENT TO RIGHT TO TRY

Legal scholars have voiced considerable concerns about the likely effectiveness of right to try acts. Some of these concerns, such as federal preemption and manufacturer nonparticipation, appear to have some cogency. Yet, the popularity of the right to try acts, as evidenced by their unanimity and bipartisanship, should signal to the FDA (and accordingly Congress) that its compassionate use program needs significan

federal right to try act should be enacted.[203] To be sure, certain members of Congress have taken notice of the nationwide desire to allow terminally ill patients to have access to investigational drugs and have introduced legislation to that effect. An analysis of this proposed legislation reveals mpt at right to try acts in assisting terminally ill patients to access investigational drugs. To date, several federal bills have been introduced to Congress in response to the state right to try acts.

### *A. Compassionate Freedom of Choice Act of 2014*

One of the first bills, known as the Compassionate Freedom of Choice [204] The CFCA

access investigational drugs.[205] Importantly, the CFCA prohibits the implementation or enforcement of any law that prevents or restricts the importation, distribution, or sale of investigational drugs or devices for terminally ill patients.[206] Thus, the CFCA would allow states to enact right to try acts that would bypass FDA regulations. The CFCA only applies to terminally ill patients and requires the patients to execute an informed consent document.[207] The CFCA also prohibits the FDA from requiring the disclosure, collecting or reporting of any information related to the use of an investigational drug or device or any information related to the outcomes experienced by a terminally ill patient given an investigational drug or device.[208] Lastly, the CFCA protects from liability any person who manufactures, imports, distributes, prescribes, dispenses, or administers an investigational drug or device in any action under state or federal law for any injury arising out of use of the investigational drug, except in cases of gross negligence or willful misconduct.[209]

---

203. Adriance, *supra* ins a creature solely

204. Compassionate Freedom of Choice of Act of 2014, H.R. 4475, 113th Cong. (2014)