HHS Public Access

Author manuscript

Clin Cancer Res. Author manuscript; available in PMC 2020 August 10.

Published in final edited form as:

Clin Cancer Res. 2020 January 15; 26(2): 340–343. doi:10.1158/1078-0432.CCR-19-2015.

Understanding the Right to Try Act

Rajiv Agarwal, **Leonard B. Saltz**

Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY USA

Abstract

Cancer patients who have exhausted standard treatments often seek access to investigational drugs. Often, however, such access is unavailable, due to either the unavailability of a trial, lack of an open recruiting spot on the trial, even when the trial itself is open, or the inability of the patient to meet one or more trial eligibility criteria. In such settings patients often seek access to investigational agents outside of a trial. The federal "Right to Try" legislation was passed to create an additional avenue, different from the FDA's Expanded Access, or "Compassionate Use" Program, through which patients might obtain access to investigational drugs. A year after this legislation was signed into law, there remains both a limited awareness of it and a substantial degree of misunderstanding on the part of those who are aware of it. The law creates an avenue to greatly facilitate off-study administration when patient, physician and the manufacturer are all in agreement regarding the off study use of an eligible investigational agent. The law does not, however, empower a patient to impose a demand on either a provider or a drug manufacturer, nor does it require any entity to provide financial coverage for the drug. Eligible drugs are those which are not approved by the FDA for any indication, have completed a phase I trial, have an ongoing pivotal trial, and have an active registration plan. We review the specific law with commentary on its implications for improved access to investigational drugs outside of clinical trials.

Introduction

On May 30, 2018, President Trump signed into law what is commonly known as the Right to Try Act (RTT). Having completed the first year of this law being in effect, opinions vary widely in terms of support for this legislation. Too few in the cancer community and elsewhere, however, are aware of exactly what is in the law, what is not, what is clear and what is unclear, and ultimately, what the law means, and what it does not. In the review that follows, we address these issues as they relate to the rights and obligations of those who are providing cancer care and those who are receiving it. Since most involved in the cancer community have little or no formal legal background, we have broken down our analysis to explain the structure and text of the law in terminology and context that we believe will be understandable to medical providers and to our patients and their caregivers.

RTT is divided into three sections. Section 1 is the title, Section 2 is the law itself, and Section 3 is a commentary entitled "Sense of the Senate." We will discuss these sections in

Address correspondence to: Leonard B. Saltz, MD, Memorial Sloan Kettering Cancer Center, 300 E 66th Street, room 1049, New York, NY 10065, Tel: 646-888-4181, Fax: 646-888-4258, saltzl@mskcc.org.

The authors declare no potential conflicts of interest.

sequence, with commentary on what is clear and what we feel is left open to interpretation. Wording that is in quotations in the text below is taken verbatim from the Act.[1]

Section 1:

The official title of the law is the "Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017."

Section 2:

This is the actual law, and starts with a statement that this Act is, in general, an amendment to Chapter V of the Federal Food, Drug, and Cosmetic Act, and is encompassed in what is now section 561B of that Act, entitled "Investigational Drugs for Use by Eligible Patients." The Federal Food, Drug, and Cosmetic Act (or Chapter 9 of Title 21 of the United States Code) was established in 1938 by Congress and signed into law by President Franklin D. Roosevelt. It established the FDA's legal authority to oversee the safety and regulations of food, drugs, and cosmetics, with Chapter V focusing specifically on Drugs and Devices and Part E of that chapter detailing the general provisions and approval process related to new drugs and devices. It is within Chapter V, Part E of the Federal Food, Drug, and Cosmetic Act, that Section 561B (or Title 21 of the United States Code 360bbb-0) is the federal Right to Try Act (RTT).[2]

The opening line, prior to Section 1, introduces the legislation with the words "An Act to authorize the use of unapproved medical products by patients diagnosed with a terminal illness…." This indicates, and the subsequent text makes clear, that this Act does not apply to drugs which are already on the market for any indication, as these would no longer be "investigational" or "unapproved," and that patients with a potentially curable condition would not be eligible patients for consideration of treatment under this Act (see table 1).

Which Patients are Eligible?

Section 2, subsection (a)(1) outlines the definitions of an eligible patient. For a patient to be eligible, he or she must have been diagnosed with a "life-threatening disease or condition," have "exhausted approved treatment options," be "unable to participate in a clinical trial involving the eligible investigational drug," and must provide to the treating physician "written informed consent regarding the eligible investigational drug."

Criterion 1:

For the definition of "life-threatening disease or condition," a reference is made to Section 312.81 of Title 21, Code of Federal Regulations.

Criterion 2:

What is meant by the word "exhausted" in relation to approved treatment options is open to some interpretation. We interpret this to mean that an eligible patient must have received all approved treatments which could be safely administered. Thus, a patient choosing to pursue an investigational agent under this law would not be able to do so prior to receiving all available approved standard treatments.

Criterion 3:

The next area of subjectivity is the definition of “unable” to participate in a clinical trial involving the drug. We would suggest that “unable” could be characterized as either not meeting eligibility criteria for an otherwise available clinical trial (different tumor type, inadequate performance status or organ function, etc.) or not being geographically able to participate in the trial due to distance from home. Another caveat of this is that a patient would not be eligible if he or she were to decline participation in an available phase III trial in which the desired investigational drug is not given in all arms and instead, attempts to invoke this law to improve his or her odds of receiving the investigational drug.

Subsection (a)(1) also outlines information regarding the prescribing physician. The physician must be in good standing with the responsible licensing organization or board, and would be required to certify that the patient is “unable” to participate in a clinical trial with the investigational agent. Moreover, the law explicitly states that the physician must not be compensated directly by the manufacturer for prescribing the investigational drug.

Criterion 4:

An eligible patient must have “provided to the treating physician written informed consent regarding the eligible investigational drug.” This raises some important, and as yet, unanswered questions. What are the standards for this informed consent? Who is responsible for assuring that it is complete and correct? By definition, an investigational drug obtained through this legislation is not part of research, and so not under the responsibility an Institutional Review Board. Presumably the treating physician, who is charged in this legislation with obtaining written informed consent, would be responsible for the completeness and accuracy of that informed consent. Logically, the manufacturer would need to provide the patient and/or the treating physician with either the consent form from the phase I trial (addressed below), or the materials necessary to construct a consent form, such as the investigator brochure. Such materials, along with the pharmacy manual, would likely be required for an institution’s pharmacy to be able to process and prepare the investigational drug for administration. If an institution is already running or has run a trial with the investigational agent, then these materials are likely already in the institution’s possession. If, however, the institution has not previously worked with the drug, then materials will be needed which are often carefully guarded under confidentiality agreements and contracts. A company would presumably require these protections of its intellectual property before releasing an agent to a physician or institution.

Which Drugs are Eligible?

Next within Section 2 of the legislation, subsection (a)(2) defines what criteria must be met for a drug to be eligible under this Act.

First, the drug must be an investigational drug (as defined by existing statutes) for which a phase I trial has been completed. While the Act does not define “completed,” we would interpret it to mean that the critical information for which the phase I trial was undertaken is available to guide decisions by the patient and the physician. In that regard, we submit that a

reasonable definition of a "completed" phase I trial would include that: the study is permanently closed to new patient enrollment, the database is locked, the maximum tolerated dose (MTD), recommended phase II dose, and dose-limiting and non-dose-limiting toxicities have all been identified, and these data have been reviewed and vetted by the sponsor and submitted to the FDA. Without this, the proper dose for treatment, as well as the potential risks and benefits, could not reliably be provided and proper informed consent could not be obtained.

Second, subsection (a)(2) stipulates that an eligible drug is one "that has not been approved or licensed for any use." Thus, a drug that is approved (we interpret this as meaning FDA-approved) for *any indication* is not eligible under this Act. For example, an immune checkpoint inhibitor that is approved only for melanoma would not be eligible under this Act for a patient with pancreas cancer.

Furthermore, this subsection states that for a drug to be eligible, it must be "under investigation in a clinical trial that is intended to form the primary basis of a claim of effectiveness in support of approval or licensure." Such a trial would necessarily be a phase II or a phase III trial. It is also states that the drug must be the subject of an active investigational new drug (IND) application, and "the active development or production of which is ongoing and has not been discontinued by the manufacturer or placed on hold." These drug eligibility criteria are summarized in table 1.

Who Must Report What?

Next in the Act is subsection (b) of Section 2, which delineates the specific codes and regulations that do not apply to eligible drugs when supplied in compliance with RTT. This includes exemption from part 312 of title 21 from the Code of Federal Regulations,[3] which contains the requirements pertaining to the FDA's Expanded Access pathway to investigational drugs. Subsection (b) does specify, however, that manufacturers who sponsor drugs under RTT must still comply with the standard requirements for investigational new drugs regarding labeling, promotion, and recovery of direct costs noted in sections 312.6, 312.7, and 312.8(d)(1) of title 21 from the Code of Federal Regulations.

This is followed by subsection (c), entitled "Use of Clinical Outcomes." This states that "the Secretary may not use a clinical outcome associated with the use of an eligible investigational drug pursuant to this section to delay or adversely affect the review or approval of such drug…unless— the Secretary makes a determination …that use of such clinical outcome is critical to determining the safety of the eligible investigational drug; or the sponsor requests use of such outcomes." This provides some, but not complete, protection to a company that might be concerned that a drug-related adverse event could undermine the approval process.

Subsection (d) details that the sponsor shall submit an annual summary of the use of the drug under this act, including: "the number of doses supplied, the number of patients treated, the uses for which the drug was made available, and any known serious adverse events." The subsection also states that the Secretary is required to report an annual summary on the

FDA's website. Thus, while the intention clearly is not to have adverse events under this Act influence the approval process, a sponsor may have concerns regarding the risk that adverse events, and the degree to which these events will be made public, could influence the approval process. Such concerns could impact a sponsor's willingness to provide a drug under this Act.

No Liability

The next subsection of Section 2 is entitled "No Liability." The first clause of this subsection states that "no liability …. shall lie against the manufacturer or sponsor, prescriber or dispenser, or other individual entity" regarding an investigational drug administered under this Act, other than for "reckless or willful misconduct, gross negligence, or intentional tort under any applicable State law." The second clause states that "No liability shall lie against a sponsor, manufacturer, prescriber, dispenser or other individual entity for its determination not to provide access to an eligible investigational drug." Thus, RTT creates no obligation for a physician, manufacturer, or other entity to provide a drug under this Act. As such, it does not provide a patient with an actual *right* to try a drug, but rather facilitates the provision of an eligible drug to an eligible patient if both the physician and the sponsor agree to do so.

Section 3:

This section, entitled "Sense of the Senate," provides context for interpretation of the statute. It is not directly incorporated into amendment 561b of the Federal Food, Drug and Cosmetic Act, as Section 2 is. Of the seven statements included, we highlight three that we feel are most important.

First, "It is the sense of the Senate that… [this Act] does not establish a new entitlement or modify an existing entitlement, or otherwise establish a positive right to any party or individual." It should be noted that there is no specific guidance regarding who covers the cost of a drug or the costs of care associated with the use of an unapproved drug under this Act. Medicare and Medicaid do not pay for drugs that are not FDA-approved or compendium listed, and only pay for the care associated with administration of investigational agents in the context of a qualifying trial. Therefore, neither Medicare nor Medicaid are intended by this Act to cover the costs of an unapproved drug, the related care of administering that drug, or the treatment of any medical consequences of that drug. Often commercial insurance follows Medicare's lead. As such, payment for care under this Act, even if a pharmaceutical company were to provide an investigational drug at no charge, could pose a considerable impediment. The specific statement here that this Act "does not establish a positive right to any party or individual" emphasizes that the legislation does not empower a patient with an overt "right to try."

Additionally, the next clause in this section states that "It is the sense of the Senate that… [this Act] does not establish any new mandates, directives, or additional regulations," confirming that this legislation does not require any individual or entity to provide an investigational drug under this Act.

Finally, clause number five offers a cautionary note to those individuals who, under the emotional stress of coping with a terminal illness may lose perspective on what investigational agents can and cannot be expected to do: “It is the sense of the Senate that… [this Act] will not, and cannot, create a cure or effective therapy where none exists.”

Discussion

It is useful to consider what is left open to interpretation in RTT, what is not included, and how RTT differs from the FDA’s Expanded Access, or Compassionate Use programs. There are no guidelines in RTT for data monitoring or follow up on any individual patient. While the manufacturer must provide a report to the FDA as noted above, the collection and transfer of data from treating physician to the manufacturer is left to be determined by those parties. The treating physician has no reporting requirements to the FDA. The only role the FDA has in RTT is limited to receiving an annual report from the manufacturer and posting a consolidated report on their website.

The FDA is not involved in review or approval of a patient being provided investigational drug under RTT. If an eligible patient seeks an eligible drug, the determination of eligibility is made purely between the patient, the treating physician, and the manufacturer. This significantly differs from the FDA’s Expanded Access program, in which treating physicians submit an FDA Form 3926 for individual expanded access to investigational drugs and biologics, or FDA Forms 1571 and 1572 are required for other intermediate access treatment INDs and industry INDs. In addition, manufacturers who agree to provide drugs via expanded access must permit the FDA to refer to their industry IND for that drug by providing the FDA with a letter of authorization, or they must support a request by providing the treating physician with medical product information. With Expanded Access or Compassionate Use, the FDA must review all request forms and then determine whether treatment can proceed.[4] There is no such regulatory requirement within RTT.

In contrast to the role of the Institutional Review Board (IRB) for Expanded Access investigational drugs, in which the IRB is mandated to review expanded access protocols and consent forms, the IRB does not have any specific role under RTT. No forms need to be submitted or approved by an IRB under RTT, and the IRB does not have any obligations regarding the administration of a drug under the RTT mechanism. While RTT requires the physician to obtain written informed consent, it does not define requirements for such consent and does not require an IRB to review or approve a consent form.

RTT does not overtly state who determines if the requirements under this Act are being followed. As currently written, it would appear that these responsibilities belong to the manufacturer, given that the company must still provide general information to the FDA regarding the number of doses, number of patients, and adverse events related to a specific drug being provided under this Act. The process to determine the eligibility of a patient and drug, the specifics of the informed consent form, and reporting of data must be agreed upon by both manufacturer and treating physician for each case, and, as the law states, neither the treating physician nor manufacturer is liable for the administration or provision of the drug.

It is also noteworthy that RTT makes no mention of publication of results, so there is no guidance as to whether the outcomes of patients treated on RTT can be published or not.

Summary.

RTT creates a pathway for patients to receive an investigational drug outside of a clinical trial if, and only if, the patient is eligible, the drug is eligible, and the patient, drug manufacturer, and treating physician all agree that they wish to pursue this path. This legislation does not empower the patient to compel either a physician or a drug company to provide a drug under this Act. For the patient to be eligible, that patient must have a life-threatening disease or condition, must have exhausted standard care options, and must not have access to the drug on a clinical trial. For the drug to be eligible, it must *not* be approved by the FDA for any indication, must have completed a phase I trial, and must have an ongoing pivotal trial. The number of times in which all eligibility criteria for the patient and the drug are met, and all parties agree to proceed, will be limited, however, in such scenarios, RTT provides a pathway which is far simpler and requires far less consultation, documentation, and reporting than the FDA's Expanded Access Program, thus facilitating access to eligible investigational agents for eligible patients.

Acknowledgements:

R. Agarwal and L. Saltz supported in part by: P30-17 CA008748.

R. Agarwal supported in part by the Conquer Cancer Foundation of ASCO. This work was funded by an Anna Braglia Endowed Young Investigator Award in Cancer Supportive Care, supported by HELSINN. Any opinions, findings, and conclusions expressed in this material are those of the author(s) and do not necessarily reflect those of the American Society of Clinical Oncology® or the Conquer Cancer Foundation.

Abbreviations:

RTT	The Right to Try Act
FDA	Food and Drug Administration

References.

1. [Accessed 10-2-19] https://www.congress.gov/115/bills/s204/BILLS-115s204enr.pdf
2. [accessed 10-2-2019] https://uscode.house.gov/browse/prelim@title21/chapter9/subchapter5/partE&edition=prelim
3. [accessed 10-2-19] https://ecfr.io/Title-21/cfr312_main
4. Jarow JP, et al. (2017). "Ten-Year Experience for the Center for Drug Evaluation and Research, Part 2: FDA's Role in Ensuring Patient Safety." Ther Innov Regul Sci 51(2): 246–249. [PubMed: 28553566]

Clinical-Translational Relevance

Cancer patients who wish to receive investigational agents are too often unable to access them through participation in a clinical trial. Reasons may include lack of availability of a trial, lack of an available opening in a trial, or failure to meet one or more eligibility requirements. The Right to Try Law is one mechanism that can be considered by patients and clinicians who are seeking off-trial access to an investigational drug. However, the law is not well known and not well understood within the cancer community. We review this Federal legislation and discuss for which drugs and which patients it might be applicable, and where it does, and where it does not, offer a potential to facilitate patient access to promising investigational treatments outside of a study. We also compare and contrast it to available expanded access and compassionate use programs within the FDA and discuss relevant differences.

Table 1.

Summary of “Right to Try” Act

Requirements for Patient
a. Life-threatening condition
b. Exhausted standard treatment options
c. Unable to participate in an ongoing trial
d. Provide informed consent
Requirements for Drug
a. Phase I trial completed
b. Ongoing pivotal phase II or III trial
c. Active development plan to seek FDA approval
d. Not approved for any indication
Requirement for the Physician
a. Be in good standing with licensing organization or board
b. Certify that patient is unable to participate in a clinical trial involving the drug in question
c. Accept written informed consent from patient or authorized representative.
d. Receive no compensation from the Sponsor/manufacturer
Requirements for Sponsor/Manufacturer
a. Comply with standard procedures for investigational drug labeling, promotion, and recovery of direct costs.
b. Submit an annual summary of the use of the drug to the FDA, including number of doses supplied, number of patients treated, the uses for which the drug was made available, and any known serious adverse events.
Liabilities and Mandates
a. No liability for a manufacturer’s decision not to provide drug
b. No liability for a physician’s decision not to prescribe drug
c. No mandate for any entity to provide coverage for drug or associated care
d. No positive right established to any individual