VIEWPOINT

Promoting Patient Interests in Implementing the Federal Right to Try Act

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On May 30, 2018, President Trump signed into law the federal Right to Try Act of 2017,[1] providing patients with life-threatening conditions a pathway to access investigational drugs without authorization from the Food and Drug Administration (FDA). Ethicists, physicians, and patient groups have raised concerns about this type of legislation at the state and national levels given its implications for patients and the FDA's public health mission.[2,3] Now that "Right to Try" has become federal law, however, there is an opportunity to clarify statutory ambiguities that may help minimize the law's potential to cause harm and advance its goal of encouraging companies to provide preapproval access to investigational drugs.

What Does the New Law Do?

The FDA has long provided seriously and terminally ill patients the ability to access investigational drugs and devices through its Expanded Access program,[4] first codified in regulations in 1987. Unlike Expanded Access, Right to Try applies only to investigational drugs and does not task the FDA or institutional review boards with ensuring that the risks and benefits of treatment are reasonable (**Table**). Instead, the investigational drug must simply have completed phase 1 testing and be under active development by a manufacturer. The law additionally exempts eligible investigational drugs provided to eligible patients from compliance with other FDA requirements for investigational use, such as strict standards for informed consent and adverse event reporting, but does mandate compliance with provisions regarding investigational labeling and restrictions on promoting and charging for investigational products. Further, the Right to Try Act grants various expansive immunities from liability not applicable to clinical trial participation or Expanded Access. As described by its primary Congressional sponsor, the law "intends to diminish the FDA's power over people's lives."[5]

What Is Next?

It is typical for new legislation to be interpreted through agency regulation and guidance. In the context of Right to Try, the FDA should clarify at least 4 areas of ambiguity by adopting interpretations that will maximally advance the interests of patients.

Eligible Patients

To be eligible for access under the Right to Try pathway, the law requires that patients be "unable to participate"[1] in a clinical trial involving the investigational drug. Defining such inability to include only patients who do not meet the eligibility criteria for a trial within a reasonable geographic vicinity will avoid interference with clinical trial enrollment. This is critical to developing the safety and effectiveness data essential for product approval, which is the best way to help patients in need.

Table. Comparing the Text of Expanded Access Regulations and Federal Right to Try Act

	Expanded Access	Right to Try
Patients with serious conditions eligible	✓	
Patients with life-threatening conditions eligible	✓	✓
Exhaustion of approved treatment options	✓	✓
Consideration of clinical trial eligibility	✓	✓
FDA authorization of access	✓	
IRB authorization of access	✓	
Specified content of informed consent	✓	
Requirements for investigational labeling	✓	✓
Restrictions on promotion	✓	✓
Restrictions on charging by sponsor	✓	✓
Completed phase 1 testing		✓
Active development ongoing		✓
Immunity from liability		✓
Specification of acceptable use of clinical outcome		✓
Safety reporting to sponsor	✓	
Rapid safety reporting to FDA	✓	
Annual safety reporting to FDA	✓	✓
Public posting of information by FDA		✓
Sponsor compelled to provide access		
Insurers compelled to reimburse		

Abbreviations: FDA, Food and Drug Administration; IRB, institutional review boards.

The law also requires that patients provide "written informed consent,"[1] while stating that FDA regulations governing informed consent do not apply. Patients, physicians, and sponsors will need guidance on what satisfies the statutory standard. At a minimum, patients should be informed of the drug's investigational status; anticipated risks and benefits; statutory limitations on the liability of a sponsor, manufacturer, prescriber, dispenser, and "other individual entity"[1]; and the existence of Expanded Access as an alternative pathway to secure access to investigational products.

Eligible Drugs

For investigational drugs to be eligible for Right to Try, the law requires that a phase 1 study be completed and active development be ongoing. This is ambiguous, however, because phase 1 studies vary significantly in design and approximately 40% fail to progress to phase 2.[6] The FDA should clarify that (1) its regulatory definition requiring that a phase 1 study "permit the design of well-controlled, scientifically valid, Phase 2 studies" applies in this context and (2) active development means that the sponsor has submitted a phase 2 protocol to its

Investigational New Drug (IND) application file.[7] The FDA should also monitor the continuation of active development for the duration of use under this pathway. This approach could help ensure that Right to Try is not used as a preapproval marketing tool or a substitute for clinical study of drug safety and effectiveness.

Reporting Requirements

Right to Try expressly requires annual reporting by the manufacturer or sponsor of at least 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."[1] However, the statute does not prohibit the FDA from seeking additional information, such as patient demographics, whether patients were charged for the drug, and if so, how much. Doing so would enable the FDA to better serve patient interests and assess implementation of the law.

These goals can also be advanced by clarifying the requirements around adverse event reporting. Although drugs provided under the Right to Try pathway must be the subject of an IND application, the law exempts Right to Try uses from most requirements imposed by IND regulations. However, the IND sponsor retains its obligations to comply with all IND requirements independent of the Right to Try use. The FDA should clarify that the requirement for IND sponsors to rapidly report certain safety information "from clinical trials or any other source" includes information obtained from Right to Try uses.[7] To facilitate this reporting, the FDA could encourage sponsors to seek agreements from physicians to share adverse event information as a condition of providing a drug for a Right to Try use.

Intersections With Expanded Access

Given concerns about Right to Try, the FDA should take steps to facilitate Expanded Access as the preferred pathway for accessing investigational drugs outside clinical trials. Because the FDA authorizes more than 99% of Expanded Access requests, generally within a matter of hours or days, patient access will not be reduced by this approach, and in July 2018 testimony to Congress, the FDA commissioner indicated that the agency is exploring further simplification of the process. Additionally, under this pathway, the FDA can recommend improvements (eg, dosing regimens), preauthorize charges pursuant to the IND regulations, and better oversee informed consent and patient safety.[8]

To assuage manufacturers' potential concerns about Expanded Access, the FDA could formalize its current practice of using clinical outcomes from Expanded Access only when a sponsor requests it or the information is critical for evaluation of a drug's safety,[9] precisely the restriction imposed for Right to Try. The FDA also could emphasize that the additional oversight associated with Expanded Access can provide important context for its determination of whether and how to use clinical outcomes in its decisions about a product. Similarly, the FDA could emphasize that there have been no reported product liability cases involving use of a drug under the Expanded Access pathway, even without the express limitations on liability exclusive to Right to Try. In the case of such a lawsuit, FDA and institutional review board authorization of Expanded Access uses may offer an important indication of reasonableness.

Conclusions

The recommendations suggested here are not intended to render Right to Try indistinguishable from Expanded Access; it is clear that lawmakers intended to create a new, distinct pathway. Instead, these recommendations may help prevent the rise of a market in unproven therapies and preserve the ability to collect critical information about investigational drugs, while enabling access as the law intended (but did not guarantee). Additionally, these recommendations are not intended to be exhaustive. For example, rigorously monitoring and enforcing the statutory requirement that manufacturers may charge only for the direct costs of their drugs under Right to Try also may help to deter those who would seek to exploit vulnerable patients.

Ultimately, one of the most important actions the FDA can take to balance access with the need to develop rigorous evidence about the safety and effectiveness of new drugs could be to encourage sponsors to design trials that include the broadest possible patient populations consistent with participant safety and scientific integrity. This approach could help to minimize the demand for preapproval access under either the Right to Try or Expanded Access pathway.

ARTICLE INFORMATION

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