VIEWPOINT

The Federal Right to Try Act of 2017—A Wrong Turn for Access to Investigational Drugs and the Path Forward

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In 2017, President Trump said that "one thing that's always disturbed"[1] him is that the US Food and Drug Administration (FDA) denies access to experimental drugs even "for a patient who's terminal…[who] is not going to live more than four weeks [anyway.]"[1] Fueled by emotionally charged anecdotes recirculated by libertarian political activists, 38 states have passed Right to Try laws. In 2017, the US Senate approved a bill that would create a national law (**Box**).[2] As of December 2017, the US House of Representatives was considering the bill.

Although the FDA has an expanded access option for utilizing experimental drugs outside of clinical trials, Right to Try laws create an alternative pathway that bypasses the agency. Moreover, the term "Right to Try" is a misnomer: the legislation creates a right for a patient to ask a company to provide a product, the same right that currently exists.[3] As is the case with the FDA program, companies are not obligated to provide access.

The proposed federal Right to Try legislation[2] sets the threshold for patients to access investigational drugs at the completion of phase I (dosage-determination) trials, grants companies and physicians broad immunity from liability, and largely blinds the FDA to safety or efficacy data from these therapeutic attempts. Such changes would upend the agency's expanded access program, which has worked successfully for decades to provide patients who are seriously ill and without therapeutic options access to investigational drugs and still assure the safety and efficacy of new drugs before these products gain marketing approval. The legislation does not solve actual concerns, such as lack of knowledge that the program exists and the very limited supply of many investigational products.

A 2016 review[4] of 10 years of FDA records found that the Center for Drug Evaluation and Research receives over 1000 expanded access applications per year. The FDA reviews such requests in days—or hours when an emergency so requires—and approves over 99%.[5] This is no mere rubber stamp of proposals: unlike individual physicians, the FDA has access to proprietary data about the risks and benefits of the investigational product or others in the same class. In some instances, the agency can improve the proposed treatment via modifications of drug dosage, dosing schedule, or other aspects.[6]

Eliminating the FDA's review of expanded access requests is perilous, because most of the drugs that succeed in phase 1 trials turn out to be too unsafe or ineffective for clinical use. Phase 1 trials are intended to find a reasonable dosage of a drug in a small number of subjects, who may not even have the disease in question. About two-thirds of successful phase 1 drugs will fail as they proceed to phase 2,[7] and even more will fail at phase 3. Given the low odds that an investigational drug will succeed, patients benefit from the agency's review. Under expanded access, the FDA does not set a threshold for when patients may access investigational drugs: the agency has permitted access to products that are in phase 1 testing, and well as in preclinical (nonhuman) testing. Such a case-by-case approach is appropriate and should be retained.

The federal Right to Try legislation[2] creates immunity for physicians who prescribe investigational agents and companies that dispense them even if they act negligently in certain circumstances or if their actions may have been influenced by financial conflicts of interest. In our view, such broad liability protection is not needed. If Congress, nonetheless, seeks to provide immunity, it should be premised on FDA review of the protocol and the patient having received independent advice from a physician who has no economic or reputational stake in the investigational drug.

Under the expanded access option, pharmaceutical companies can only charge shipping and manufacturing costs for their investigational products. The Senate bill[2] has no such restrictions, opening the door for companies to profit from selling unproven drugs. The FDA policy of limiting what companies can charge for their investigational products provides an important incentive for companies to complete clinical trials.

In addition, the bill includes no mechanisms or incentives for insurance coverage, which would be essential if companies were to charge, as private and government health insurance plans generally exclude coverage for experimental treatments. Instead, the Senate bill creates a very real opportunity for vulnerable patients to be taken advantage of financially. Furthermore, 19 state Right to Try laws specifically allow insurers to deny hospice coverage to patients who try investigational products via the Right to Try pathway: 5 of those laws also allow denial of coverage for home health care (as does the law of an additional, sixth state, which does not have the hospice provision). Three of the 19 state laws allow, in addition to denial of both hospice and home health care coverage, denial of insurance coverage altogether for up to 6 months after treatment with the investigational product ends. One state law allows denial of home health care and insurance coverage without mention of hospice coverage.[8] If investigational products are to be treatment options—as advocates of Right to Try laws intend—then federal law should prohibit insurers from

Box. **Provisions of Senate Bill 204, The Right to Try Act of 2017**[2]

- Applies to patients diagnosed with a life-threatening disease or condition who have exhausted treatment options and are unable to participate in a clinical trial.
- Provides an alternative to current expanded access procedures, which include US Food and Drug Administration (FDA) review of individual protocols and limit pricing of such drugs.
- Requires patient's informed consent and certification by the treating physician.
- Prohibits the certifying physician from being directly compensated by the drug manufacturer, but allows ownership of company stock and/or charging patient treatment fees.
- Applies to drugs for which a phase 1 clinical trial has been completed and are undergoing further testing but have not yet been approved by the FDA.
- Prohibits the FDA from using outcomes data to adversely affect approval or review of the drug unless the Secretary of the Department of Health and Human Services deems that such data are "critical to determining the safety of the eligible investigational drug"[2] or the sponsor requests its use.
- Immunizes from liability manufacturers, physicians, and pharmacies (as long as conduct is not reckless or willful misconduct, gross negligence, or an intentional tort).
- Affirms manufacturers, prescribers, and dispensers are able to not provide access to an investigational product.

discriminating against patients who use such products, as these state laws allow.

In our view, there are better ways for the federal government to improve access to investigational drugs. For example, the FDA Reauthorization Act of 2017[9] identified regulatory requirements for institutional review board (IRB) oversight of expanded access applications for possible streamlining. Subsequently, the FDA announced that expanded access applications can be reviewed by a designated member of an IRB, not the full board, as previously required.[10] Other modifications that improve the expanded access process should be considered, as long as FDA oversight is maintained.

Congress and the FDA should also continue to examine ways to increase enrollment in clinical trials so that patients can access investigational products while contributing to the production of generalizable knowledge. To enroll patients who would otherwise have no options other than expanded access, trial reforms may include changes in where trials are located, inclusion and/or exclusion criteria, and the costs for patients to participate. Such changes would fit with current federal efforts to encourage the production of data that better predict clinical outcomes of approved therapies in the "real world."

Although the emotional appeals on behalf of patients who are terminally ill and concerns about government intrusions are understandable, the proposed federal Right to Try legislation would not create an alternative and realistic mechanism for preapproval access to investigational drugs. Rather, by removing the FDA from the process, companies would have fewer incentives to provide their investigational products to very sick patients. Instead of undercutting the FDA, Congress should focus on pragmatic reforms. Efforts to expand patient access to investigational medical products, however well intentioned, should not harm drug development or clinical trials.

ARTICLE INFORMATION

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REFERENCES

1. Mezher M. Trump signals support for 'Right-to-Try' movement. Regulatory Focus. 2017. http://www.raps.org/Regulatory-Focus/News/2017/02/02/26759/Trump-Signals-Support-for-Right-to-Try-Movement/. Accessed December 1, 2017.

2. *Right to Try Act of 2017, S 204*, 115th Cong, 1st Session (2017). https://www.congress.gov/bill/115th-congress/senate-bill/204?r=1. Accessed October 26, 2017.

3. Zettler PJ, Greely HT. The strange allure of state "right-to-try" laws. *JAMA Intern Med*. 2014;174(12):1885-1886.

4. Jarow JP, Lemery S, Bugin K, Khozin S, Moscicki R. Expanded access of investigational drugs: the experience of the Center of Drug Evaluation and Research over a 10-year period. *Ther Innov Regul Sci*. 2016;50(6):705-709.

5. Jarow JP, Moscicki R. Impact of expanded access on FDA regulatory action and product labeling [published online December 1, 2017]. Ther Innov Regul Sci. doi:10.1177/2168479017707800

6. Jarow JP, Lemery S, Bugin K, Lowy N. Ten-year experience for the Center for Drug Evaluation and Research, part 2: FDA's role in ensuring patient safety. *Ther Innov Regul Sci*. 2017;51(2):246-249.

7. Waring MJ, Arrowsmith J, Leach AR, et al. An analysis of the attrition of drug candidates from four major pharmaceutical companies. *Nat Rev Drug Discov*. 2015;14(7):475-486.

8. Folkers KM, Kearns L, Bateman-House A. Senate passes a "right to try" bill; harm to patients comes next. *Cancer Lett*. 2017;43(31):17-21.

9. *FDA Reauthorization Act of 2017, HR 2430*, 115th Cong, 1st Session (2017). https://www.congress.gov/bill/115th-congress/house-bill/2430. Accessed December 1, 2017.

10. Gottlieb S. Expanded Access: FDA Describes Efforts to Ease Application Process. FDA Voice, 2017. https://blogs.fda.gov/fdavoice/index.php/2017/10/expanded-access-fda-describes-efforts-to-ease-application-process/. Accessed December 1, 2017.