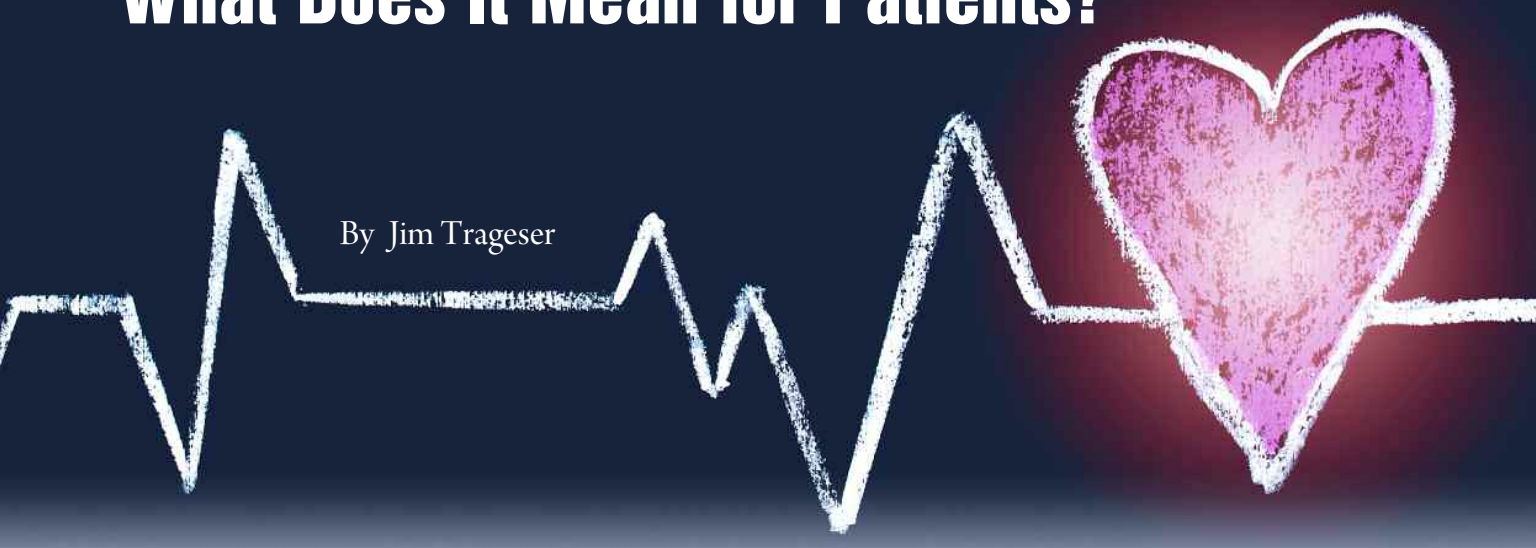
The "Right to Try" Law: What Does It Mean for Patients?



By Jim Trageser

While this new law offers hope for terminally ill patients who have exhausted approved treatment options, the jury is out on whether it will help patients until more questions are answered.

ON MAY 30, 2018, President Trump signed into law SB 204, the "right to try" law allowing terminally ill patients the legal right to request access to experimental drugs not yet approved by the U.S. Food and Drug Administration (FDA). While much discourse has been made by activists on both sides of the political debate surrounding the new law, the few neutral analyses indicate the law is more of a symbolic victory for "right-to-try" advocates that will likely have relatively small practical ramifications for patients and their families.

The uncertainty of its value to patients is due to the fact that even though Congress approved the bill and the president signed it, until lawsuits are filed and the courts decide exactly what the law means, the legal landscape surrounding it will remain murky — leaving many pharmaceutical companies reluctant to take part.

Unfortunately, relatively little is written about the new law in the medical or legal literature. Most of the analysis is found in political outlets, both conservative and liberal, with both claiming to represent the true interests of patients and their families.

What the Law Says

The law, formally known as the "Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017," removes certain federal regulations regarding unapproved drugs for terminal patients who have exhausted all existing approved options.[1] It amends Chapter V of the Federal Food, Drug and Cosmetic Act that allows a patient who has been diagnosed with a terminal illness by a licensed physician to apply for access to unapproved drugs. The patient must sign a letter of consent, accepting the risks inherent to using a nonapproved drug, and only drugs that have passed Phase I clinical trials can be requested or provided.

The law specifically does not require pharmaceutical manufacturers to provide drugs to patients who request them. Further, while the law stipulates manufacturers and physicians are largely protected from being sued for providing or prescribing an experimental drug under the law, it does allow lawsuits for reckless and willful misconduct, but it does not define what constitutes either.

Another provision in the law says, except in narrowly defined cases, the outcome of a patient's use of the drug will not be used by FDA when weighing approval of a drug once its clinical trials are completed. The law also directs the Department of Health and Human Services (HHS) to report to Congress each year on how many requests are made under the law, and it requires pharmaceutical companies to provide that information to the HHS.

Left unaddressed is whether any such drug requested and provided will be covered by a patient's insurance carrier.

What Supporters Say

Supporters argue it is cruel and makes no sense to deny experimental drugs to terminally ill patients. They contend if doctors are allowed to prescribe drugs to let patients take their own lives in some states (known as medically assisted suicide), then doctors should be allowed to prescribe drugs that may save or prolong their lives.

Proponents also argue that FDA's approval process can take years to complete (about 10 years, on average[2]), and any drug that has passed Phase I clinical trials is known to not be immediately dangerous (i.e., poisonous). They also point out that 38 states already have right-to-try laws on the books, and they argue the federal law evens the playing field for patients living in the other 12 states.

What Opponents Say

Critics argue the law was a political stunt designed to generate positive headlines without doing anything to truly help patients. They point to an existing FDA regulation known as the expanded access rule (sometimes called compassionate use)[3] that has already allowed almost 9,000 patients to receive experimental drugs that have passed Phase I approval. Opponents of the law also argue that allowing patients to take experimental drugs outside the normal testing protocols will hamper the ability of pharmaceutical companies to derive meaningful knowledge from controlled tests.

Critics such as Steven Joffe, MD, professor in medical ethics and health policy at the University of Pennsylvania's Perelman School of Medicine, have expressed concern that the law may be a first step in deregulating the drug industry and exposing patients to dangerous, untested drugs.[4]

What Lawyers Say

Almost a year after its passage, there is surprisingly little written on the right to try law in legal journals. In one article published in the *American Society of Clinical Oncology,* law professor Thaddeus M. Pope of the Mitchell Hamline School of Law in Saint Paul, Minn., interpreted the law as a somewhat more streamlined application process than FDA's expanded access rule, but requiring less disclosure to the physician by the drug manufacturer. He argued this is a trade-off (less knowledge to guide their treatment of patients) that many physicians may find troubling.[5]

In June, the Connecticut law firm Shipman & Goodwin LLP analyzed the law in a white paper that included bullet points of incentives and risks for drug companies. Incentives included generating good will and social capital, gaining additional data and increasing brand awareness for any new drug. But the law firm cautioned the law is vague on what defines "written informed consent" and "life-threatening disease or condition."[6]

Will Insurance Cover It?

The pro right-to-try website, righttotry.org, has a frequently asked questions section that states the law will work the same as FDA's expanded access program for insurance coverage. In short, it's up to insurance companies, including Medicaid and Medicare, to determine whether to cover the cost of experimental treatments.[7]

But, this is also true when doctors prescribe a drug "off label" (to treat a disease for which the drug is not FDA approved). For a drug to receive approval for treating a new condition, it has to complete Phase II and III trials for that disease. Reviewing the roster of ongoing trials at clinicaltrials.gov, many drugs already on the market are back in additional trials to see if they are effective at treating other, often related conditions or diseases.

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Still, any drug already on the market would not be governed either by FDA's existing expanded access policy or the right to try law, even if it is undergoing additional clinical testing. A physician can prescribe a drug legally even though an insurance company may decline to cover it. (One caveat to this is federal law requires Medicare to cover off-label cancer prescriptions if there is evidence to support such use.[8])

How the FDA Approval Process Works

When a pharmaceutical company or academic research institution discovers a new substance or develops a new compound

that it believes can treat a disease or other condition, it files an investigation new drug (IND) application with FDA for permission to conduct human tests. With the IND, researchers must submit results of any lab tests they've conducted, often introducing the new compound into test tissue with the virus, bacteria or cancer they're looking to treat, or in some cases testing it on animals. If the new compound appears safe and shows promise for treating or curing a disease, it will be approved for clinical testing, which has four phases. Phase I, as mentioned, is designed to study the drug's safety to determine whether it will cause immediate side effects when given to human patients. FDA says about 70 percent of prospective drugs pass Phase I, which normally involves two dozen to as many as 100 volunteers, and lasts a few months.[9]

Phase II of clinical testing generally takes a few months to a couple of years to complete. This is where the rubber starts to meet the road. The purpose is to determine whether the drug actually treats or cures the disease in question, and if so, in a safe manner. Depending on the disease or condition targeted, the manufacturer or university conducting the research will recruit as many as a couple of hundred volunteers who have the disease or condition. The research typically divides research subjects into two groups with some receiving the new drug and others a placebo. Patients have their condition monitored over a course of months or even years, and are observed for any side effects. Roughly one-third of drugs submitted for Phase II testing pass. (This means two-thirds of drugs available under the right to try law, as well as FDA's existing expanded access rule, will eventually fail to do what they were intended to do, or will pose so much adverse risk that they are deemed unsafe.)

Phase III is a continuation of Phase II. The volunteer pool is expanded to up to several thousand test subjects. The drug continues to be studied to see if it is effective in treating a disease or condition. Phase III can last as long as four years, and during this period, researchers watch for any long-term adverse reactions that may not have manifested during the earlier, shorter phases. Only about 25 percent to 30 percent of drugs submitted for study pass Phase III. (Thus, of all potential drugs submitted for FDA clinical trials, only about 7 percent will ever make it to market.)

Phase IV is an ongoing study, again looking to ensure the new drug is safe over the course of years. Phase IV trials can continue even as the drug is submitted to FDA for permission to market and sell, and even after approval.

Once Phase III clinical trials are successfully completed, the manufacturer then submits a new drug application to FDA. FDA then has up to 10 months to review all study results and any other documentation to decide whether the drug can be sold. (Drug companies often express frustration about the length of time it can take to complete preclinical testing and the three required phases of FDA clinical tests before gaining approval on new drugs. This is because a patent for a new drug lasts only 20 years, and it usually takes eight to 10 years from developing a new drug to getting it on the market. Once the patent expires, competitors are free to sell generic versions.)

Even after a drug is approved for marketing and sale, FDA continues to monitor its safety.

What It All Means

For patients whose prognosis is grim, who have exhausted all existing treatments and for whom only a drug not yet available through normal channels offers any hope, the right to try law may offer a last chance at a cure and a shorter process to gain access to experimental drugs than FDA's expanded access program. But, with many questions about liability, cost recovery and use of data generated by out-of-trial use unanswered, it is unclear how many pharmaceutical companies will be willing to honor requests for experimental drugs — no matter how urgent the plea. Until more data is available about how many patients and their physicians request new drugs, and whether those requests are honored, it will be impossible to know whether the law is accomplishing the goals of its supporters.

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