Vermont Ethics Network

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Right to Try Legislation – S.258

We live in a time of tremendous capability to treat and cure disease. Yet with all our advancements in medicine and technology, there are still times when despite our best efforts and available therapies, we are unable to slow—let alone reverse—the outcome of advancing terminal disease. Over the past few years, "right-to-try" legislation has been proposed in a growing number of states to enable terminally ill patients who have exhausted all other therapeutic options quicker access to unapproved, experimental drugs, biologics and devices. Many would argue why not? What do these patients have to lose and there is the potential to prevent a real tragedy. Others, while sympathetic, are not as convinced about the benefit of such policies and have expressed concern about the promise of false hope and the potential harms that could be inflicted on sick and vulnerable patients. The Vermont Ethics Network takes no position either for or against any proposed "right-to-try" legislation. Rather, we see our role as that of providing information and opportunity for discussion about the ethical considerations that surround this issue.

BACKGROUND

FDA approval for experimental drugs typically occurs in 3-phases:

- Phase I trials – small (20 – 80) healthy volunteers, primarily for assessing safety and dosage ranges.
- Phase II trials – larger (100 – 300 patients), designed to show early evidence of efficacy in patients that the drug is intended to treat.
- Phase III trial - much larger (may involve hundreds or thousands of patients), designed to show that the drug is effective compared to a control or the standard treatment.

"Right-to-Try" laws are intended to permit terminally ill patients the ability to request access to investigational drugs or devices that have only completed Phase I trials but have not yet been approved by the FDA.

CURRENT DEBATE

The current debate centers around whether the gain in providing terminally ill patients with a slim chance at prolonging life is worth possibly endangering a process designed to protect the public health and ensure the development of safe and effective medicines. Supporters argue that patients have the right to determine what risks they are willing to take at the chance to save their own lives and "right-to-try" laws seek to provide an accelerated timetable for gaining access to experimental drugs by removing federal regulatory barriers. Opponents argue that "right-to-try" laws expose vulnerable patients to unproven and potentially harmful drugs or other products without any expert safeguards or oversight (ethics or IRB

review), thereby undermining current processes intended to protect the public health and patient welfare.

FDA EXPANDED ACCESS

Expanded access sometimes called "compassionate use" refers to the existing FDA process for allowing a physician to request access for a terminally ill patient to an investigational agent prior to FDA approval. The goal is to introduce some degree of flexibility into the regulatory process and allow patients with no other treatment options a chance to try therapies they may not otherwise be able to access. Criticism of the FDA's expanded access is that the paperwork is unnecessarily lengthy and burdensome and the approval process is too slow to be useful to patients. This isn't a new criticism. It reflects an ongoing tension between the need to balance access to new therapies against the requirements that these therapies be safe and effective before they can be marketed. In February of 2015 the FDA revised their compassionate use application process to make it less cumbersome.

ETHICAL CONSIDERATIONS

- **Informed Consent:** Drugs that have only gone through Phase I trials are not yet tested for efficacy and may still have serious side effects. Concerns have been expressed that under "right-to-try" laws patients may be exposed to significant harms with no guarantee or even potential for benefit. And, in choosing this path, they may end up foregoing care that could lengthen or at the very least increase the quality of their remaining time. In the absence of phase II or phase III data on the experimental drug being requested, it is unclear how a patient can weigh the risks, benefits and alternatives and provide a truly informed consent. It also poses challenges for physicians in meeting their professional and ethical obligations to communicate these issues to patients and provide recommendations.

  Related to this is the existing problem of therapeutic misconception. Therapeutic misconception exists when individuals do not understand that the defining purpose of clinical research is to produce generalizable knowledge, regardless of whether the subjects enrolled in the trial may potentially benefit from the intervention under study or from other aspects of the clinical trial. Concern has been expressed that right-to-try laws could promote this misconception by thinking that the research drug is actually a treatment.

- **Autonomy:** The bedrock principle of medical ethics which speaks to respecting and preserving a patient's right to make their own decisions about medical treatment. Historically, in law and ethics, the way autonomy has been protected is as a "negative right"--the right of noninterference or to refuse treatment—not as a "positive right"—the right to access treatment. Critics of the FDA's experimental use and access policy claim that it

interferes with a patient's right to determine their own treatment. But opponents of "right-to-try" laws claim that autonomy needs to be protected for patients who are most vulnerable.

- **False Expectations:** Opponents of "right-to-try" laws have expressed concerns about the fact that these laws do not actually create any additional "rights" for patients since the law does not compel anyone or any company to fulfil a patient's request for an experimental drug, device or biologic. This could result in false hope and unmet expectations on the part of patients who have no therapeutic options left but think that because this law exists in their state, that experimental drugs will be available to them. According to one study published in the Annals of Internal Medicine in November of 2015, there had been no reports of patients gaining access to products through right-to-try legislation.

- **Justice:** Because insurers are not required to cover the costs of experimental agents under "right-to-try" laws, access may be limited only to patients who have the resources to cover the costs associated with the therapy (direct drug costs and any potential fees associated with administration, treatment or side effects that may occur). This raises concerns about equity and fairness with regard to access.

- **Research Integrity:** Concerns have been expressed that broader access to experimental therapies outside of the regulated clinical trial process could undermine and/or delay existing research leading to FDA approval of needed new therapies. Specifically issues have been raised about increased risks of higher rates of adverse events that may discourage patients from joining clinical trials thereby jeopardizing the approval process.

References:

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2. Health Policy Brief: Right-to-Try Laws, *Health Affairs,* Updated April 2015.

3. Yang YT, Chen B, Bennett, C. Right-To-Try Legislation: Progress or Peril? *Journal of Clinical Oncology,* Vol 33, No.24, 2015.