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Testimony Senate Health & Welfare Committee – February 9, 2017
Right to Try (S.37)

We live in a time of tremendous capability to treat and cure disease. Yet with all the advancements in medicine and technology, there are still times when despite best efforts and available therapies, we are unable to slow—let alone reverse—the outcome of progressive, life-limiting and terminal disease.

"Right-to-try" legislation has been proposed in a growing number of states in recent years to enable terminally ill patients, who have exhausted all other therapeutic options, access to unapproved, experimental drugs, biologics and devices. These laws are not without controversy. Many in the public favor them—seeing them as a last hope for terminally ill patients and the opportunity to prevent an untimely death. Others, namely health care professionals, researchers and most ethicists I have encountered, while sympathetic, are not convinced about the benefit of right-to-try laws—expressing concern about the promise of false hope and the potential harm and suffering that could be inflicted on sick and vulnerable patients.

The Vermont Ethics Network takes no position on the proposed legislation. Rather, we see our role as that of providing information and opportunity for discussion about the complex ethical questions and concerns that are raised by right-to-try laws.

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 public policy debate centers on whether the gain in providing terminally ill patients with a slim chance at prolonging life is worth 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 provide an accelerated timetable for gaining access to experimental agents by removing federal regulatory and institutional 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 committee, FDA or IRB review), thereby undermining current processes intended to protect public health, patient welfare and research integrity.

FDA EXPANDED ACCESS (Compassionate Use)

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 before it has been approved for public use by the FDA. The goal is to introduce some flexibility into the regulatory process and allow patients with no other treatment options a chance to try therapies they would otherwise not be able to access. Access to drugs via compassionate use still requires approval by the FDA and by the IRB at the institution where the drug will be dispensed. Criticism of the FDA's expanded access program is that the paperwork is lengthy and burdensome and the approval process is too slow to be useful to patients in the last stages of terminal disease. This criticism reflects an ongoing tension between the need to balance timely access to new therapies against the requirements that these therapies be safe and effective before they are marketed.

ETHICAL CONSIDERATIONS

- **Autonomy:** Patient autonomy (the ability to be self-governing) is a bedrock principle of medical ethics and speaks to respecting and preserving a patient's right to make their own decisions about medical treatment. This concept is central to proponents of right-to-try laws and also to their criticism of FDA expanded access programs. That is, patients should have a right to choose and access an agent that might prolong their life and should not be burdened by FDA and IRB approval when their life expectancy is short. Conversely, critics argue that historically, in both law and ethics, autonomy has long been represented as a "negative right"--the right of noninterference or to refuse treatment—not as a "positive right"—the right to demand or access treatment.

- **Voluntary & Informed Consent:** Terminally ill patients are considered a vulnerable population and as such, should be afforded protections to assure that they understand the choice they are making. Drugs that have only gone through Phase I trials are not yet tested for efficacy and may still have serious side effects. In the absence of phase II or phase III data, it is unclear how or if a patient can weigh the risks, benefits and alternatives and provide a truly voluntary and informed consent. This also poses ethics challenges for physicians in meeting their obligations to communicate information to patients such that they can understand, appreciate in the context of their own situation and communicate a reasoned a choice.

Related to the issue of informed consent is the existing problem in medical research of *therapeutic misconception*. Therapeutic misconception exists when individuals do not understand that the primary purpose of clinical research is to produce generalizable knowledge, regardless of whether the subject enrolled in the trial would 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 or perpetuate this misconception---with patients thinking that the research agent is actually a viable treatment.

- **Beneficence/Non-maleficence:** Since there are real risks to patients seeking access to investigational agents, ethics concerns have been expressed that under "right-to-try" laws patients will be exposed to significant harms with minimal or no potential for benefit. Furthermore, by circumventing FDA and IRB approval an important layer of patient protection is removed. Finally, concerns have been raised that terminally ill patients who pursue this course may end up foregoing care that could lengthen or at the very least increase the quality of their remaining time.

- **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 they do not compel anyone or any company to fulfill a patient's request for an experimental agent. 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.

- **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, etc.). This raises concerns about equity and fairness with regard to access. Another emerging ethics concern has been the use of social media by patients and others with the means to pressure companies into providing unapproved agents. This has the potential to exacerbate disparities in how unapproved treatments are distributed.

- **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, prevent the approval of a promising therapies, or result in earlier death of the patient.

Thank you for the opportunity to testify on this proposed legislation on behalf of the Vermont Ethics Network.

Sincerely,
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