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August 28, 2017

The Honorable Greg Walden, Chairman
Committee on Energy and Commerce
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Walden:

On behalf of the International Society for Stem Cell Research (ISSCR), the leading professional organization of stem cell science and regenerative medicine, I am writing to express strong opposition to S. 204, the "Trickett Wendler Right to Try Act of 2017," which is currently pending in the Energy and Commerce Committee. This legislation would allow investigational agents to be provided to patients outside of the context of a clinical trial, without first establishing their safety and efficacy through rigorous clinical trials. The ISSCR, which represents more than 4,200 members in the United States and over 65 countries, opposes this legislation because it would lower standards for new regenerative medicine therapies.

Using unproven interventions on significant numbers of patients, particularly in a for-profit context, raises major ethical and integrity concerns and jeopardizes patient safety. The practices that would be permissible under this legislation are contrary to the principles of the ISSCR 2016 Guidelines for Stem Cell Research and Clinical Translation. These guidelines have been widely adopted internationally and help assure the integrity of stem cell science and its translation to medicine.

Eliminating phases of the clinical trial process would be dangerous to patients.

Currently, the Food and Drug Administration (FDA) reviews clinical trial data and determines whether the benefits of new therapies outweigh the risks. Historical data show that most experimental therapies that initially look promising based on Phase I clinical trials subsequently fail, proving to be either unsafe or ineffective in Phase II and Phase III clinical trials. This means that if the lower standards in this legislation are enacted, many of the new treatments that would become available to patients would ultimately prove to be unsafe or ineffective. It may sound like an appealing idea to allow seriously ill patients accelerated access to experimental therapies; however, in the absence of full clinical testing, this legislation will allow snake oil salesmen to sell unproven and scientifically dubious therapies to desperate patients. Indeed, patients have been blinded and paralyzed by receiving unproven cell "therapies" from physicians in the United States.

Typically, investigational medical treatments are tested for toxicity in Phase I trials, preliminary evidence of therapeutic efficacy in Phase II, and for definitive evidence of safety and efficacy in carefully controlled Phase III clinical trials. This phased approach minimizes

harm to patients during the testing process and ensures that physicians and patients have as much information as possible on the risks and benefits of these products. Indeed, physicians depend upon the information from Phase III clinical trials to make informed decisions about what therapies might benefit their patients. In the absence of later stage clinical trials, patients and their physicians will have to make life-and-death decisions without information on efficacy.

Allowing investigational therapies to be available after only Phase I trials risks harming recruitment to randomized controlled trials (RCT), as patients will want the available "treatment" option, and therefore limit the important control group data, skewing the results. This will also harm our healthcare system by reducing the validity of RCT results and the ability to do adequately designed studies. Data should be collected on the safety and efficacy of the experimental therapeutics in all patients, and these data should be made broadly available. Neither physicians nor patients should be forced to make treatment decisions without information on the results that such treatments have achieved in other patients.

Current law already provides a pathway for patients to receive unapproved interventions through expanded access programs.

Under current law, the FDA permits patients and physicians to petition to receive access to unapproved drugs. The FDA approves more than 99 percent of the applications it receives under "compassionate use" or "expanded access" procedures, while continuing to monitor the effects of the drug. Additionally, over the past few years, review times for U.S. drugs have decreased considerably and the FDA has created several kinds of fast-track approval mechanisms and a priority-review designation. Therefore, there is no need for "right to try" legislation because patients in crisis already have timely access to last-chance products.

Approval for marketing and reimbursement should remain conditional upon the completion of clinical investigations that demonstrate safety and efficacy, as judged by rigorous, independent, and expert regulatory review. By potentially allowing companies to market unproven therapies, the bill removes the incentive to invest in the research needed to validate safety and efficacy, and without this investment, the cost of treatment failure will be transferred to patients. Ensuring the health and welfare of patients should be a top priority in the approval process, along with guarding against the sale of unproven therapies.

If the ISSCR can be of any assistance as you consider this critical issue, please contact me directly, or contact Kaye Meier on my staff (KMeier@ISSCR.org).

Sincerely,

Hans Clevers, MD, PhD
President, ISSCR
Professor of Molecular Genetics at Hubrecht Institute/University Medical Centre Utrecht