PhysiciansCommittee
for Responsible Medicine
PCRM.ORG
5100 Wisconsin Ave. NW, Suite 400 • Washington, DC 20016 • Tel: 202-686-2210 • Fax: 202-686-2216 • pcrm@pcrm.org

**Statement for the Record**

**U.S. House Subcommittee on Health of the Committee on Energy and Commerce**

**March 17, 2022**

**Submitted by: Kristie Sullivan, MPH, Vice President, Research Policy**

On behalf of the Physicians Committee for Responsible Medicine, thank you for the opportunity to submit this statement for the record regarding the need for policy and program changes that integrate human-specific *in vitro* and computational methods in nonclinical drug safety and efficacy testing. Legislative efforts to improve the way drugs are developed and tested must compel FDA action to remove the requirements for animal experiments and expand FDA efforts to evaluate and accept human-specific approaches.

The Physicians Committee is a 501(c)(3) nonprofit organization supported by over 175,000 members nationwide working for effective, efficient, and ethical medical research and product testing. We collaborate with federal and state agencies, the private sector, and academia to improve public health and medical practice. We request this statement be included in the record for the Subcommittee on Health's March 17, 2022 hearing entitled "The Future of Medicine: Legislation to Encourage Innovation and Improve Oversight."

Fundamentally, human-specific approaches are more relevant to humans and predictive of human outcomes than traditional animal studies because they utilize human cells, tissues, and data, and even offer the ability to model diverse patient populations prior to clinical trials. Traditional nonclinical studies rely heavily on the biology of other animal species, frequently that of dogs, mice, rats, and non-human primates. Increasingly, scientists spanning various stakeholder groups, affiliations, and backgrounds, including the FDA and industry, acknowledge that these animal studies do not always provide accurate information for humans and that there is a need to integrate methods that are more predictive for humans. The 95% failure rate of investigational medicines moving from nonclinical to clinical studies indicates that we can do better to overcome translational challenges – for humans that need safe and effective medicines and for non-human animals who are used in testing.

## FDA's Policies and Practices

The FDA's regulations and guidance play a key role in the continued use of animal studies over modern human-specific approaches because they require and recommend animal use. While human-specific methods have significantly advanced in recent years, and many are

commercialized, many FDA policies have not been updated to account for this progress. Currently, FDA policies include requirements and recommendations for the submission of data from animal tests, without providing flexibility for submission of data from human-specific approaches. Without certainty that new approaches will be accepted, companies will continue to submit data from traditional animal tests.

The code of federal regulations definition of 'nonclinical' should be amended to include *in vivo*, *in vitro,* and *in silico* approaches, rather than just *in vivo* and *in vitro*. The word 'nonclinical' should then be used throughout the regulatory text instead of inconsistent references to 'animal' or '*in vivo'* data. These regulatory changes would help to ensure that the best methods for predicting human outcomes are included in drug review, whether they include *in vivo* animal tests or not. In addition, many FDA guidance documents include language stating that alternative methods to the enumerated animal tests are accepted where appropriate. Unfortunately, many guidance documents also include a disclaimer that alternative methods may be used if they meet the requirements of applicable statutes and regulations, making the intended flexibility impractical until the regulations allow flexibility. Additionally, some FDA guidance contain conflicting recommendations for testing.

For these reasons, the Physicians Committee recommends that any effort to encourage innovation and improve drug development outcomes should require agency action to update regulations and guidance to explicitly communicate acceptance of human-specific nonanimal approaches.

*Draft Legislative Text to Advance Human-Specific Methods:*

*TITLE VI--REAUTHORIZATIONS AND IMPROVEMENTS RELATED TO DRUGS*

*SEC. ___. Human-Specific Translational Models and Tools.*

*Regulations and Guidance for Nonclinical Laboratory Studies.*

*1) Regulations. – Not later than September 30, 2023, the Secretary, acting through the Commissioner of Food and Drugs, shall publish in the Federal Register notice of proposed rule changes, including—*

> *A. Amendment to the definition of 'nonclinical' in 21 C.F.R. § 58.3(d) to include in vivo, in vitro, and in silico approaches;*
>
> *B. Amendments to regulations promulgated under 21 C.F.R. to employ 'nonclinical' in lieu of references to 'animal,' 'in vivo,' or 'in vitro' data.*

*2) Guidance. – Not later than September 30, 2023, the Secretary shall conduct a review of existing guidance documents for nonclinical testing to—*

> *A. Identify and amend guidance that recommend animal tests to explicitly communicate acceptance of alternative methods;*

*B. Of the relevant guidance, identify which guidance contain conflicting recommendations and amend or delete to resolve inconsistencies;*

*3) Report. – Not later than September 30, 2024, the Secretary shall publish in the Federal Register the issuance, reissuance, modification, and/or deletion of regulations and guidance identified during the review under this section.*

**FDA's Innovative Science and Technology Approaches for New Drugs (ISTAND)**

To encourage innovation and improve drug development outcomes while reducing animal testing, PDUFA VII should fund qualification of human-specific nonanimal approaches via FDA's ISTAND program and include commitments from the FDA regarding deliverables.

In November 2020, the FDA launched the ISTAND pilot program, which created a much-needed path for the agency to consider and potentially accept new approaches through a scientific evaluation process called qualification. Once qualified through ISTAND, a method gains the FDA's stamp of approval for the qualified purpose, and all drug sponsors may confidently use the human-specific approach.

ISTAND is a broad program that also includes other drug development tools, so dedicated funds for qualifying human-specific approaches with deliverables would help ensure the agency prioritizes human-specific approaches.

For these reasons, the Physicians Committee recommends that PDUFA VII fund the FDA's ISTAND program, with dedicated funds allotted for qualification of human-specific approaches.

*Draft Legislative Text to Advance Human-Specific Methods in PDUFA VII:*

*TITLE VI--REAUTHORIZATIONS AND IMPROVEMENTS RELATED TO DRUGS*

*SEC. ___. Human-Specific Translational Models and Tools.*

*Qualification of Drug Development Tools.*

*1) Funding for the Qualification of Human-Specific Approaches.– This Act designates $5,000,000 to be spent on activities to support the qualification of nonanimal approaches within the Innovative Science and Technology Approaches for New Drugs (ISTAND) pilot program. ISTAND provides a pathway for regulatory acceptance of innovative human-specific methods that can better protect public health, improve the safety and efficacy of drug development, and reduce animal testing. Allocated funds should cover salaries for designated staff to qualify nonanimal methods through the ISTAND program, to update agency guidance to recommend qualified methods, and to train staff on qualified nonanimal approaches, in addition to other activities.*

*2) Report.– Not later than September 30, 2025, the Secretary shall publish in the Federal Register a report on activities related to the qualification of human-specific approaches through ISTAND, including eligibility criteria, a list of qualified methods, guidance changes*

*recommending the use of human-specific methods qualified through ISTAND, and information on agency training on qualified human-specific methods, in addition to other activities.*

Delivering safer and more effective therapeutics requires agency and industry policies, practices, and programs to keep pace with scientific and technological advances. Human-specific approaches have the potential to transform nonclinical drug safety and efficacy testing by providing information specific to humans, allowing companies and the agency to make more informed decisions earlier in the drug development pipeline.

The Physicians Committee appreciates the Subcommittee's efforts to encourage innovation in medicine. Please do not hesitate to reach out with any questions.