Congress of the United States
House of Representatives
Washington, DC 20515

Norman E. Sharpless, M.D.
Acting Commissioner
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

June 19, 2019

Dear Acting Commissioner Sharpless:

Over the past year, the FDA has prioritized the integration of predictive nonclinical tools for assessing drug safety and efficacy through initiatives such as the Predictive Toxicology Roadmap. We look forward to continued prioritization and implementation under your leadership.

To help implement roadmap goals and ensure the most predictive tests are integrated into the drug development pipeline, we urge the agency to take the following complementary actions.

- Modify the attached regulations that mandate or prioritize the use of animal tests over modern human-based nonclinical approaches. The references to 'animal' data in these regulations could be changed to 'nonclinical,' which encompasses *in vivo* (animal), *in vitro* (animal and human-based) and *in silico* (animal and human-based) approaches. This would neither indicate a ban on animal testing nor a mandate for human-based approaches. It would merely neutralize the regulations to reflect the agency's discretion to accept any valid nonclinical method. These changes remove regulatory barriers and will help ensure the longevity of the regulations in the face of rapidly advancing nonclinical approaches.
- Establish a qualification program for *"in vitro* and computational" methods. The roadmap describes *in vitro* platforms and sophisticated computer models as having the potential to improve drug development and suggests qualification may help with integration of such approaches. It remains unclear how the methods the roadmap seeks to integrate may be qualified, because qualification is limited to three existing programs. Launching an "*in vitro* and computational" qualification program would assist with roadmap implementation and extend qualification eligibility to these approaches. To address global harmonization of method acceptance, we ask the agency to work with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) to harmonize acceptance of qualified approaches.

While nonclinical tests are crucial for understanding whether a potential medicine is likely to be safe and effective in humans, a large percentage of new medicines that appear safe in animals later fail in humans. Significant progress is being made with advanced human-based *in vitro* and *in silico* approaches. Indeed, the FDA has played an integral role in many of these successes, such as the National Institutes of Health (NIH) Tissue Chips Program.

In light of such progress, we believe FDA must ensure its regulatory framework and evaluation programs create a path for integrating innovative human-based nonclinical approaches.

For the reasons outlined above, we respectfully urge the FDA to modify the attached regulations to clearly allow for use of modern human-based nonclinical approaches and establish a qualification program for "*in vitro* and computational" methods.

Thank you for your consideration of our views. We respectfully request a thorough written response by August 1, 2019.

Sincerely,

Brendan F. Boyle
Member of Congress

Earl Blumenauer
Member of Congress

James P. McGovern
Member of Congress