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The Honorable Anna Eshoo
Chairwoman
Subcommittee on Health
Committee on Energy and Commerce
Washington, D.C. 20515

The Honorable Brett Guthrie
Ranking Member
Subcommittee on Health
Committee on Energy and Commerce
Washington, D.C. 20515

**Testimony of
Hope R. Ferdowsian, MD, MPH, FACP, FACPM, Phoenix Zones Initiative
Before the Subcommittee on Health, Committee on Energy and Commerce**

Thursday, March 17, 2022

The Future of Medicine: Legislation to Encourage Innovation and Improve Oversight

Dear Chairwoman Eshoo, Ranking Member Guthrie, and members of the Subcommittee,

Thank you for the opportunity to provide written testimony in support of the FDA Modernization Act of 2021 (H.R. 2565 and S. 2952). This legislation is essential to encourage scientific and ethical innovation and to improve the lives of patients who are desperate for safer and more effective therapeutic interventions.

As a double board-certified internal medicine, preventive medicine, and public health physician, I have 20 years of experience treating patients who suffer from various medical and mental disorders that range from the top killers of Americans, including heart disease and cancer, to debilitating psychiatric disorders such as posttraumatic stress disorder and major depression. I regularly teach medical students, residents, and other healthcare professionals how to evaluate and treat patients living with these conditions.

Additionally, I have designed and led human clinical research trials and consulted with pharmaceutical companies on human and animal research ethics, and I have received National Science Foundation awards to investigate opportunities to advance scientific and ethical innovation in medicine. My publications on these subjects have appeared in peer-reviewed journals and popular science magazines. I have worked with professionals at government agencies, including the FDA and the NIH; executives at pharmaceutical companies; decision makers at health charities; and innovators at academic institutions around the world.

After serving on the faculty of the George Washington University School of Medicine and Health Sciences and the Georgetown University School of Medicine, I now serve as an associate professor of medicine at the University of New Mexico School of Medicine. Additionally, my professional responsibilities include acting as a medical expert for Physicians for Human Rights and as president and CEO of Phoenix Zones Initiative (PZI), an organization that advances the interconnected health and well-being of people, animals, and the planet through education, research, and advocacy. One of PZI's goals is to transform medical research in ways that benefit people and animals. My testimony is submitted in my role as a physician, scientist, educator, patient, and caregiver, and as president and CEO of PZI.

The Need for Greater Innovation

The FDA Modernization Act of 2021 is promising news for medicine and public health. This landmark legislation marks a major milestone in transforming medical research to embrace testing platforms that are more innovative and relevant to human health than are outdated, formulaic animal tests.

The science of nonclinical testing has been transformed over the past several decades, but in the absence of regulatory acceptance of more modern testing methods, practical change has occurred at a glacial pace that endangers the nation's health. Passage of the FDA Modernization Act will ultimately streamline drug development and stimulate innovation, benefitting both patients and those of us who care for them.

Views about animal experimentation are often presented in polarizing ways. Both defenders and skeptics of the scientific merits of animal experiments have made far-reaching claims that are frequently based on anecdotal evidence.

In human medicine, we rely on an evidence-based process to make clinical and population-based decisions. Similarly, in considering questions about the validity and reliability of animal testing and research, it is important to examine internal and external variables that affect study design as well as systematic analyses of the animal research literature.

When physicians and scientists have examined how animal experimentation translates to human outcomes, they have found serious problems with methodology, clinical relevance, predictive value, and the reproducibility of results.

Concerns about the predictive value of animal testing have led to dramatic changes in the field of toxicology, including a move toward an evidence-based, integrated, non-linear approach, which includes chemical characterization, toxicity testing, and dose-response and extrapolation modeling. At each step, population-based data and human exposure information are considered, as is the question of what data are needed for decision-making.

Similar strategies are available and necessary for predicting the safety and effectiveness of various therapeutic interventions, including medications.

Drug absorption is a complex process that is dependent upon numerous biochemical and physiological factors. Animal tests have not been reliable predictors of bioavailability behavior in humans. Absorption, Distribution, Metabolism, Excretion, and Toxicology (ADMET) studies in animals repeatedly show that there is no clear relationship between human bioavailability and animal bioavailability, particularly in dogs, nonhuman primates, and rodents—animals who are commonly used in drug development. As a result, high rates of false negatives and false positives are common, which increases the risk for both adverse events in humans and delays in drug discovery. When researchers have analyzed the sum of published animal studies through systematic reviews and meta-analyses, they have likewise shown that the predictive value of animal studies in determining clear evidence of human benefit approximates the flip of a coin.

Discordance between animal and human studies can be explained by threats to internal and external validity in animal experimentation, including methodological flaws, publication bias, disease-specific disparities, profound differences in outcome measures, human genetic variability, and the effects of behaviors and the environment on gene expression.

Additionally, various unknown variables affect the validity and reproducibility of animal tests. The effects of captivity, maternal-infant separation, social isolation, and the induction of fear,

anxiety, pain, and discomfort in animals result in changes to their physical, mental, and physiological health and well-being. Decades of research in humans and animals have shown how adverse experiences affect the manifestation of multiple diseases. Various physical, cognitive, and emotional stressors influence immunological, endocrine, neurological, cardiovascular, and other organ systems. These problems are not resolved with improvements in traditional animal welfare standards or other standardization procedures.

As a result of these problems, executives and scientists at pharmaceutical companies and government agencies have expressed how a mandated overreliance on animal research impedes their work. Decision makers at these companies have privately shared that they fear the legal consequences of foregoing animal tests in the setting of existing regulatory requirements administered through the FDA.

The Need for Improved Oversight

The past six decades have marked a significant revolution in research ethics in the United States. Following several research scandals, in 1979, the Congressionally appointed National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research published *The Belmont Report*, which established foundational ethical principles to guide research involving human subjects. *The Belmont Report* and resulting legal codifications dramatically transformed human research for the better. Human research now requires informed consent, a full assessment of the risks and benefits of research, and special protections for vulnerable individuals and populations such as children, who cannot provide informed consent.

The situation is much different for animals, who overwhelmingly bear the burdens of research, despite their inability to provide informed consent or to benefit from the research. The U.S. Animal Welfare Act still does not cover most animals used in research, and animals who are covered under the Animal Welfare Act are not protected from serious harm.

As a result, Americans have become increasingly skeptical of animal research. Roughly half of Americans think that medical testing on animals is morally unacceptable, and public opposition to animal research has steadily increased over the past decade because of moral, ethical, and scientific concerns.

Although the U.S. spends more on healthcare and research than does any other industrialized nation, high levels of spending do not translate into meaningful health outcomes or increased life expectancy. In fact, over the past twenty years, the percentage of deaths linked to preventable causes has remained about the same.

Scientific and ethical innovators should not be held back by an eighty-year-old misleading mandate that requires animal testing and slows progress. If government scientists and regulators require education and training on the latest innovative methods, it should be provided.

The FDA Modernization Act of 2021 will enable drug companies to test a drug's safety and efficacy using more advanced and ethical methods in place of animal testing wherever possible.

During the COVID pandemic, many of us realized that the drug and vaccine approval process needs to be overhauled. Fortunately, government and scientists brought urgency to the pandemic response, cut through organizational red tape, and developed successful vaccines in less than a year. Now is the time to bring this commitment and innovation to other areas of medicine for patients who need our help.

The FDA Modernization Act will free the FDA to allow for the best science to address the diseases that afflict patients.

Thank you for your attention to this important matter.

Sincerely,



Hope Ferdowsian, MD, MPH, FACP, FACPM
President and CEO, Phoenix Zones Initiative