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Written Testimony for the Record Submitted by
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The Future of Medicine: Legislation to Encourage Innovation and Improve Oversight

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To Chairwoman Eshoo, Ranking Member Guthrie, and Members of the Subcommittee:

On behalf of the Michelson Center for Public Policy, a 501(c)(4) social welfare organization that propels legislative change through meaningful collaboration with elected officials, government agencies, and civic leaders to achieve positive outcomes in education, equity, medical research, and animal welfare, I submit the following testimony in support of H.R. 2565, the FDA Modernization Act of 2021.

With strong bipartisan support, House leaders introduced the FDA Modernization Act of 2021 to revise a long-standing statute that limits preclinical studies to animal testing for new drugs. This follows action by the European Parliament in September to adopt a resolution—by a vote of 667 to 4—to phase out animal testing.

This is great news for public health as it marks a major milestone in transforming the biomedical sciences to embrace testing platforms that are more innovative and could be more relevant to human health than the standard animal testing platforms. The public expects the FDA and pharmaceutical companies to deploy first-rate science to develop and approve treatments for millions of Americans suffering from diseases. However, the current statute limits drug developers into antiquated methods that drive up costs, delay treatments, leave the afflicted without life-saving therapies, and churn through animals used in testing.

We are in desperate need of a reboot when it comes to drug development.

An outdated approach

Since its enactment in 1938, the Federal Food Drug and Cosmetics Act (FFDCA) has required data for safety and efficacy from animal tests for all new drugs and vaccines. But this 80-year-old statute has not caught up with the science.

Over the past several decades technology advancements have provided new nonclinical testing methods that have proven to be more effective in predicting the safety and effectiveness of drugs and vaccines for humans for certain disease areas. There are also several instances where we know animals testing is a poor method for predicting safety and effectiveness. For

example, in 2003, Elan Pharmaceuticals was forced to terminate a Phase II trial when an investigational Alzheimer's vaccine was found to cause brain swelling in humans.[1] No significant adverse effects were detected in genetically modified mice or nonhuman primates. In another example from 2006, six volunteers who were injected with an immunomodulatory drug, TGN 1412, suffered severe adverse reactions resulting from a life-threatening cytokine storm that led to catastrophic systemic organ failure.[2] TGN 1412 was tested in mice, rabbits, rats, and nonhuman primates with no ill effects.[3] Even recently, the FDA's Cellular, Tissue, and Gene Therapies Advisory Committee concluded that animal models are "problematic" in assessing the safety risks of gene therapies derived from adeno-associated virus (AAV) vectors.[4] There have been severe adverse events in AAV vector clinical trials, including acute liver failure and encephalopathy, in children.[5]

Time and again, drugs and vaccines that proved promising in animal tests failed when tried in humans. At least 172 drugs that showed promise in animals for the treatment of Alzheimer's disease failed in humans,[6] as did 150 drugs tested successfully in animals for inflammatory diseases.[7] More than 114 therapies for stroke tested in animals failed in human trials.[8] More than 700 human trials of potential HIV/AIDS vaccines have been conducted, all of which gave encouraging results in animals, including monkeys and chimpanzees.[9] Yet not one has worked in humans.

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[1] Lemere CA. Developing novel immunogens for a safe and effective Alzheimer's disease vaccine. *Prog. Brain Res.* 2009; 175: 83–93.

[2] Allen A. Of Mice or Men: The Problems with Animal Testing. *Slate*. Published June 1, 2006.

[3] Attarwala H. TGN1412: From Discovery to Disaster. J. Young Pharm. 2010; 2(3): 332–336.

[4] Eglovitch JS. Animal models have limitations for safety assessment of gene therapies: FDA adcomm. Regulatory Affairs Professionals Society. Published September 2, 2021.

[5] George LA. Systemic AAV: Clinical Findings of Hepatotoxicty. Presentation at: CTGTAC: Toxicity Risks of AAV Vectors for Gene Therapy. September 2–3, 2021.

[6] Schneider LS, Mangialasche F, Andreasen N, et al. Clinical trials and late-stage drug development in Alzheimer's disease: An appraisal from 1984 to 2014. *J. Int. Med*. 2014; 275: 251–283.

[7] Seok J, Warren HS, Cuenca AG, et al. Genomic responses in mouse models poorly mimic human inflammatory diseases. *Proc. Natl. Acad. Sci. USA* 2013; 110: 3507–3512.

[8] O'Collins VE, Macleod MR, Donnan GA, et al. 1,026 experimental treatments in acute stroke. *Ann. Neurol.* 2006; 59(3): 467–477.

[9] Bailey J. Letter. *Altern. Lab. Anim*. 2017; 45(4): 213–218.

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The FDA Modernization Act of 2021 would lift the requirement for animal testing and provide the FDA the opportunity to authorize the best testing methods, whether animal or non-animal, to determine the safety and efficacy of a new drug.

We must also consider the drugs and vaccines that did not work in animals that may prove to be effective in other nonclinical methods. For example, cyclosporine, a drug widely and successfully used to treat autoimmune disorders and prevent organ transplant rejection, was delayed because of animal tests.[10] How many potential cures were thrown out due to relying only on animal testing?

New methods

Bioprinted organ models, organ-on-a-chip models, "virtual humans," and artificial intelligence applications have been developed to predict human responses to new drugs more accurately and quickly. The benefit of these methods is that they are based on human biology. Recognizing the need for better models for human diseases, the Biomedical Advanced Research and Development Authority issued awards in September for human vaccine organ-chips[11] and lung-chips[12] for COVID-19 research.

Despite these signs of progress, the FDA continues to operate within the parameters of this outdated statute, compelling researchers to rely on animal testing, when evaluating new drug submissions.

Whatever role animal testing may have played in the past, we know that there are now new advanced methods to predict the safety and effectiveness of drugs and vaccines for humans.

Fortunately, Democrats and Republicans have joined together to push the FDA Modernization Act 2021 would lift the requirement for animal testing and provide the FDA the opportunity to authorize the best testing methods, whether animal or non-animal, to determine the safety and efficacy of a new drug. This measure will enable greater innovation in biomedical research and allow for the use of methods that are more likely to predict human outcomes.

A call to action

As physicians, we know that people come to medical professionals desperate for life-saving treatments. During the COVID-19 crisis, we as a nation realized that a protracted, bureaucratic,

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[10] Greek R, Greek J. Animal research and human disease. *JAMA* 2000; 283: 743–744.

[11] Walrath R. Draper inks $719K BARDA contract to develop lung chip for Covid-19 research. *Boston Business Journal*. Published September 23, 2021.

[12] Marx U, Andersson TB, Bahinski A, et al. Biology-inspired microphysiological system approaches to solve the prediction dilemma of substance testing. *Altern. Anim. Exp*. 2016; 33(3): 272–321.

and inaccurate drug and vaccine approval process must be revamped. Thus, government and scientists brought urgency to the pandemic response, cut through organizational red tape, and developed successful vaccines in less than a year. We must bring this commitment and innovation to other drug development programs and get cures and treatments to those who desperately need them.

The FDA Modernization Act 2021 will free the FDA to allow for the best science to address the diseases that afflict us. This is an essential reform, and Congress and the Biden administration should pursue it with the same urgency they are bringing to the fight against COVID-19.