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The end of animal testing? Transitioning to models is promising — but no silver bullet

No single method can replace using animals to test new drugs

The U.S. Food and Drug Administration's recently published Roadmap to Reducing Animal Testing in Preclinical Safety Studies may have caused a stir across the pharmaceutical and biotech industries, but I wasn't surprised. I've been working in drug development for 30 years and can tell you that the truth is the 3Rs (reduce, replace, and refine) principle for animal testing has been a goal in development for decades.

Beyond the ethical implications, relying on animals to test new drugs is inherently imperfect. More than 90% of drugs that appear safe and effective in animals fail in human trials due to safety or efficacy issues. Traditional animal models often fall short of predicting human outcomes. High costs and supply chain limitations (such as scarce non-human primates) underscore the urgency to adopt human-relevant alternatives.

I've spent my career — primarily as the co-founder of biosimulation company Simcyp, which was acquired by Certara — focusing on translational modeling to predict the behavior of drugs in the human body with the aim of accelerating the development and regulatory approval of safer drug products and bringing them to the patients. Through this work, I've seen the potential of alternatives to animal testing but also how challenging it will be to make the FDA's vision a reality within the three-year timeframe it set out.

For that to happen, sponsors, technology companies, consulting companies, and regulators all need to support creating a matrix of new approach methodologies (NAMs) like advanced in vitro assays, AI-driven computer modeling, and organ-on-a-chip technologies, as opposed to a singular method.

There's no magic fix that will eliminate animal testing at the push of a button, but with NAMs, we have the tools to work toward a future where it is significantly reduced and we are utilizing more effective, modern, and ethical methods.

Drug developers need to be confident that a drug candidate can go into the clinic and not cause serious harm to patients. Currently, animal models are used to assess the safety liability of drug candidates.

The rate-limiting step to developing drugs without using animals is the development and validation of alternatives to using animals for toxicological assessment. For example, instead of examining a mouse liver to assess if a drug is hepatotoxic, researchers can look at a drug's effect on human hepatocytes in a 3D liver organoid model.

Another important use of animal testing is to generate the data needed to build computer models. As experimental alternative methods mature, they will be able to provide the data needed to build computer models instead of using animals.

Embracing computer modeling will also be critical to eliminating animal testing. The wave of regulatory use of non-animal-based methods — such as physiologically-based pharmacokinetic (PBPK) models that started over a decade ago to independently review, analyze, and verify developer claims — will accelerate with these changes.

While computer-simulated models for pharmacokinetics (what the body does to the drug) and pharmacodynamics (what the drug does to the body) may seem avant-garde to some, the foundations of the technology are not new or unfamiliar. Our society uses simulations every day — for example, weather forecasting models have been around for many decades. They are used to predict the exact chance of rain today. On a more consequential scale, they are relied upon to determine when and where the next hurricane will hit. Weather simulations ensure safety and save lives. They also guide evacuations and placement of rapid response equipment and personnel to deal with the aftermath of natural disasters. The accuracy of these models is at an all-time high, with a four-day forecast today more accurate than a one-day forecast 30 years ago.

In the pharmaceutical space, techniques like quantitative systems pharmacology (QSP) modeling (where PBPK modeling is a subgroup) allow researchers to take the advantage of increasing knowledge of human biology, incorporate them in models alongside drug information obtained in humanized systems in the lab, and accurately predict how drugs will perform in humans without collecting additional animal data. These models can be used to determine first-in-human doses that will be safe and effective, predict potential side effects, and help with dose adjustment in special patient populations (such as pregnancy). These represent many of the same circumstances when we would traditionally turn to animal testing for answers.

Modeling also takes medical research a step further, simulating “what-if” scenarios that cannot safely or feasibly be tested in animals or humans, such as testing drug interactions in pregnant women, neonates, or patients with rare diseases.

In one such recent case, GRIN Therapeutics and Certara used a PBPK model to determine doses in an efficacy study for a new therapy for pediatric patients with GRIN-related neurodevelopmental disorder (NDD). GRIN-related NDD can cause seizures and developmental delays in children, but there are currently no FDA-approved therapies available to treat it. This was a sensitive situation where we needed to ensure the doses were efficacious for the vulnerable patient population while remaining below previously established limits. Making matters more complicated was the inherent variability in dosing drugs in children and the rarity of GRIN-related NDD.

The only option was estimating dosing at an individual patient level. This would not be possible with in vivo testing. After the initial starting dose was administered, we performed “virtual twin” simulations in real time to estimate individualized dose escalation options for each patient.

Another example is that of antiviral monoclonal antibodies (mAbs) against Covid-19. The urgency created by the pandemic forced the pharmaceutical industry to develop these therapies faster than ever before. The use of models was essential for determining the dosing of investigational mAbs for humans based on very limited data. These models were so trusted that we at Certara used them to determine the president’s dose.

However, these models shouldn’t be used in isolation.

Again, consider weather models. While they are valuable tools to aid decision making as a storm approaches, once the storm is imminent, common sense is to look out the window and make decisions based on what is right in front of you. Fail to do so, and you risk being caught outside in the rain, unprepared.

Shifting an entire industry doesn’t happen overnight. Phasing out animal testing requires collaboration among sponsors, regulators, and technology pioneers. Success will hinge on addressing common concerns, such as trust in these methodologies and ensuring rigorous validation. Biosimulation tools, like animal studies, undergo rigorous model qualification. What differentiates them is their superior translation to human biology and scalability across various drug candidates.

Moving away from animal testing using NAMs also has a competitive advantage in an industry that demands innovation at every stage. A recent study from Pfizer found the use of model-informed drug development saved on average 10 months of cycle time and $5 million per program. We must ask ourselves if we want to stay stuck in the past, or if we want to embrace and help shape a future where speed, ethics, and efficiency define drug development.

The theoretical removal of animal testing from the drug development industry is nothing new, but at times, it has felt more like a pipe dream than reality. I hope that this announcement from the FDA is the push the industry needs to embrace advanced NAMs and make the bold changes required to bring about a substantial reduction in animal testing.

Amin Rostami-Hodjegan is professor of systems pharmacology and director of Centre for Applied Pharmacokinetic Research at the University of Manchester and chief scientific officer and senior vice president of R&D at Certara.