Attention: Scientific Advisory Committee on Alternative Toxicological Methods Meeting
Date received: September 3, 2025
Federal Register Notice: (90FR29572-29573)
Private Citizen

Comments: “Dear Sir or Madam,
As an researcher and associate director of the Institute for Molecular Life Sciences at Texas State University, I am encouraged by recent policy actions taken by the FDA and NIH to advance biomedical research and enhance the translation of biomedical knowledge. As a scientist doing research with animals since many decades, I fully support all measures which reduce, refine and replace animal usage wherever and whenever it is possible. But there are clearly research areas which cannot abandon model organism. Only a few diseases are restricted to the malfunctioning of a single cell type or tissue. Most are systemic, and the full-blown clinical picture can only be studied, understood and modeled in an intact organism. As frontline scientists, we believe it is our responsibility to provide informed perspectives to support comprehensive policymaking on the future of biomedical research, particularly as it pertains to the use of model organisms.

There is broad consensus within the scientific community that the ultimate goal of model organism research is to improve human health. Animal models contribute to biomedical research through two primary strategies:

Conserved Disease Modeling: This approach leverages the biological similarities between model organisms and humans to investigate disease development, progression, and intervention. Common vertebrate models, e.g., mouse, rat, and zebrafish,are chosen for their well-characterized genomes, physiological relevance, and high degree of evolutionary conservation. These models have been indispensable for studies in embryonic development, neuroscience, drug discovery, molecular mechanisms of disease, and importantly, toxicology. Engineered mutant models, developed through mutagenesis, transgenesis, or genome editing, have played foundational roles in these efforts.

Evolutionary Medicine Models: This emerging and complementary strategy focuses on the unique biology of certain model organisms that differ markedly from humans. These evolutionary mutant models reveal natural resistance or adaptation to disease, offering powerful insights into mechanisms of disease resilience.

These systems provide unprecedented opportunities to understand how evolution shapes disease resistance and adaptation, knowledge that is unattainable through in vitro or in vivo human studies alone.

We recognize that some traditional animal models, particularly in preclinical drug testing, have shown limitations in predictive validity. This includes certain mammalian models used in the safety and efficacy assessments of mRNA vaccines and monoclonal antibodies. While these shortcomings underscore the growing role of New Approach Methodologies (NAMs), it is critical to emphasize that model organisms remain irreplaceable in fundamental discovery science. They enable the identification of previously unknown biological processes, therapeutic pathways, and gene-environment interactions that drive disease.

Furthermore, many human diseases arise from maladaptation to environments or are driven by complex genetic and epigenetic factors. Evolutionary models, by virtue of their naturally evolved resilience to

such pressures, are uniquely positioned to reveal protective mechanisms that can inform future therapeutics.

Finally, we respectfully urge the SACATM to consider the following recommendations in research policy development:

1.Identify areas where animal models remain necessary for discovery science and knowledge translation;

2.Specify assessment criteria that NAMs need to meet to be eligible in replacing certain animal models;

3.Identify limitations of NAMs and areas where further development is pressingly needed."