



**AMERICAN
PSYCHOLOGICAL
ASSOCIATION**
SERVICES, INC.

August 16, 2023

Advisory Committee to the Director
Working Group on Catalyzing the Development and
Use of Novel Alternative Methods to Advance Biomedical Research
National Institutes of Health
Bethesda, MD 20892

RE: Request for Information (RFI) on Catalyzing the Development and Use of Novel Alternative Methods to Advance Biomedical Research

Submitted electronically via portal and e-mail: lyric.jorgenson@nih.gov and jessica.creery@nih.gov

Dear Working Group Members:

On behalf of the American Psychological Association (APA) and its Committee on Animal Research and Ethics, I am writing in response to Request for Information (RFI) (NOT-OD-23-140) regarding the development and use of Novel Alternative Methods (NAMs). APA is the nation's largest scientific and professional nonprofit organization representing the discipline and profession of psychology, as well as over 146,000 members and affiliates who are clinicians, researchers, educators, consultants, and students in psychological science.

APA's mission is to advance the creation, communication, and application of psychological knowledge to benefit society and improve people's lives. Our comments recognize the Association's broad and diverse membership, which is committed to leading with science to promote health and welfare. The charge of the Committee on Animal Research and Ethics is to safeguard responsible research with animals other than humans, and to establish and maintain cooperative relations with organizations sharing common interests; to disseminate in cooperation with other organizations accurate information about such research; to review the ethics of such research and recommend guidelines for its ethical conduct; and to disseminate in cooperation with other organizations, guidelines for the protecting the welfare of animals other than humans that are used in research, teaching and practical applications; and to consult on the implementation of these guidelines.

APA recognizes that the development of new methods and tools will propel biomedical and behavioral research forward, including both animal and non-animal models. We support the Advisory Committee to the NIH Director's decision to investigate how NAMs may enhance NIH research studies. However, APA agrees with the [comments](#) of the Federation of American Societies for Experimental Biology (FASEB) that animal studies are at present and in the foreseeable future the most valid and reliable method for numerous areas of research. Clarifying the contexts in which NAMs may be appropriate and highlighting their use to supplement research with animals is an important step in adjusting end-user and public expectations until validation strategies, metrics, and regulatory pathways become more defined.

APA.ORG

APASERVICES.ORG

Advocating for APA members and psychology

750 First Street, NE

Washington, DC 20002-4242

202.336.5800

202.336.6123 TDD

Topic 1: The use of novel alternative methods to study human biology, circuits, systems, and disease states. (a) How NAMs are currently being developed and/or used successfully, including features that maximize scientific utility; (b) How NAMs are advancing progress into understanding specific biological processes or human states, including potential limitations to addressing human variability; (c) How NAMs could be truly revolutionary for understanding/treating human health, including currently underserved areas of biomedical research.

The development of new technologies to extend the boundaries of understanding is a touchstone of scientific progress. New and emerging technologies such as *in chemico* methods, computer simulations, organs-on-chips and 3D digital imaging are making exciting contributions to our understanding of biology and behavior. Each of these technologies must proceed through the development pipeline with common steps: undergoing testing, providing convincing data and clear endpoints, rigorous benchmarking studies, and evaluation metrics. To maximize scientific utility and achieve clinical and regulatory acceptance, continuous collection and evaluation of NAMs data through pilot programs and comparative assessments are essential. Scientists who are acting within the high standards of NIH's peer review guidelines, rather than pressure from outside advocacy organizations, must determine when and how novel alternative technologies should be employed to ensure the health and safety of the public.

Topic 2: Approaches for catalyzing the development and validation of novel alternative method technologies. (a) Challenges for building robustness, replicability, reproducibility, and reliability of technologies and the ensuing datasets; (b) Strategies for bolstering technology readiness and reliability of these technologies; (c) Factors potentially limiting the successful integration of these technologies across research approaches and potential solutions.

New models must be validated to receive acceptance. As NIH outlines future areas of investment, APA agrees that model development and validation should be considered concurrently and that providing parallel funding for validation studies alongside future NAM grants, initiatives, or projects seems reasonable. *Consistent validation guidelines and confirmatory data from human and animal studies alike are needed. Otherwise, the development of NAMs will continue to outpace scientific standards and applications, resulting in inefficient use of research time and federal dollars (and increased pressure for NIH to apply technologies before they can be considered safe and ready).*

To inform NIH's future investment strategy in NAMs, APA supports FASEB's recommendation to conduct cost-effective analyses of proposed technologies with existing methods, including animal studies, looking at time, scalability, and resource efficiency. It is possible that combinations of multiple NAMs may not outperform single tests involving animals, further increasing costs. While this type of analysis may be resource-intensive, this information would facilitate proper investment of federal dollars and may support the public's understanding of the state of the science involving NAMs.

Topic 3: Strategies for maximizing the research value of novel alternative method technologies. (a) Areas in which coordinated approaches across research disciplines or research sectors would dramatically advance the development and/or use of these technologies; (b) Approaches for sharing technology deployment equitability across labs, including incentives for reliable and reproducible methods integration; (c) Factors for consideration when maximizing translatability and minimizing bias regarding human variability.

APA agrees with a recent National Academy of Sciences, Engineering and Medicine (NASEM) [recommendation](#) that NIH develop new mechanisms to foster collaboration between animal researchers and NAM developers. The NASEM report, “Nonhuman Primate Models in Biomedical Research,” underscores how nonhuman primates (NHPs) remain essential for NIH-supported biomedical research given the lack of qualified and validated NAMs to answer complex research questions, such as those pertaining to brain function and behavior (Homberg, et al., 2021). To address this, the report emphasizes the importance of enhanced collaboration between NHP researchers and NAMs developers to expand the applicability of non-animal systems. APA encourages NIH to establish multi-laboratory funding opportunities, cross-disciplinary challenge programs, and annual conferences or symposia that mobilize varying perspectives and expertise. For the latter, we strongly advise partnering with scientific societies to leverage their knowledge and networking capabilities for maximal impact and effective policy implementation.

APA and its Committee on Animal Research and Ethics appreciate the opportunity to comment on these important questions and are eager to collaborate with NIH on issues involving research with non-human animals. For more information, please contact Dr. Kim Boller (kboller@apa.org), Sr. Director for Science Affairs.

Sincerely,



Katherine B. McGuire, MS
Chief Advocacy Officer
American Psychological Association

References

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