PhysiciansCommittee
for Responsible Medicine
PCRM.ORG
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September 11, 2024

Re: Physicians Committee for Responsible Medicine Written Comment; September 17-18, 2024, SACATM Meeting

Dear SACATM members:

Thank you for seeking this input, submitted on behalf of the Physicians Committee for Responsible Medicine, a nonprofit organization supported by nearly one million members and supporters worldwide, including scientists, physicians, and healthcare professionals who advocate for effective, efficient, and ethical medical and scientific practices. We greatly appreciate the opportunity to provide input on activities of the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).

Support for the NICEATM Method Developer Forum

We applaud the recently launched Method Developers Forums for New Approaches for Carcinogenicity Testing, which provides a collaborative platform for stakeholders and scientists to engage in the development and validation of New Approach Methodologies (NAMs). The open exchange of ideas and findings is essential to advancing the field and improving regulatory acceptance of NAMs. We believe that these forums will accelerate the validation process, thus contributing to reducing animal testing in regulatory contexts, and we look forward to additional MDF events.

Encouraging Regulatory Harmonization and Broader Adoption of NAMs

We encourage SACATM to continue supporting efforts to harmonize the use of NAMs across agencies and sectors. While significant strides have been made, particularly in chemical testing, through activities of the Organisation of Economic Co-operation and Development, NICEATM, and the Environmental Protection Agency, broader regulatory adoption in the United States remains necessary, including at the EPA and other agencies, like the Food and Drug Administration. We recommend clear communication to industry stakeholders about NAMs' applicability in different contexts, ensuring that companies can confidently integrate these methods into risk assessments and testing strategies. Formal policy updates through guidelines, regulations, and guidance are preferred, but workarounds to these onerous processes are also welcome, as long as the communications are clear and strong, communicating to regulatory affairs specialists, lawyers, and scientists, that companies may indeed rely on the policy communications when deciding to use nonanimal approaches instead of traditional animal tests.

There is often industry interest in using NAMs, but a lack of confidence within companies that NAMs will be embraced. The clearer agencies can be in writing regarding the circumstances in which NAMs will be accepted, the better. Agency scientists can then use these communications to propose and advocate for NAM use in regulatory testing packages.

Promoting the Use of Human-Relevant Data in Evaluation of NAMs

We would like to reiterate the importance of leveraging human-relevant data, particularly in the context of regulatory decisions. Human epidemiological and clinical data, alongside biomarkers from in vitro and patient studies, should be prioritized when evaluating NAMs. Acknowledging that accessing human data is more difficult than utilizing animal data, to fully embrace the benefits of human-based approaches, more human data is needed. While companies ultimately own the data, ICCVAM agencies can encourage partnerships to share anonymized human data for the purposes of validation.

Supporting SACATM's Role in Advancing NAMs in Response to the 2022-2023 ICCVAM Biennial Progress Report

The Physicians Committee commends ICCVAM'S advancements in NAMs, highlighted through tools like CATMoS and ICE, and SACATM's pivotal role in promoting nonanimal methods. The focus on microphysiological systems and organs-on-chips is a promising step toward replacing animal testing. As stated above and included in the report, we urge SACATM to continue advocating for regulatory harmonization and global acceptance of NAMs. Additionally, we encourage SACATM to press ICCVAM agencies to address the importance of including metrics on animal testing. ICCVAM agencies are setting goals to integrate NAMs and reduce animal use, but without a baseline to measure against, it is hard to see how progress will be assessed in a meaningful way. SACATM's ongoing leadership in this space is key to reducing and replacing animal use.

Appreciation for the Complement Animal Research in Experimentation (Complement-ARIE) Program

We would like to commend the National Institutes of Health (NIH) on the new Complement-ARIE Common Fund program. This initiative is a crucial step forward in the ongoing effort to replace animal research with innovative, human-relevant methods. We also greatly appreciate the strategic planning activities for this initiative, which comprehensively engaged federal and non-federal stakeholders. The Common Fund hosted a series of listening sessions to gather broad stakeholder input on the goals and structure of the forthcoming program.[1] A crowdsourcing competition was also conducted to garner ideas from diverse research teams for new ways of using NAMs to conduct basic research, uncover disease mechanisms, and translate knowledge

[1] Executive Summary of the NIH Listening Sessions on the Complement-ARIE Program Concept. National Institutes of Health (NIH). Published March 14, 2024. Accessed May 14, 2024. https://commonfund.nih.gov/complementarie/strategicplanning/listeningsessions.

into products and practice.[2] Exercises like these that engage the research community help those developing the Complement-ARIE program to understand diverse research perspectives and to integrate practical strategies for overcoming barriers and maximizing research impact. Complement-ARIE's structured approach is vital to reducing animal use in biomedical research while ensuring that scientific rigor is maintained. and we encourage other institutes, centers, offices, and programs to look to Complement-ARIE's strategy for inspiration. The Physicians Committee fully supports this initiative and looks forward to its further development and application, welcoming any opportunities to support this important work.

Catalyzing the Development and Use of New Approach Methods to Advance Biomedical Research

We commend the NIH's efforts to advance NAMs in biomedical research, including through the recently convened Advisory Committee to the Director Working Group in Catalyzing the Development and Use of Novel Alternative Methods to Advance Biomedical Research.[3] The Working Group's focus on multidisciplinary collaboration, data interoperability, and comprehensive training will be crucial for empowering researchers to adopt NAMs and enhancing regulatory acceptance. Additionally, the public-private partnerships led by FNIH in conjunction with Complement-ARIE will play a vital role in accelerating the validation and implementation of NAMs. These initiatives will help ensure global regulatory compliance and foster broader use of NAMs across the scientific community. We support continued efforts to drive the integration of NAMs into biomedical research.

The final NAMs Working Group recommendations[4] (which were subsequently accepted by NIH Director Bertagnolli[5]), discussed among other things the important role of scientific review in the successful use and deployment of NAMs, suggesting that reviewers need to understand the unique value of NAMs when evaluating proposals. As the NIH begins implementing the recommendations, we encourage the agency to explore the following measures to ensure that NAMs are fairly evaluated during scientific review:

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[2] Complement-ARIE Challenge Prize Winner Summaries. National Institutes of Health (NIH). Published May 8, 2024. Accessed September 9, 2024. https://commonfund.nih.gov/complementarie/challengewinnersummaries.
[3] ACD Working Group on Catalyzing the Development and Use of Novel Alternative Methods to Advance Biomedical Research. NIH Advisory Committee to the Director. Published December 16, 2022. Accessed September 10, 2024. https://acd.od.nih.gov/working-groups/novel-alternatives.html.
[4] Advisory Committee to the Director Working Group on Catalyzing the Development and Use of Novel Alternative Methods to Advance Biomedical Research. Catalyzing the Development and Use of Novel Alternative Methods. Published online December 2023. https://www.acd.od.nih.gov/documents/presentations/Working_Group_Report.pdf.
[5] Statement on catalyzing the development of novel alternative methods. National Institutes of Health (NIH). Published February 1, 2024. Accessed September 9, 2024. https://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-catalyzing-development-novel-alternatives-methods.

1. Broaden the pool of NAMs expertise available for scientific review groups (including *ad hoc* or external input and by allowing potential reviewer recommendations from non-scientific society nonprofit groups);
2. Create NAMs specific funding streams so that NAM-based proposals are not competing with animal-based proposals;
3. Include additional review criteria specificity regarding NAMs in funding opportunities;
4. Ensure NAMs-based proposals are not held to different standards than animal-based proposals; and
5. Promote educational opportunities to the scientific community on the value of NAMs.

Thank you for your continued efforts and dedication to advancing non-animal methods. We look forward to continuing to work together toward a future where animals are no longer in biomedical research and toxicology, and instead predictive, human-based approaches are utilized to better inform human outcomes.

Sincerely,

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