

10/23/2026

Re: Advancing Nonanimal Research in Federal Priorities; November 4-5, 2026, Scientific Advisory Committee on Alternative Toxicological Methods Meeting Written Comment

Dear Dr. Marty and SACATM members:

On behalf of the Physicians Committee for Responsible Medicine, a 501(c)(3) nonprofit organization supported by nearly one million members and supporters worldwide working for effective, efficient, and ethical medical research and product testing, thank you for the opportunity to provide input on this meeting and the activities of the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).

We commend the continued efforts of federal agencies to advance new approach methodologies (NAMs) and recognize the growing momentum toward their regulatory acceptance. As increasingly sophisticated human-relevant methods become available, the challenge is no longer solely their development, but ensuring that these approaches can be efficiently evaluated, validated, and implemented to replace animal testing. The 2026 SACATM agenda presents an important opportunity to address these challenges through harmonized validation frameworks, clearer regulatory acceptance pathways, advancement of integrated testing strategies, and improved accessibility of computational tools. We offer the following recommendations to help translate scientific innovation into meaningful regulatory progress.

1. Advancing Federal Leadership in NAM Development and Implementation Through ORIVA and Interagency Coordination

The Physicians Committee commends the National Institutes of Health (NIH) for its continued commitment to advancing human-relevant research, particularly through the establishment of the Office of Research Innovation, Validation, and Application (ORIVA) in June 2026. We welcome ORIVA's early efforts to foster scientific collaboration and accelerate the development, validation, and implementation of NAMs. Recent initiatives, including the October 20-21 workshop on Alternative Methodologies in Pharmaceutical Development and the October 22-23 workshop on Recent Developments in Human-Based Models, demonstrate important progress in bringing together researchers, regulators, and other stakeholders to address scientific and regulatory barriers to NAM adoption.

Building on this momentum, we encourage ORIVA to translate the outcomes of these workshops into coordinated actions that advance NAM implementation across federal agencies. We particularly emphasize the importance of dedicated funding opportunities, harmonized validation approaches, and expanded training and infrastructure to support human-relevant methods. We also encourage ORIVA, through its Division of the National Interagency Center for the Evaluation of Alternative Test Methods (D-NICEATM), to strengthen interagency coordination and ensure that experts in nonanimal methods are meaningfully represented in NIH grant review and scientific decision-making. These efforts will be critical to accelerating the transition toward human-relevant research and reducing reliance on animal testing.

2. International Harmonization and Validation

We commend SACATM agencies for engaging in activities such as the revision of the Organisation for Economic Co-operation and Development's (OECD) Guidance Document No. 34 (GD 34), on the Validation and International Acceptance of New or Updated Test Methods for Hazard Assessment. We encourage SACATM to support the development of harmonized, fit-for-purpose guiding principles for assessing the technical readiness of NAMs, including biological relevance, reliability, reproducibility, transferability, and performance.

We further encourage SACATM to consider how validation frameworks can accommodate the increasing complexity of NAMs, particularly when evaluating large assay batteries and extensive chemical datasets with varying levels of data quality and biological coverage. Validation expectations should distinguish between individual assays and integrated testing strategies, with performance criteria tailored to their intended contexts of use. Establishing scalable, transparent, and internationally harmonized evaluation frameworks will be essential to ensuring scientific confidence while avoiding unnecessary barriers to regulatory acceptance.

3. Advancing NAM Validation and Regulatory Implementation

A. Leveraging the Validation and Qualification Network (VQN) to Address Method Development Challenges

The Physicians Committee commends U.S. agencies for their proactive response to the OECD's 2023 call for "[urgent mobilisation of national and regional resources](#)" to support method validation. The establishment and implementation of the Validation and Qualification Network (VQN) through the Foundation for the National Institutes of Health (FNIH) represents important progress. Pilot projects addressing acute oral toxicity, developmental neurotoxicity, and inhalation toxicity offer opportunities to overcome practical barriers to NAM validation and regulatory acceptance. We encourage SACATM to recommend that ICCVAM and D-NICEATM facilitate early engagement among developers, regulators, and end users; define context-of-use-specific performance and evidence requirements; and apply lessons learned to develop transparent, harmonized validation frameworks across toxicological endpoints.

B. Identifying and Addressing Barriers to NAM Validation and Regulatory Replacement

Regulatory end users should articulate, at the outset of method development, the decision a NAM is intended to support and the evidence needed to replace an existing animal test. ICCVAM agencies should publish endpoint-specific acceptance criteria and identify who is responsible for reviewing and implementing successful methods.

Validation should assess reliability and human relevance against the intended context of use, explicitly accounting for the uncertainty and variability of animal reference data. Agencies should state when available evidence is sufficient to discontinue an animal test, rather than treating additional animal comparisons as the default requirement.

We encourage SACATM to support early engagement between method developers and regulators to identify opportunities for emerging technologies to replace existing animal tests. Establishing clear regulatory contexts of use, standardized protocols, appropriate reference materials, and reproducibility criteria early in method development would help ensure that promising human-relevant approaches can advance efficiently toward regulatory acceptance and animal test replacement.

C. Broader Implementation of EPA's Nonanimal Test Methods and Strategies

The Physicians Committee welcomes the U.S. Environmental Protection Agency's (EPA) expanded list of nonanimal test methods and strategies under the Toxic Substances Control Act, its new nomination process, and its progress toward phasing out mammalian testing by 2035. In August, the EPA announced two further advances: a human airway tissue model to assess respiratory irritation from surfactants and acceptance of the Globally Harmonized System mixtures equation to support replacement of acute oral animal studies for certain pesticide formulations.

We are particularly encouraged by EPA's increasing integration of NAMs into chemical risk assessments. Recent assessments demonstrate the use of computational approaches, transcriptomic data, and weight-of-evidence frameworks, including Rethinking Carcinogenicity Assessment for Agrochemicals Project (ReCAAP), to inform hazard characterization and regulatory decisions. These developments highlight opportunities to incorporate human-relevant evidence, address data gaps, and reduce reliance on additional animal testing. We encourage SACATM to support broader implementation of such approaches across federal regulatory programs.

D. FDA Regulatory Modernization to Advance Nonanimal Methods

The Physicians Committee also commends the U.S. Food and Drug Administration (FDA) for its September 2026 direct final rule updating regulatory terminology to replace references to animal tests and studies with broader nonclinical terminology that accommodates scientifically valid NAMs. This important step is expected to remove animal-specific regulatory language and helps clarify opportunities for using scientifically valid NAMs in drug development. We encourage continued efforts to update remaining regulations and guidance to facilitate broader adoption of nonanimal approaches.

4. Advancing Integrated Approaches to Testing and Assessment (IATAs) Toward Regulatory-Ready Defined Approaches (DAs)

As secretariat for the International Council on Animal Protection in OECD Programmes (ICAPO), the Physicians Committee commends federal agencies for their leadership in developing Integrated Approaches to Testing and Assessment (IATAs), including those addressing developmental neurotoxicity, systemic toxicity, and respiratory sensitization. We encourage SACATM to build on these efforts by identifying representative IATA case studies that can inform the development of regulatory-ready Defined Approaches (DAs), where appropriate.

We encourage SACATM to consider developing a harmonized framework for advancing IATAs toward DAs, emphasizing clearly defined regulatory contexts of use, predefined information sources, assay-selection criteria, data interpretation procedures, and uncertainty assessments. Such a framework could also provide guidance on progressing toward regulatory acceptance when complete adverse outcome pathways (AOPs) or comprehensive mechanistic information are unavailable, including how remaining knowledge gaps can be characterized and evaluated in relation to the intended regulatory decision.

These case studies offer opportunities to address challenges involving large assay batteries and uneven chemical coverage (developmental neurotoxicity), reference chemical selection (respiratory sensitization), and integration of diverse experimental and computational evidence (systemic toxicity). We encourage ICCVAM and OECD partners to establish transparent, proportionate performance criteria and publish practical examples demonstrating how suitable IATAs can advance toward DAs and regulatory implementation without unnecessary validation barriers.

5. Computational Tools and Databases

We welcome D-NICEATM's continued efforts to develop and improve computational tools and resources, including CAMERA, NICE, SARA-ICE, the DASS App, OPERA, MoVIZ, and CATMoS. To improve accessibility and facilitate broader regulatory adoption, we encourage D-NICEATM to establish a **centralized, user-friendly platform that serves as a single-entry point to all tools and resources developed or hosted by D-NICEATM**. This would allow regulators, researchers, and other stakeholders to access available tools through one link, rather than navigating multiple websites or platforms. The platform should support interoperability through standardized chemical identifiers, compatible data formats, and linked workflows. Individual tools should also provide intuitive interfaces, clearly defined applicability domains, transparent measures of prediction confidence and uncertainty, where appropriate, and information on their intended regulatory contexts of use. Such an integrated platform, supported by user training and regular updates, would improve the accessibility, consistency, and practical application of NAMs in regulatory decision-making.

The Physicians Committee appreciates the continued leadership of SACATM, ICCVAM, D-NICEATM, and participating federal agencies in advancing human-relevant approaches to toxicological assessment. As NAM development and validation continue to advance, their ultimate success should be reflected in their adoption for regulatory decision-making and their contribution to replacing animal testing. We encourage SACATM to build on the current momentum by strengthening interagency coordination, facilitating knowledge sharing, and supporting the timely implementation of scientifically robust, human-relevant methods. The Physicians Committee remains committed to collaborating with federal agencies and other stakeholders to advance these shared goals while strengthening the protection of human health and the environment.

Sincerely,



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