



May 20, 2024

Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)  
National Institutes of Health  
Bethesda, MD 20892

**Re: ICCVAM Public Forum, May 2024**

Dear ICCVAM Members,

The 3Rs Collaborative (3RsC) appreciates the opportunity to provide written and oral input on ICCVAM-related activities. We are a U.S.-based non-profit whose mission is to advance better science – for both people and animals – through facilitating collaborative 3Rs efforts. Forwarding the use of the 3Rs and coordinating efforts across all stakeholders is therefore a central part of our organization.

ICCVAM and the 3RsC have multiple shared interests and goals that could serve as opportunities for potential future partnerships. Two areas of focus that may be of particular interest to ICCVAM include our initiatives devoted to advancing microphysiological systems (MPS) and artificial intelligence for preclinical safety and risk assessment. Similar to the broad range of stakeholder representation on ICCVAM's workgroups, the 3RsC prioritizes evidence-based decision-making by collecting input from the full range of interested parties. For example, our MPS initiative includes 96 members from 44 organizations (primary commercial developers) including a formal consortium agreement and active participation from the FDA's Center for Drug Evaluation and Research (CDER) and an MOU with the IQ MPS. Additionally, our Artificial Intelligence initiative includes 21 members from 15 diverse organizations including EPA, FDA, NIH/NIEHS, and USDA-AWIC.

We would like to congratulate ICCVAM members for a productive year of activities that are advancing the use of the 3Rs, validating new test methods, and coordinating efforts related to alternative methods across U.S. federal agencies.

To build on this momentum, the 3RsC would like to provide 3 key commendations & recommendations for ICCVAM to continue focusing on in the coming years.

**1. Continue to enhance collaborations between governmental and non-governmental agencies such as non-profits especially those that are balanced in their work across all 3Rs and encourage collaboration between various stakeholders (e.g., researchers utilizing animal models and/or NAMs, NAMs developers, etc.) and sectors (e.g., academics, industries, contract research organizations, regulators, developers, and IACUCs).**

- This recommendation aligns with the NIH ACD NAMs Working Group final report that emphasizes the need for combinatorial NAMs; for this effort to be effective, there is a need to ensure clear communication, expectations, and goals.

- For example, we commend and recommend continued or extended participation of ICCVAM members with the 3RsC such as ad hoc directors on our board and in our MPS, AI, and other initiatives to promote such collaboration.
- To help better advance the scientifically supported use of non-animal methods in regulatory submissions, we recommend that end-users, regulators, and technology developers should work together on (a) the development and validation of methods for specific contexts of use, (b) considerations for standards and outcome measures for specific contexts of use, and (c) to show the advantages of replacements in regulatory submissions.
- We also recommend funding a national U.S.-based, balanced 3Rs (replacement, reduction, refinement) center whose focus is on harnessing the power of collaboration to increase broad implementation of all 3Rs using evidence-based techniques is recommended.

**2. Continue to provide investments for the independent characterization and validation of NAMs (especially those that have been commercialized) to ensure that these technologies are well-characterized and validated for contexts of use.**

- For example, this may include projects under the NIH's Complement-AIRE efforts and common fund as well as projects directly with the 3RsC such as the 3RsC-FDA collaborative DILI project.
- Of note, we recommend balanced, accurate messaging on non-animal models that neither over-promises nor holistically condemns animal research – as this can alienate and activate cognitive dissonance in scientists currently utilizing animal models. Progress will be facilitated by all researchers working together to develop the best model possible to support the scientific objective with ethical considerations for both animals and humans. Partnering with non-profits such as the 3RsC may be valuable in these efforts.

**3. Continue to endorse and invest in implementing scientifically justified NAMs using evidence-based techniques to create change by promoting positive attitudes, providing training on implementation, and assisting in the normalization and socialization of 3Rs progress.**

- Supporting non-profits such as 3RsC that provide educational materials and advocate for responsible inclusion and analysis of NAMs in partnership with an understanding of the *in vivo* human and animal models.



In conclusion, the 3RSC appreciates the opportunity to give feedback on ICCVAM activities over the past year. Stakeholder feedback is crucial to policy making. There is a clear need for funding to focus on 3Rs research, reproducibility, translation, and dissemination. As scientists that strongly support the development and implementation of the 3Rs in biomedical research, we look forward to the next year of ICCVAM activities that advance our mutual goals.

Sincerely,

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3RSC Executive Director

[www.3rc.org](http://www.3rc.org)