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Dear SACATM members,

RTI International is an independent scientific research institute dedicated to improving the human condition through the development and application of science-based solutions. Our interdisciplinary teams work across the discovery, clinical, and regulatory spaces, combining in vitro, computational, and regulatory toxicology expertise with deep capabilities in bioinformatics, statistics, data science, and cheminformatics. This perspective informs our strong support for the leadership that the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and the National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) have demonstrated in advancing New Approach Methodologies (NAMs) through rigorous validation, data standards, and cross-agency coordination.

The progress made by ICCVAM and NICEATM in establishing validation frameworks, advancing data standards, and promoting transparent qualification processes is laying the groundwork for a new era of toxicological assessment. Sustained investment in these efforts will ensure that NAMs innovate regulatory science while also being rigorous, trusted, fit-for-purpose, and globally harmonized.

Recognizing NICEATM and ICCVAM's Progress and Leadership in Encouraging Adoption of Alternative Methods

We commend ICCVAM and NICEATM for their sustained attention to scientific rigor in NAMs development and qualification. Initiatives such as Complement Animal Research in Experimentation (Complement-ARIE), the Data Standards Work Group, and the planned Collection of Alternative Methods for Regulatory Application (CAMERA) resource build off ICCVAM and NICEATM's past work to exemplify the infrastructure and leadership needed to ensure that innovative approaches are both scientifically credible and decision-making ready. These efforts not only build confidence in science but also foster global harmonization, reduce duplication, and create transparent and accelerated pathways for regulatory acceptance.

Sustaining Trust and Adoption Through Standards, Validation, and Fit-for-Purpose Use

Building on this strong foundation, we encourage ICCVAM and NICEATM to continue prioritizing these objectives:

1. Establish and communicate clear criteria for determining when a method is fit-for-purpose for hypothesis generation versus regulatory or clinical decision-making.

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2. Expand cross-agency harmonization of data and metadata standards and reporting frameworks to ensure interoperability of NAMs datasets for regulatory applications and secondary data use.
3. Embed transparency and reproducibility measures into all validation and qualification processes to reinforce public trust in regulatory and clinical science.
4. Support the characterization and validation of in vitro methods to ensure rigor and reproducibility in in regulatory applications and basic science research.

Through our work with both data generators and secondary data users, we have seen firsthand the difference between exploratory science and decision-making applications. Although hypothesis generation is acceptable and advantageous during exploratory research and development (R&D) phases, decision-making that carries consequences for human health, environmental safety, and economic stability demands validated, context-specific methods. In an era when data misuse, deepfakes, and artificial intelligence "hallucinations" threaten the credibility of information, NICEATM and ICCVAM's discipline in setting high standards for method validation and data integrity is essential to optimal decision-making and sustaining public confidence.

By clearly delineating the evidentiary standards for different contexts, ICCVAM and NICEATM can foster accelerated scientific discovery while ensuring that decision-making remains grounded in rigorously validated science.

RTI's Experience and Commitment to Advancing NAMs

RTI has developed and used biologically complex human-derived in vitro co-culture models for R&D as well as in the generation of health effects data for regulatory submission. These complex models have demonstrated the importance of considering biological complexity and inter-individual variability in the identification of adverse effects of inhaled toxicants while also allowing mechanistic exploration at the molecular and cellular level, and capturing differences across populations. The resulting data can be integrated with advanced computational approaches such as in vitro to in vivo extrapolation (IVIVE) to translate laboratory insights into real-world predictions of human health impacts.

In parallel, RTI supports data harmonization and standards through efforts such as work leveraging the Adverse Outcome Pathway (AOP) framework. Frameworks such as these enable aggregation of scientific knowledge linking targets testable by NAMs to human-relevant outcomes. This work directly supports ICCVAM's emphasis on structured, interoperable data for risk assessment, regulatory review, and environmental management. Similarly, RTI's leadership in projects like the PhenX Toolkit, Biodata Catalyst, and the ECHO Program demonstrates our capacity to design and operate large-scale, reproducible pipelines for data ingestion, harmonization, and integration. These skills are directly transferable to the validation and qualification of NAMs for critical human-relevant outcomes.

Conclusion

RTI is committed to continuing its engagement with ICCVAM, NICEATM, and SACATM to advance these shared priorities. We bring decades of experience in data interoperability, computational modeling, experimental method development, and regulatory support, and we stand ready to contribute both thought leadership and executional capacity. Together, we can ensure that the next generation of safety assessment tools is innovative, credible, and capable of informing decisions that protect human and environmental health.

Sincerely,

Shaun D. McCullough, PhD
Senior Principal Investigator
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