



Interagency Coordinating Committee on the Validation of Alternative Methods

Presentation Abstracts and Background Materials

SCIENTIFIC ADVISORY COMMITTEE ON ALTERNATIVE TOXICOLOGICAL METHODS

Session IV: Computational Tools and Databases

Thursday, November 5, 2026

CAMERA v2.0: Enhancing Functionality and Test Method Discovery Through Improved Search and Visualization

Presenter: Dr. Alex Cole, Dynanet

The Collection of Alternative Methods for Regulatory Application (CAMERA) is an interactive database and user interface that provides online access to validated alternative methods for U.S. regulatory and other contexts of use. Supported by the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), CAMERA operates under the direction and oversight of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).

CAMERA serves as a central hub and unified resource for validated new approach methodologies (NAMs), enhancing access to validation study reports, data, protocols and standard operating procedures (SOPs), performance information, and regulatory guidance. Users can filter searches by alternative method type, defined approach, test-method endpoint, and regulatory guidance, and can visualize and compare key data and metadata from validation studies, including reference chemicals, reference test methods, and performance metrics such as reproducibility and predictive capacity.

The platform also identifies validated NAMs capable of measuring key events (KEs) within OECD-endorsed adverse outcome pathways (AOPs). This functionality helps users identify methods relevant to specific biological events and supports risk assessment when the domain of applicability of a given KE or AOP is appropriate. By integrating study reports, protocols, performance data, and regulatory guidance within a unified interface, CAMERA enhances transparency and facilitates the consistent application of NAMs in chemical safety evaluation.

CAMERA has recently migrated from NIEHS-hosted servers to the Amazon Web Services cloud and now features a redesigned user interface, enhanced visualization tools for comparing test methods and their performance, and an integrated AI-powered smart-search capability. Ongoing development will expand the range of methods and predicted endpoints, strengthen interoperability with databases such as the NIH Integrated Chemical Environment (NICE) and the AOP-Wiki, add interactive analytical tools, and incorporate user feedback to further enhance CAMERA's usability and scientific value.

This presentation will give a demo of CAMERA v2.0 for feedback and suggestions.

Background

1. Website: Collection of Alternative Methods for Regulatory Application (CAMERA). <https://camera.od.nih.gov/>



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NICEATM Computational Efforts Update: From Curated Data to Interoperable Tools

Presenter: Dr. Kamel Mansouri, on Detail to ORIVA, DPCPSI, NIH OD

This presentation provides a 2026 update on NICEATM's expanding computational ecosystem for the development, evaluation, and application of new approach methodologies. It describes the transition from individual software tools toward an interoperable environment in which curated *in vivo*, *in vitro*, *in silico*, exposure, and chemical-property data can be carried across interactive tools, automated workflows, and predictive models. Updates to the NIH Integrated Chemical Environment include the NICE v5.0 release, refinements to PBPK and IVIVE modeling, new visualizations, and ongoing cloud and platform modernization. A propylparaben case study demonstrates this interoperability in practice: Chemical Quest and Chemical Characterization identify and refine relevant analogs; Curve Surfer and IVIVE evaluate estrogen-related bioactivity and translate *in vitro* concentrations into equivalent administered doses; and NICE Search and PBPK modeling connect predicted exposure with tissue-level concentration profiles.

The presentation also highlights efforts to democratize cheminformatics through MoVIZ, which packages advanced computational methods into transparent, guided no-code and low-code workflows. Examples include LLM-assisted extraction of structured study information, QSAR-ready chemical-structure standardization, and endpoint-specific chemical grouping for read-across and method evaluation. OPERA updates include a major CATMoS revision that expands coverage of highly toxic chemicals, improves the consensus weight-of-evidence approach, and strengthens the handling of counterions, salts, and solvents, along with refreshed physicochemical-property models. The international CoMPAIT collaboration extends this consensus-modeling strategy to acute inhalation toxicity, with planned implementation in OPERA and a manuscript in preparation. Additional efforts include OECD guidance for *in silico* methods, pubertal IVIVE, quantitative translation of lung microphysiological-system data, and AI-assisted method development. The overarching message is that **accessible tools, curated data, interoperability, and transparent consensus models together provide a stronger computational foundation for regulatory adoption of computational tools.**

Background

- Mansouri K, Moreira-Filho JT, Tieghi RS, Kleinstreuer NC. 2026. Democratizing artificial intelligence in toxicology: real-world applications and automated computational workflows. *Chem Res Toxicol* 39(2):1072–1083. <https://doi.org/10.1021/acs.chemrestox.6c00093>.
- Moreira-Filho JT, Ranganath D, Tieghi RS, Patton R, Sutherland V, Schmitt C, Rooney AA, Fostel J, Walker VR, Saddler T, Reif D, Mansouri K, Kleinstreuer N. 2025. Automating data extraction from scientific literature and general PDF files using large language models and KNIME: An application in toxicology. *WIREs Comput Mol Sci* 15(1):e70047. <https://doi.org/10.1002/wcms.70047>.

Reimagining the SARA-ICE Tool for Regulatory Application

Presenter: Dr. Emily Reinke, General Dynamics Information Technology

The Skin Allergy Risk Assessment – Integrated Chemical Environment (SARA-ICE) model for derivation of a human relevant point-of-departure (PoD) for skin sensitization is one of many successes by NICEATM in developing and providing tools that advance the use of NAMs in a user-friendly manner. This is reflected by the acceptance of SARA-ICE into the Organisation for Economic Co-operation and Development (OECD) Guideline 497 “Defined Approaches on Skin Sensitisation” in 2025, a first-of-its-kind addition to the guideline [1]. With the acceptance of SARA-ICE, the model falls under the Mutual Acceptance of Data for OECD member countries and has seen several regulatory authorities explore its use and apply it within hazard assessments. The PoD for SARA-ICE is defined as the geometric mean of ED₀₁, the dose, in µg/cm², at which 1% of a human population is likely to be sensitized [2,3]. This metric differs from traditionally utilized



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PoDs derived as a weight-of-evidence under a quantitative risk assessment framework, which are termed no expected skin induction level (NESIL), and are the doses at which no sensitization is expected [4,5]. Due to the difference in the SARA-ICE PoD from the NESIL, robust uptake and understanding of how to apply the SARA-ICE PoD in a risk assessment has been an ongoing conversation, including what uncertainty factors, if any, need to be applied to the PoD and what an appropriate margin of exposure (MoE) would be for a 1% sensitization dosage. The former was explored by the U.S. Environmental Protection Agency (EPA) Office of Pollution Prevention and Toxics in a draft health hazard assessment for phthalic anhydride [6]. The assessment determined that the model was robust and only required an uncertainty factor of 1 for intraspecies variability, as the model is already human-based and incorporates variability and uncertainty into the predictions. Unilever, the co-developers of SARA-ICE developed a statistical approach to convert precedent safety assessment factors (SAF)/MoE utilized with NESILs into equivalent thresholds for models such as SARA-ICE or other NAM-based PoDs approaches [7]. Their assessment showed that where a SAF/MoE of 100 was typically used, the SARA-ICE PoD and the NESIL were equivocal. At larger SAFs, the MoE for SARA-ICE diverges from the NESIL SAF, but less than for other approaches. These assessments show that while the current approach to SARA-ICE is feasible, it does require some nuance to understand the application of the PoD. Additionally, the EPA explored extrapolating the dose-response curve for estimated PoDs, in order to get closer to an effective non-induction level.

These discussions and publications have led the SARA-ICE development team, in continued collaboration with Unilever, to explore a new approach that predicts a more NESIL-like value. This presentation will discuss this new approach for SARA-ICE, which will instead predict an implied NESIL (iNESIL) and explore the development and evaluation of the SARA-NESIL.

Background

- Webpage: SARA-ICE: Skin Sensitization Risk Assessment - Integrated Chemical Environment Model. <https://ntp.niehs.nih.gov/whatwestudy/niceatm/test-method-evaluations/skin-sens/da/SARA-ICE>
- Reynolds, J., Aleksic, M., Gilmour, N. & Reynolds, G. Determination of acceptable margins of exposure (MoE) for NAM-based skin sensitisation risk assessment. NAM Journal, 100062 (2025). <https://doi.org/10.1016/j.namjnl.2025.100062>
- Reinke, E. N. et al. Deriving a point-of-departure for skin sensitization risk assessments, application of the SARA-ICE tool to a diverse set of chemicals. NAM Journal 2 (2026). <https://doi.org/10.1016/j.namjnl.2026.100078>

Citations

1. OECD. Guideline No. 497: Defined Approaches on Skin Sensitisation. Report No. OECD TG 497, (Organisation for Economic Co-operation and Development, Paris, France, 2026). <https://doi.org/10.1787/e1f1244b-en>
2. Reinke, E. N. et al. Deriving a point-of-departure for skin sensitization risk assessments, application of the SARA-ICE tool to a diverse set of chemicals. NAM Journal 2 (2026). <https://doi.org/10.1016/j.namjnl.2026.100078>
3. Reinke, E. N. et al. The skin allergy risk assessment-integrated chemical environment (SARA-ICE) defined approach to derive points of departure for skin sensitization. Current Research in Toxicology 8, 100205 (2025). <https://doi.org/10.1016/j.crttox.2024.100205>
4. Api, A. M. et al. Updating exposure assessment for skin sensitization quantitative risk assessment for fragrance materials. Regul Toxicol Pharmacol 118, 104805 (2020). <https://doi.org/10.1016/j.yrtph.2020.104805>
5. Api, A. M. et al. Dermal sensitization quantitative risk assessment (QRA) for fragrance ingredients. Regulatory Toxicology and Pharmacology 52, 3-23 (2008). <https://doi.org/10.1016/j.yrtph.2007.10.008>
6. EPA, U. S. Draft Human Health Hazard Assessment for Phthalic Anhydride. (Washington, D.C., 2026). <https://www.epa.gov/system/files/documents/2026-04/16-phthalic-anhydride-draft-human-health-hazard-assessment-public-release-march-2026.pdf>
7. Reynolds, J., Aleksic, M., Gilmour, N. & Reynolds, G. Determination of acceptable margins of exposure (MoE) for NAM-based skin sensitisation risk assessment. NAM Journal, 100062 (2025). <https://doi.org/10.1016/j.namjnl.2025.100062>



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SACATM Discussion

Lead Discussants: Dr. Sally Thompson-Irritani, University of Washington; Dr. Ellen Berg, Alto Predict LLC; Dr. Adrian Nanez, Exelixis, Inc

Discussion Questions

1. How well are NICEATM's computational tools currently meeting your needs and expectations? How would you ideally like to use them in your work?
2. Detailed use case descriptions help NICEATM develop needed capabilities. Please provide detailed descriptions of use cases that require interactions between CAMERA and NICE.
3. How will computational models impact risk assessment? On which tools, features, or other related area should NICEATM/ICCVAM focus future efforts to maximize this impact?