Presentation Abstracts and Background Materials

SCIENTIFIC ADVISORY COMMITTEE ON ALTERNATIVE TOXICOLOGICAL METHODS

Session III: Computational Resources
Friday, September 12, 2025

Collection of Alternative Methods for Regulatory Application (CAMERA)

Presenter: Dr. Katie Needham, Axle

CAMERA - The Collection of Alternative Methods for Regulatory Application - is a publicly available, web-based application designed to provide streamlined access to validated and qualified new approach methodologies (NAMs) for regulatory and other contexts of use. CAMERA was developed in response to a proposal from U.S. regulatory agency members of ICCVAM, recognizing a critical need for a centralized resource that enhances the visibility and accessibility of NAMs that have been accepted for regulatory application. NAMs refer to innovative scientific tools, technologies, and approaches – or combinations thereof – that can be used to inform chemical, drug, or product safety assessments and regulatory application, with the goal of improving human relevance and reducing reliance on traditional vertebrate animal models. CAMERA features user-friendly search and filtering capabilities tailored to diverse user needs, including tools to compare the performance and key characteristics of different NAMs. Users can access a range of supporting information, including validation study data, protocols, validation study reports, applicability information, and relevant guidance or guidelines.

Background

- ICCVAM Authorization Act (42 U.S.C. 285l-3)
- CAMERA webpage
- OECD (2025), *Guideline No. 497: Defined Approaches on Skin Sensitisation*, OECD Guidelines for the Testing of Chemicals, Section 4, OECD Publishing, Paris, https://doi.org/10.1787/b92879a4-en.

Updates to the Integrated Chemical Environment (ICE)

Presenter: Dr. Kamel Mansouri, NICEATM, DTT, NIEHS

The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) developed the Integrated Chemical Environment (ICE, https://ice.ntp.niehs.nih.gov/), a free online resource that provides toxicologically relevant data and computational tools to support the development and evaluation of NAMs. ICE offers access to both reference and non-reference chemical lists, as well as curated, high-quality datasets for toxicity endpoints of regulatory concern. This presentation will provide an overview of the various uses of ICE and briefly introduce ICE data and its suite of interoperable tools. Examples will be presented to show how these tools can be used to identify structurally similar chemicals, explore high-throughput screening assays, predict tissue concentrations, relate in vitro measurements to in vivo equivalent administered doses, and characterize chemical space through physicochemical properties and use categories. Recent updates to these features in ICE v4.1.1 (January 2025) and ICE v4.2 (July 2025) will also be highlighted. These include updates to the PBPK (Physiologically Based Pharmacokinetics) and IVIVE (In Vitro to In Vivo Extrapolation) tools to allow users to upload their own physicochemical and absorption, distribution, metabolism, and excretion (ADME) parameters. Additionally, curated high-throughput screening data were updated to align with the U.S. Environmental Protection Agency's invitrodb v4.2, which has new points-of-departure, new curve-fit models, and updated

biological annotations. Information fields in the Curve Surfer tool were expanded to accommodate these changes. In the Chemical Characterization tool, the principal component analysis plots now have loadings that show how various physicochemical properties contribute to overall chemical clustering. Additional updates to various chemical quick lists, datasets, help videos, and website aesthetics were made to improve overall user experience. Feedback from this presentation will be used to inform priorities for future ICE improvements.

Background

- ICE Website: https://ice.ntp.niehs.nih.gov/
- Reisfeld B, Borrel A, Chang X, Daniel A, Hill B, Hull V, To KT, Unnikrishnan A, Green A, McAfee E, Phillips J, Reinke E, Mansouri K, Kleinstreuer N The Integrated Chemical Environment (ICE): Advancing Data Availability and Computational Tool Accessibility for the Development, Evaluation, and Application of New Approach Methods. Poster Presentation to ASCCT 2024. https://ntp.niehs.nih.gov/sites/default/files/2024-11/Reisfeld_ASCCT2024_poster.pdf
- Daniel AB, Choksi N, Abedini J, Bell S, Ceger P, Cook B, Karmaus AL, Rooney J, To KT, Allen D, Kleinstreuer N. 2022. Data curation to support toxicity assessments using the Integrated Chemical Environment. Front Toxicol. 4:987848. https://doi.org/10.3389/ftox.2022.987848

New Apps for Skin Sensitization

Presenter: Dr. Emily Reinke, Inotiv

As part of NICEATM's goals for supporting the advancement of NAMs, a focus on developing applications that help to advance the science in a user-friendly manner has been in place for several years. With the development and acceptance of the "Defined Approaches on Skin Sensitisation" test guideline (TG 497) by the Organisation for Economic Co-operation and Development (OECD) in 2021 and subsequent updates in 2023 and 2025, these web applications help in application of the defined approaches or related test methods. Three user-friendly web applications have been developed and released since 2022: the DASSapp, the SARA-ICE model, and the HPPTapp (to be released prior to the SACATM meeting). The DASSapp allows users to take their in vitro, in chemico, and in silico data and apply the decision trees for each of the different variations of the defined approaches in Sections 1 and 2 of TG 497. SARA-ICE is a first-of-its-kind statistical model for deriving a point-of-departure for use in a skin sensitization risk assessment, using only NAMs data. The model is predicated on a robust database of sensitizers and non-sensitizers, using a variety of input parameters from both in vivo and in vitro methods. This web app was recently launched and provides users an easily accessible way to run the model for both application within the TG 497 parameters and in an extended model for increased functionality. The HPPTapp was developed to help users derive a point-of-departure for skin sensitization for human patch tests, following a decision tree recently published by NICEATM and collaborators.

Background

- Reinke EN, Reynolds J, Gilmour N, Reynolds G, Strickland J, Germolec D, Allen DG, Maxwell G, Kleinstreuer NC. 2025. 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. https://doi.org/10.1016/j.crtox.2024.100205
- To KT, Strickland J, Reinke E, Borrel A, Truax J, Maldonado H, Allen D, Kleinstreuer N. 2024. Computational application of internationally harmonized defined approaches to skin sensitization: DASS App. BMC bioinformatics. 25(1):4. https://doi.org/10.1186/s12859-023-05617-1
- Unnikrishnan A, To KT, Herzler M, Germolec D, Reinke E, Kleinstreuer N. Web Application to Classify and Subcategorize Skin Sensitizers Using Human Data. Poster presentation to SOT 2025. https://ntp.niehs.nih.gov/sites/default/files/2025-03/Unnikrishnan_SOT2025_poster.pdf