Presentation Abstracts and Background Materials

SCIENTIFIC ADVISORY COMMITTEE ON ALTERNATIVE TOXICOLOGICAL METHODS

Session IV: Computational Resources
Wednesday, September 18, 2024

NICEATM's Integrated Chemical Environment (ICE): Updates, Enhancements, and Advances

Presenter: Dr. Brad Reisfeld, Inotiv

The NTP Interagency Center for the Evaluation of Alternative Toxicological Methods' (NICEATM) Integrated Chemical Environment (ICE) provides a convenient and user-friendly platform to aid in the development, evaluation, and application of new approach methodologies (NAMs). In this presentation, we detail some of the updates and advances to ICE in response to evolving stakeholder needs. As an open access, web-based tool (https://ice.ntp.niehs.nih.gov/) with over 2400 page views and 600 file downloads per month, ICE has made significant contributions to supporting chemical assessments and advancing NAMs by providing users with curated toxicology-relevant data and interactive analysis and visualization tools.

The most recent ICE releases (4.0.2 in March 2024 and 4.1 in August 2024) included enhancements to tools for data exploration and interpretation, more intuitive search features, and new Chemical Quick Lists that provide users with curated sets of related compounds to use in analyses and visualizations. Recent ICE updates also improved the curated high-throughput screening (cHTS) pipeline. Outputs now include flags for potential technological interference and updated assay annotations using standardized terminologies to encompass a broader range of biological and toxicological processes. We also improved the ICE Curve Surfer tool to include these new cHTS flags and annotations, as well as an activity concentration at cut-off (ACC) overlay that allows users to conduct focused analyses of concentration-response curves. Finally, users can now access the concentration-response information within ICE using the REST application programming interface.

Background

- Abedini JA, Cook B, Bell SM, Chang XQ, Choksi NY, Daniel AB, Hines DE, Karmaus AL, Mansouri K, McAfee E, Phillips J, Rooney JP, Sprankle CS, Allen D, Casey WM, Kleinstreuer NC. 2021. Application of new approach methodologies: ICE tools to support chemical evaluations. Comput Toxicol. 20:100184. https://doi.org/10.1016/j.comtox.2021.100184.
- Bell SM, Abedini JA, Ceger P, Chang XQ, Cook B, Karmus AL, Lea I, Mansouri K, Phillips J, McAfee E, Rai R, Rooney J, Sprankle C, Tandon A, Allen D, Casey WM, Kleinstreuer NC. 2020. An integrated chemical environment with tools for chemical safety testing. Toxicology In Vitro. 67:104916. https://doi.org/10.1016/j.tiv.2020.104916.

Collaborative Computational Modeling of Inhalation Toxicity

Presenter: Dr. Kamel Mansouri, Division of Translational Toxicology (DTT), National Institute of Environmental Health Sciences (NIEHS)

In response to the need for efficient and humane alternatives to traditional in vivo studies, the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) has initiated a collaborative effort to develop a computational approach for predicting inhalation LC50 values. This project arises from a

2016 workshop focusing on alternative methods for acute inhalation toxicity assessment. A curated dataset comprising in vivo LC50 values for approximately 760 chemicals has been established to facilitate this endeavor. Unlike other modeled endpoints, the unique complexities of inhalation data and regulatory frameworks necessitate innovative and tailored approaches. Beginning in mid-2024, participating groups started collaborating to define and refine predictive modeling methodologies, with a focus on accommodating categorical hazard/classification systems to align with regulatory requirements. Through iterative refinement and consensus-building, this collaborative effort aims to deliver robust and applicable computational tools for acute inhalation systemic toxicity hazard and risk assessment.

Background

- Strickland J, Clippinger AJ, Brown J, Allen D, Jacobs A, Matheson J, Lowit A, Reinke EN, Johnson MS, Quinn Jr. MJ, Mattie D, Fitzpatrick SC, Ahir S, Kleinstreuer N, Casey W. 2018. Status of acute systemic toxicity testing requirements and data uses by U.S. regulatory agencies. Regul Toxicol Pharmacol 94:183–196. https://doi.org/10.1016/j.yrtph.2018.01.022.
- Strickland J, Haugabrooks E, Allen DG, Balottin LB, Hirabayashi Y, Kleinstreuer NC, Kojima H, Nishizawa C, Prieto P, Ratzlaff DE, Jeong J, Lee JH, Yang Y, Lin P, Sullivan K, Casey W. 2023. International regulatory uses of acute systemic toxicity data and integration of new approach methodologies. Crit Rev Toxicol 53(7):385–411; https://doi.org/10.1080/10408444.2023.2240852.

Collection of Alternative Methods for Regulatory Application (CAMERA)

Presenter: Dr. Nicole Kleinstreuer, NICEATM, NIEHS DTT

NICEATM and ICCVAM support coordinated efforts among federal government agencies to advance alternatives to animal models that are based on human biology while providing information of equivalent or better scientific quality and relevance, and align with the 3Rs principles: Reduce, Refine, and Replace animal testing. There is a critical need for a unified resource that enhances accessibility to validated/qualified NAMs that have been accepted for regulatory application. CAMERA aims to become a central hub for alternative methods and validation reports, both those that are currently validated as well as future methods, e.g. arising from the NIH Complement-ARIE program. The project seeks to provide access to standardized methodologies and their associated validation data to ensure consistency and reliability across biomedical research and regulatory submissions, facilitating global regulatory compliance and cooperation and promoting reproducibly of NIH-funded research. CAMERA will be a comprehensive database and user-friendly, interactive web-based interface that provides advanced search capabilities, allowing users to easily locate and access information on validated NAMs, including data from validation studies, standardized protocols, and information on applicability and regulatory acceptance.

Background

- National Toxicology Program. 2024. Alternative Methods Accepted by US Agencies. https://ntp.niehs.nih.gov/go/regaccept.
- European Commission. TSAR – Tracking System for Alternative Methods Towards Regulatory Acceptance. https://tsar.jrc.ec.europa.eu/.