

Building Confidence in Alternative Methods Through ICE

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New approach methodologies (NAMs) are generally defined as non-animal methods using one or more in vitro assays or in silico tools to provide information on chemical hazard and risk assessment. While scientific and policy advances have enabled adoption of some NAMs for specific applications, barriers remain to widespread regulatory acceptance of NAMs, with animal-based testing paradigms remaining standard. Two critical resources must be provided to foster development of, and build confidence in, NAMs. One of these is access to high-quality data, including context and provenance. The other is opportunity for stakeholder engagement through increased familiarity and use of interpretable, approachable language and controlled terminology. These needs are met by the National Toxicology Program's (NTP's) Integrated Chemical Environment (ICE, <https://ice.ntp.niehs.nih.gov/>), a user-friendly, open-access resource that provides high-confidence, curated reference data and in silico predictions of chemical properties. Processes used for ICE data acquisition and curation are transparent and include citations of original data sources. Use of controlled vocabularies and standard IDs (CASRNs, DTXSIDs) aids in data interoperability and linkage between ICE, the U.S. Environmental Protection Agency's Chemicals Dashboard, and NTP's Chemical Effects in Biological Systems (CEBS) database. ICE computational tools allow users to search for, visualize, and obtain context for these data. High-throughput screening assays from ToxCast and Tox21 have been annotated to mechanistic targets and modes of action to provide biological context for assay results. Curated data from these assays can be viewed as concentration–response curves using the Curve Surfer tool. Other tools available in ICE allow users to run physiologically based pharmacokinetics and in vitro to in vivo extrapolation models and search for structurally similar chemicals. These tools are designed to be accessed by diverse end-users through simple user interfaces and provide a bridge between subject matter experts and computational scientists. This project was funded by the National Institute of Environmental Health Sciences, National Institutes of Health, under Contract No. HHSN273201500010C.

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