

Evaluating New Chemicals in the U.S under the Toxic Substances Control Act (TSCA): Application of New Approach Methods (NAMs) to Evaluate Eye Irritation

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US Environmental Protection Agency's Office of Pollution Prevention and Toxics, New Chemicals Division (NCD) is responsible for conducting risk assessments under the Toxic Substances Control Act (TSCA). In 2016, TSCA (amended under the Frank R. Lautenberg Act) directed EPA to "promote the development and implementation of alternative test methods and strategies to reduce, refine, or replace vertebrate animal testing and provide information of equivalent or better scientific quality and relevance for assessing risks of injury to health or the environment". To incorporate NAM data for eye irritation hazard identification, NCD is collaborating with colleagues from National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), Institute for *In Vitro* Sciences, Inc. and PETA Science Consortium International e.V. to develop a decision framework to evaluate eye irritation hazards for new chemicals under TSCA. This framework proposes to prioritize use of data from NAMs over *in vivo* studies in animal models for the prediction of eye irritation in humans. In using the framework, acceptable NAMs data on the new chemical substance from OECD test guideline or other acceptable studies are considered first. If information on the new chemical substance is not available or acceptable, a close analogue that has information is identified to evaluate eye irritation of the new chemical substance. Under the framework, all information is collected and evaluated in the following order: (1) data from human cell/tissue-based test methods that have been demonstrated to be reproducible and relevant to eye irritation; (2) data from *in chemico* or non-human *in vitro* and/or *ex vivo* test methods that have been demonstrated to be reproducible and provide information on the mechanisms of toxicity relevant to eye irritation in humans; and (3) data from *in vivo* animal studies. If no acceptable information on eye irritation is available, the framework allows for consideration of skin irritation data that predict irritating or corrosive properties to make inferences about eye irritation hazard of the new chemical substance. The decision tree framework as well as case studies will be presented. *These views are those of the authors and do not reflect views or policies of the US EPA or other respective organizations. This project was funded in part with federal funds from the NIEHS, NIH under contract No. HHSN2722015000010C.*