Development and Curation of an Acute Inhalation Toxicity Database

Reinke EN[1], Daniel AB[1], Hull VH[1], To KT[1], Karmaus AL[1], Allen DG[1], Mansouri K[2], Kleinstreuer NC[2]

[1]Inotiv, RTP, NC, United States; [2]NIH/NIEHS/DTT/PTB/NICEATM, RTP, NC, United States

Interest is increasing in using computational modeling tools to predict toxicity endpoints for regulatory decision-making. Developing such tools requires robust, well-curated, and chemically diverse training data. NICEATM has compiled and curated rat acute inhalation data for approximately 1700 chemicals from a variety of sources, including ECHA, EPA, the U.S. National Institute for Occupational Safety and Health, the U.S. Department of Defense, and PubChem/ChemIDPlus. We used manual and automated curation techniques to extract LC50 values and/or ranges. Metadata collected for each entry included exposure type, exposure route, species, sex, and number of animals tested. Duplicate studies were removed. All qualifying LC50 values were converted to 4-hour exposures using Haber's Law to allow for direct comparison to, and assignment of, GHS categories. For many studies, details were not available on whether the substance was delivered via aerosol, vapor, or gas. Therefore, a rule-based decision process was applied to determine the GHS category of each chemical based on its physicochemical properties. The data were analyzed for variability across categories for chemicals with multiple studies and exposure types. The curated data will be made publicly available and used for a collaborative modeling effort to predict continuous, binary, and multicategory endpoints based on the regulatory use of the LC_{50} value for hazard assessment. The development and curation of this acute inhalation database for consensus models will support progress in the use of NAMs for regulatory decision-making. Project was funded by NIEHS under Contract No. HHSN273201500010C.