

Compilation and Standardization of Rat Acute Inhalation Study Data to Support Predictive Modeling

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Computational models for predicting acute inhalation toxicity have been proposed as alternatives to animal tests to support regulatory decision making. Developing such models requires robust, well-curated, and chemically diverse training data. NICEATM has compiled and curated rat acute inhalation data for approximately 1200 chemicals from a variety of sources, including the European Chemicals Agency, the U.S. Environmental Protection Agency, the U.S. National Institute for Occupational Safety and Health, the U.S. Department of Defense, and PubChem/ChemIDPlus. Concentrations lethal to half the test animals (LC50) values and study metadata were extracted and evaluated for quality using manual and automated techniques. For data meeting predetermined quality standards, LC50 values were converted to 4-hour exposures using Haber's Law to facilitate direct comparison and hazard category assignments. For nearly 70% of studies, details were not available on whether the chemical was delivered via aerosol, vapor, or gas. For these chemicals, a rule-based decision process based on physicochemical properties was applied to assign the phase of exposure and associated hazard category. Data were analyzed for variability across categories for chemicals with multiple studies and exposure types. Nearly 200 chemicals had at least three LC50 point-estimates, and more variability was found between chemicals than within chemicals. The curated data will be made publicly available in NICEATM's Integrated Chemical Environment and used in a collaborative modeling effort to generate consensus predictions for continuous, binary, and multicategory endpoints for regulatory hazard assessment. This project was funded with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.