Retrospective Analysis of Acute Toxicity Tests for Pesticides

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Systemic toxicity from exposure to toxic chemicals, chemical products, and pharmaceuticals is a significant cause of illness and death in the United States. U.S. regulatory agencies use data from in vivo rodent acute oral and dermal toxicity tests to determine potential systemic toxicity of chemical products following ingestion and topical skin exposure. These data are used to derive an LD_{50} value (dose expected to produce lethality in 50% of the animals tested) for hazard classification and labeling to protect human health and the environment when handling and transporting chemicals. In this study, we considered whether rat acute oral toxicity LD_{50} values for pesticide formulations and active ingredients (AIs) could be used to determine acute dermal toxicity hazard classifications for the U.S. Environmental Protection Agency (EPA) categorization system and the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). This retrospective analysis used high-quality acute toxicity data for 910 formulations and AIs from various EPA toxicity reports, peer-reviewed publications, and databases. Oral hazard classifications based on rat oral LD_{50} values were compared to dermal hazard classifications based on rat dermal LD_{50} values. The concordance of oral and dermal hazard classification was 52% for dermal hazard using the EPA system and 65% for dermal hazard using the GHS system. Using oral hazard classifications overestimated dermal hazard for 37% of the compounds using EPA classifications and 34% using GHS classifications. Predictivity of classification for substances that do not require hazard labeling (EPA Category IV [LD_{50} >5000 mg/kg] and GHS unclassified [>2000 mg/kg]), was 73% for the EPA system and 99% for the GHS system. Underprediction of dermal hazard was 11% for the EPA system and 2% for the GHS system, which indicates that acute oral hazard categories are sufficiently protective for acute dermal hazard classification. *This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.*

Keywords: acute toxicity, alternatives to animal testing, hazard classification