

Performance of the GHS Mixtures Equation for Predicting Acute Oral Toxicity

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The United Nations Globally Harmonized System for Classification and Labeling (GHS) provides a mathematical approach to estimate the acute oral toxicity of a mixture based on the combined toxicities of its individual components. We evaluated how well toxicity values calculated using the GHS formula, and the corresponding U.S. Environmental Protection Agency (EPA) and GHS hazard categories, agreed with those obtained from in vivo acute toxicity studies of the same formulations. Data were compiled for approximately 700 formulations submitted for pesticide registration including agrochemical and antimicrobial product formulations, most of which were classified in the less hazardous EPA Categories III and IV and GHS Categories 4, 5, and Not Classified (NC). The extent to which more toxic formulations might be underpredicted by the mixtures equation could not be addressed with full confidence. Overall concordance was between 55% to 82% depending on the classification system and the ranges of LD50 values used. Most discordant results were associated with substances with a limit test LD50 >2000 mg/kg or a measured LD50 between 2000 and 5000 mg/kg, which were predicted using the mixtures equation as having minimal toxicity LD50 >5000 mg/kg. Therefore, most of the discordance observed may be of lesser concern than if more toxic substances were underpredicted. Our results suggest the mixtures equation is a promising approach for identifying substances that would not be expected to induce toxicity. The lack of more toxic formulations in the data set preclude us from reaching definitive conclusions across the spectrum of hazard categories. This project was funded with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C. The views expressed above do not necessarily represent the official positions of any federal agency.