

## Defined Approaches for GHS Categorization to Assess Eye Irritation Potential of Agrochemical Formulations

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Accuracy of non-animal alternatives for assessing eye irritation has historically been determined by comparison to the Draize rabbit eye test. However, because of the rabbit test's demonstrated lack of reproducibility and human relevance, there has been movement away from evaluating alternatives via one-to-one comparisons with it, in favor of evaluating based on the reliability and human-relevance of the method. We used a common set of non-animal assays in a multi-phase study to assess the eye irritation potential of agrochemical formulations. Test articles represented major agrochemical formulation types and the complete range of GHS eye irritation hazard classifications. Assays were selected for inclusion based on their relevance to humans, and results were assessed to determine which assays should advance to subsequent testing phases. A total of 29 formulations were tested in as many as five assays: bovine corneal opacity and permeability (with histopathology), EpiOcular, SkinEthic Time-to-Toxicity, in vitro depth of injury, and EyeIRR-IS. Data generated were used to analyze alignment of predictions across non-animal assays and the rabbit test. Consensus GHS predictions were determined based on majority alignment among individual assay results (achieved for 27 formulations). Interestingly, the historical rabbit test classification differed from the consensus prediction for five formulations. This suggests that the rabbit test may not be a suitable reference method for deriving GHS eye irritation hazard classifications for agrochemical products. These data will support ongoing work to develop defined approaches for assessing eye irritation potential of agrochemical formulations. Project was funded by NIEHS under Contract No. HHSN273201500010C.