

Interpretation of In Vitro Concentration-Response Data for Risk Assessment and Regulatory Decision-making: Report from 2022 IWGT Quantitative Analysis Expert Working Group Meeting

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Abstract

Quantitative risk assessments of chemicals are routinely performed in rodents; however, there is growing recognition that non-animal approaches can be human-relevant alternatives. There is an urgent need to build confidence in non-animal alternatives given the international support to reduce the use of animals in toxicity testing where possible. In order for scientists and risk assessors to prepare for this paradigm shift in toxicity assessment, standardization and consensus on in vitro testing strategies and data interpretation will need to be established. To address this issue, an Expert Working Group (EWG) of the 8th International Workshop on Genotoxicity Testing (IWGT) evaluated the utility of quantitative in vitro genotoxicity concentration-response data for risk assessment. The EWG first evaluated available in vitro methodologies and then examined the variability and maximal response of in vitro tests to estimate biologically relevant values for the critical effect sizes considered adverse or unacceptable. Next, the EWG reviewed the approaches and computational models employed to provide human-relevant dose context to in vitro data. Lastly, the EWG evaluated risk assessment applications for which in vitro data are ready for use and applications where further work is required. The EWG concluded that in vitro genotoxicity concentration-response data can be interpreted in a risk assessment context. However, prior to routine use in regulatory settings, further research will be required to address the remaining uncertainties and limitations.

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