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Evaluation of the Standard Battery of In Vitro Genotoxicity Tests for Human Health Risk Assessment through Mathematical Modelling: A Report of the International Workshop on Genotoxicity Testing (IWGT)

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In human health risk assessment of chemical substances, assessment of genetic toxicity for regulatory purposes usually starts with a standard battery of in vitro genetic toxicity tests. This battery, comprising multiple tests, is needed to cover the different genetic toxicity endpoints. The tests that are commonly included in the battery (partly) differ in biology, due to which resulting data may seem contradictory, thereby complicating accurate interpretation of the findings. This could be overcome by using mathematical modelling. To test and discuss the utility of mathematical modelling for evaluating the predictivity of a test battery, a workgroup of the International Workshops for Genotoxicity Testing was convened. We applied mathematical modelling to a large database comprising *in vitro* and in vivo data for genotoxicity, with the aim to evaluate the performance of the *in vitro* test battery to predict in vivo genotoxicity. The results obtained indicate when using a battery of three genotoxicity tests, i.e. a bacterial gene mutation test (Ames), a mammalian cell gene mutation test, and a mammalian in vitro clastogenicity test, combination of two mammalian cell tests showed the highest predictive value for *in vivo* genotoxicity and adding Ames test results has no impact on the prediction of *in vivo* genotoxicity. Further research comparing *in vitro* genotoxicity data with *in vivo* data for the same genotoxicity endpoint will provide additional insights on the predictivity of the standard in vitro genotoxicity battery.

Keywords:
Genetic toxicology, Toxicity prediction, Uncertainty, Hazard assessment, Bayesian modelling, Chemicals.