

# Science Question 6: In vitro Mutagenicity/Genotoxicity

Chad Thompson, Ph.D.

ToxStrategies, Inc.

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The logo for ToxStrategies, Inc. features the company name in a white, serif font. The letter 'x' is stylized with a small dot above it. The text is set against a green, curved background that resembles a rising sun or a horizon line.

# Genotoxicity Should be Assessed in the Context of Dose and Toxicity

...In the final peer review report (2011), it was emphasized by several reviewers that for in vitro studies of mutagenicity and genotoxicity, positive results are only observed following very high concentration exposures that are toxic to the cells exposed....

Dr. Toby Rossman (NYU) in 2011 report: *“Unless assays for cytotoxicity are performed, it is not possible to know whether DNA damage occurs in the relatively nontoxic dose-range that one can relate to carcinogenesis...”*

EU Guidance (2003)\*: *“Evaluation of genotoxicity test data should be made with care. Regarding ‘positive’ findings, responses may be generated only at highly toxic/cytotoxic concentrations, and the presence or absence of a dose-response relationship should be considered.”*

Comment:

- **released database contains little/no information on dose levels, dose-response, or markers of cytotoxicity**

\*European Commission. (2003) Technical guidance document in support of commission directive 93/67/EEC on risk assessment for new notified substances and commission regulation (EC) No 1488/94 on risk assessment for existing substances, Part I.