

**Re: GUIDANCE ON A STRATEGY FOR GENOTOXICITY TESTING AND MUTAGENIC HAZARD ASSESSMENT OF CHEMICAL SUBSTANCES**

Since I only recently learned of the request for comments on this document, I will only be able to provide a brief overview. Over the years the mutagenicity strategies in Canada (e.g. the Canadian Environmental Protection Act) and the UK have taken similar approaches. I commend the COM for its continued work to respond as new developments in the field emerge.

While there is much to praise in this draft Guidance Document, my main concern is that whilst the stated goal of the document is “Mutagenic chemicals may present a hazard to health since exposure to a mutagen carries the risk of inducing germ-line mutations, with the possibility of inherited disorders, and the risk of somatic mutations including those leading to cancer” (para 11), and the *in vivo* strategies conserve the germ cell risk assessment intent, the *in vitro* strategies do not. The *in vitro* strategies are mostly based on the performance of *in vitro* tests for the prediction of carcinogenicity despite the statement at the end of para 40 indicating that “no convincing evidence that any rodent carcinogen or *in vivo* genotoxin would be “missed” ”.

There is a need to use similar statistics for the prediction of *in vivo* mutagenicity by *in vitro* tests, as are widely used for the prediction of carcinogenicity, in order to balance the rationale for the section on appropriate *in vitro* tests. I have found it helpful in the pursuit of a full understanding of the relationships among the various endpoints to regard mutation a toxicological endpoint per se, which also is a predictor of carcinogenicity, rather than the reverse.

Yours sincerely,

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