Endogenous Chemical Risk Assessment: Formaldehyde as a Case Example

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ABSTRACT

Conducting a dose-response assessment for endogenous compounds presents several challenges. The Science and Decisions (2009) report has indicated that it is possible that the dose-response curves for these types of compounds may be threshold-like, depending upon the magnitude of the background concentrations and toxic response. In addition, the dose-response curves may also appear to be linear if a detectable background level of toxicity occurs even without exogenous exposure and the exogenous exposure adds to or augments the background toxicity process, assuming the exogenous exposure does not induce an adaptive response. Formaldehyde provides an example of research and modeling activities being conducted to understand the endogenous concentrations of formaldehyde and the potential contribution of exogenous formaldehyde to the potential for health effects following inhalation exposure. The approaches demonstrate both the challenges in collecting the information needed to characterize internal doses in the low-concentration range, which is of significance to ambient exposure, as well as interpreting the results and the impact on understanding the dose-response for an endogenously present compound. These approaches can be extended to other compounds with endogenous DNA adducts that are identical to those produced by such chemicals as acetaldehyde, ethylene oxide and vinyl chloride. They may also be indicative of general phenomena related to endogenous DNA damage, as our DNA contains large amounts of endogenous DNA damage that are the reason for the well-known non-zero background of mutations, the biomarkers of effect that may be considered causal key events in carcinogenesis.