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Ms. Stephanie Sanzone
Designated Federal Officer
EPA Science Advisory Board

Re: Comments on 5/4/11 DRAFT "SAB Review of EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments"

Dear Ms. Sanzone:

Thank you for the opportunity to provide comment to the Chartered SAB on the draft report "SAB Review of EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments." These comments address the section of the Draft SAB report regarding the review of the EPA reference dose derivation, and I offer them on behalf of the Chlorine Chemistry Council.

We support the conclusions of the Panel that the derivation of the proposed RfD values would be strengthened by placing the chosen datasets into the context of other available studies in a weight of evidence evaluation. Specifically, as noted in our July, 2010, comments to the panel and reviewed in Goodman et al. (2010), the numerous studies that are available for examining associations between maternal TCDD or TEQ concentrations and infant thyroid hormone status support the findings of the Baccarelli et al. (2008) authors that no statistically significant relationship between TCDD or TEQ and TSH is seen below maternal TCDD or TEQ concentrations of 50 ppt (lipid-adjusted). Consideration of the full range of available human epidemiological data supports selection of this level as a no-observed-adverse-effect-level (NOAEL) for use in derivation of an RfD. Because the conclusions are robust across many studies with more than 500 maternal-infant pairs included, the studies address interindividual variability and sensitivity, and no additional uncertainty factors would be appropriate on this target maternal level. The SAB Panel report should be more explicit on the strong pattern of results and support reliance on the wide range of studies for selection of a point of departure (POD) from Baccarelli et al. that reflects the strength of the available datasets.

The Draft Panel report mentions, but does not sufficiently emphasize the importance of, consideration of the contribution of non-TCDD TEQ. In both the Baccarelli et al. (2008) and Mocarelli et al. (2008) datasets, non-TCDD contributors to TEQ were present at levels comparable to or exceeding the TCDD contribution. If the TEQ framework is appropriate, these contributions must be considered in the

quantitative assessment of the POD and RfDs from these studies. This should be reemphasized in the final Panel report.

Several corrections and clarifications would be appropriate in the draft report. Specifically, in the Draft Panel report, on p. 18, in reference to the EPA RfD calculations regarding the association between maternal serum TCDD and neonatal TSH levels, the following statement is made:

The Panel also suggests that since the bulk of the calculations were based on zonal averages of exposed individuals in Baccarelli et al. (2008), EPA should clarify how these measurements relate to ranges and variations in exposure *in utero*.

This statement is not correct. The calculations were not made based on zonal averages, but rather based on measured concentrations in maternal-infant pairs in a sample of women from Seveso with a range of serum TCDD concentrations, without regard for Zone of exposure. Zonal averages were not used in the RfD calculations. This comment is incorrect and should be deleted.

A second issue should be addressed in the report. Specifically, regarding selection of uncertainty factors, the following statement is made, also on p. 18 of the draft report:

However, a short discussion of the decision not to include an uncertainty factor for data quality is needed.

No category of uncertainty factor for “data quality” currently exists in the risk assessment paradigm used by EPA. While uncertainty factors for database deficiencies are sometimes assigned when toxicological data are sparse or missing in a particular toxicological category, it would be absurd to suggest that the database for TCDD is deficient relative to any other chemical assessed by EPA. The Panel report should be edited to remove the reference to this novel category of uncertainty factor.

Thank you for the opportunity to comment.

Sincerely,

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