



March 30, 2009

Wendy Cleland-Hamnett, Acting Office Director
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Re: Additional Tier 3 toxicology studies for the Xylenes Voluntary Children's Chemical Evaluation Program (VCCEP) Assessment.

Dear Ms. Cleland-Hamnett:

The American Chemistry Council Benzene, Toluene and Xylene (BTX) VCCEP Consortium (the "Consortium") appreciates the opportunity to comment on EPA's proposal for VCCEP Tier 3 testing. Following careful evaluation, the Consortium does not believe conducting an additional developmental neurotoxicity study and an adult neurotoxicity screening battery will provide meaningful contribution to the overall risk characterization or risk assessment for xylenes¹.

The Xylene VCCEP submission provides summaries of a number of repeat dose studies of xylene isomers and mixed xylenes. Included in these summaries are studies that address potential developmental neurotoxicity (Hass) and adult neurotoxicity (Korsak). The Consortium believes that these studies provide sufficient information to adequately characterize the potential risks from exposure to xylenes on this endpoint. Clearly, the EPA considered the Korsak study to be of sufficient quality to use the study as the basis for the current IRIS reference concentration. Furthermore, repeating either of these studies would likely not result in a lower NOEL than that used as the point of departure in the xylenes VCCEP documents.

Ethylbenzene (EB) is a significant component (~20%) of mixed xylenes and a common component in other potential sources of xylene exposure. EB was recently evaluated in both a developmental neurotoxicity study and adult neurotoxicity study as presented in EB's VCCEP document. The evidence for identified NOEL for both endpoints was 500 ppm, the highest dose tested. This lack of neurotoxicity or developmental neurotoxicity up to 500 ppm of EB, a close structural analog of the xylenes, suggests that exposure to xylenes would also not demonstrate activity in these tests.

¹ ortho-, meta-, para- and mixed xylenes



Although the lack of a neurotoxicity study with exposures beginning at or before birth was considered a limitation in the xylene data set by a few member(s) of the EPA sponsored VCCEP Peer Consultation Panel (the “Panel”) for xylenes, this view was not shared by the majority of the Panel. In their final recommendation, the Panel did not specifically identify a developmental neurotoxicity study or an adult neurotoxicity screening battery as a potential “data need” and/or potential “data gap” and therefore did not consider these studies necessary to adequately characterize the hazards and risks associated with chronic exposure to xylenes. The Organization for Economic Cooperation and Development Screening Information Data Set (SIDS) Initial Assessment Report reviewed the existing xylenes dataset and concluded that the xylenes were a low priority for further work.

Multiple sources of potential xylenes exposure have been identified. Most of these xylenes exposure sources are complex mixtures where xylenes represent only a fraction of the many different components present. Examples include complex mixtures of hydrocarbons like gasoline, emissions from wood burning stoves and fireplaces, automobile exhaust, environmental tobacco smoke and cooking.

Overall the VCCEP exposure assessment suggests that potential exposures to xylenes are low and the calculated Hazard Indexes (HI) (ratio of exposure / Reference Dose) indicate an ample margin of safety. The majority of exposures were more than 20 times below the Reference Concentration/Dose; the highest calculated exposure was to nursing infants of occupationally exposed mothers, but the Hazard Index was 0.13, well below 1.00. In addition, emissions from production sites have decreased over the years even though production volumes have increased. Technology changes such as reformulated fuels, lower emission automobiles and reformulated consumer products suggest that potential exposures are likely to decrease in the future. The large margin between the Reference Concentration/Dose and the estimated potential exposures along with a decreasing trend in future exposures indicate that new studies will not likely have a significant impact on the risk estimates.

In summary, a substantial database already exists to characterize the potential risks from exposure to xylene isomers and mixed xylenes. Results from the VCCEP report suggest a reasonable margin of safety already exists between estimated exposure levels and predicted effect levels. It is unlikely that the proposed studies would result in the need for a more conservative point of departure than that used in the VCCEP risk assessment. The Consortium believes that the additional studies proposed by the EPA would not result in any meaningful contribution to the overall risk characterization or risk assessment of xylenes. The Consortium, for the above mentioned reasons, will not commit to sponsor xylenes in tier 3 of VCCEP.



The American Chemistry Council Benzene, Toluene and Xylene (BTX) VCCEP Consortium appreciates the opportunity to submit these comments. If you have any questions, please contact Leslie Berry at 703.741.5612
Leslie_Berry@americanchemistry.com

Sincerely,



Leslie Berry
BTX VCCEP Consortium Manager,
Chemical Products and Technology

cc: Jim Willis, Director
Chemical Control Division
Office of Pollution Prevention and Toxics