

**Hydrocarbon Solvents Panel/American Chemistry Council Oral Comments to EPA/SAB Teleconference on SAB Draft Report on EPA IRIS Assessment of Trimethylbenzene (November 5, 2014)**

Good Afternoon,

I am David Adenuga, a toxicologist with ExxonMobil Biomedical Sciences, presenting public comments today on behalf of the hydrocarbon solvents panel of the American chemistry council.

We have read your draft report and would like to appreciate the SAB panel for their considerations of some of the key industry concerns that were raised at the face-to-face meeting in June. Those include the recommendation to the EPA to consider the inclusion of the complex C9 aromatic solvent studies, improving literature search and inclusion of the 135-TMB oral subchronic toxicity study as a potentially more appropriate study for the derivation of a reference dose. This reaffirms the panel's belief that sound science must remain the basis for which IRIS assessments are conducted.

As was mentioned by the last commenter, the EPA Office of Pesticides Program published a final rule on complex C9 aromatic hydrocarbons exemption from the requirement of a tolerance<sup>1</sup>. It is important to stress that the final rule essentially eliminates the need to establish a maximum permissible level for residues of complex C9 aromatics used as inert ingredients in pesticide formulations applied to animals.

Essentially by considering these substances as "safe", the EPA/OPP determines that there is a reasonable certainty that no harm will result from aggregate exposure to pesticide chemical residue that may result from all anticipated dietary exposures and all other exposures for which there is reliable information, including through drinking water and residential exposure (for example exposure via inhalation during refueling and transport of gasoline – for which the EPA/IRIS office has determined as the largest exposure point source for trimethylbenzenes). The conclusions reached in this final rule are very pertinent as it addresses some of the issues that are the basis for some of the conclusions reached in the IRIS assessment. Without taking too much time, I'd like to go through the key conclusions made by the OPP:

1. It is clearly demonstrated that the risks from aggregate exposure to complex C9 aromatics pose no appreciable risks to human health through all possible general population exposure routes considered (excluding occupational exposure).
2. The C9 aromatic studies could be used to address hazard assessment for trimethylbenzenes, as the individual constituents were structurally and toxicologically similar. The OPP also concluded that the results of these studies were "valid, complete and reliable" for use in assessing the potential for human risk. The OPP indicated that they found the toxicity database for C9-rich aromatic hydrocarbons to be "complete, except for an immunotoxicity study".

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<sup>1</sup> Federal Register Notice Vol 79, No. 187, September 26, 2014

3. Although no ADME data is available on the complex C9 aromatics, the OPP concluded that there was sufficient metabolism data on other aromatic hydrocarbons (most likely individual constituents) to show that “as a class they are typically well absorbed, widely distributed between tissues, extensively metabolized and rapidly excreted”. The OPP concluded that the C9-rich aromatic hydrocarbons are of low toxicological concern for developmental and reproductive effects and are not expected to be carcinogenic based on available toxicity data.
4. OPP concluded that “there is no indication that C9-rich aromatic hydrocarbons are neurotoxic chemicals” and that there is no need for a developmental neurotoxicity study or additional UFs to account for neurotoxicity.
5. Based on data on the C9-rich aromatic hydrocarbons, the OPP developed an RfD value of 1.5 mg/kg/day, a value that is at least 2 orders of magnitude higher than the values proposed in the IRIS assessment of TMB. Using this RfD value, assuming a standard adult body weight of 70 kg and breathing volume of 20 m<sup>3</sup>/day, the equivalent RfC = 5 mg/m<sup>3</sup>.

$$\text{Where RfC (mg/m}^3\text{)} = [\text{RfD (mg/kg/day)} \times 70 \text{ kg}] / 20 \text{ m}^3$$

Despite 3 different studies, this value is virtually identical to the RfD of 1.2 mg/kg/day calculated in Adenuga et al. (2014) with an equivalent RfC of 4.2 mg/m<sup>3</sup>.

To conclude, we believe that there is a need to return to the drawing board to understand why there is such a huge disparity in the EPA IRIS and EPA/OPP assessments of practically the same substances. Once again thank you for the opportunity to present these comments.

## Reference

Adenuga, M., Carrillo, J.C., and McKee, R. (2014). The sub-chronic oral toxicity of 1,3,5-trimethylbenzene in Sprague-Dawley rats. *Regulatory Toxicology and Pharmacology* 69:143-153.