



September 10, 2012

Ms. Monet Vela
Office of Environmental Health Hazard Assessment
P.O. Box 4010, MS-23B
Sacramento, California 95812-4010
Submitted Via E-Mail to: P65Public.Comments@oehha.ca.gov

Re: Notice of Augmentation and Clarification of Record for Proposed Regulation on Chloroform

Dear Ms. Vela:

On June 27, 2012 the American Chemistry Council (ACC)¹ submitted written comments on the Office of Environmental Health Hazard Assessment's (OEHHA) Notice of Proposed Rulemaking for Chloroform². ACC's comments focused on the "Initial Statement of Reason for the Chloroform Maximum Allowable Dose Level (MADL)" (Statement). We specifically noted that OEHHA did not provide the reference citations or details for all the studies noted in the Statement nor did OEHHA include any detailed information on the weight of evidence framework used to select the most sensitive study (i.e. Baeder and Hofmann 1990). ACC commends OEHHA for augmenting the record to include the references for the studies and for providing a copy of the unpublished Baeder and Hofmann study; however the documentation and justification for the proposed MADL is still lacking.

Several areas in the Statement that require additional review and clarification are included below.

¹The American Chemistry Council (ACC) represents the leading companies engaged in the business of chemistry. ACC members apply the science of chemistry to make innovative products and services that make people's lives better, healthier and safer. ACC is committed to improved environmental, health and safety performance through Responsible Care®, common sense advocacy designed to address major public policy issues, and health and environmental research and product testing. The business of chemistry is a \$674 billion enterprise and a key element of the nation's economy. It is one of the nation's largest exporters, accounting for ten cents out of every dollar in U.S. exports. Chemistry companies are among the largest investors in research and development. Safety and security have always been primary concerns of ACC members, and they have intensified their efforts, working closely with government agencies to improve security and to defend against any threat to the nation's critical infrastructure.

² Proposed Rulemaking Title 27, California Code of Regulations Amendment To Section 25805 Specific Regulatory Levels: Chemicals Causing Reproductive Toxicity for Chloroform.
<http://oehha.ca.gov/prop65/law/051812Chlor.html>



Weight of Evidence for human data lacks transparency

- OEHHA notes in the Statement that *“Human data on chloroform exposures (mostly through water disinfection by-products, as well as some workplace exposures) provide some evidence on developmental toxicity; however, these studies provide only a limited basis for establishing quantitative dose-response relationships.”* However, neither the Statement nor the augmentation to the record includes any discussion of the available human data. The record should be augmented to specifically provide a discussion of the applicable human studies which provide *“some evidence on development toxicity”* as referenced by OEHHA.
- The Statement also does not provide any discussion regarding applicable chloroform exposures although it mentions specifically that they occur *“mostly through water disinfection by-products as well as some workplace exposures.”* OEHHA should provide specific information on applicable and relevant exposures.

Weight of Evidence for animal studies lacks clarity, transparency and the confidence of peer review

- In a clarification to the record, OEHHA notes that it reviewed five animal inhalation studies and one animal oral study to determine the MADL for chloroform. However, in addition to the Thompson *et al.* (1974) oral study, the Ruddick *et al.* (1983) study does not appear to be an inhalation study. A review of the study indicates that rats were administered chloroform by oral intubation and not through inhalation. This should be corrected in the record.
- OEHHA selected the Baeder and Hofmann³ 1990 study as the most sensitive study to derive the MADL. However, this is an unpublished study that was submitted to the U.S. Environmental Protection Agency pursuant to Section 8(e) of the Toxic Substance Control Act. Considering that this is an unpublished study, OEHHA should have this study independently peer reviewed prior to using it as the basis for regulatory activity.
- The Baeder and Hofmann 1990 and 1988⁴ studies appear to represent the best available dose response information for developmental toxicity associated with chloroform exposure in rats. The authors of the Baeder and Hofmann 1990 study report noted that *“After concentrations of 10 ppm and 30 ppm the dams displayed a slight reduction in feed consumption and body-weight development. The fetuses were slightly stunted.”* and *“On the basis of the results of the embryotoxicity studies, it can therefore be concluded that the no observed adverse effect level for chloroform in the rat, as regards maternal and embryonal toxicity in the case of inhalative exposure, lies at 3 ppm.”* OEHHA also

³ Baeder C and Hofmann T (1990). Chloroform: supplementary inhalation embryotoxicity study in Wistar rats. Report No. 91.0902. Hoechst Aktiengesellschaft Pharma Development Toxicology.

⁴ Baeder C, Hofmann T (1988). Initial submission: inhalation embryotoxicity study of chloroform in Wistar rats (final report) with attachment and cover letter dated 2/21/92. Pharma Res Toxicol Pathol Conducted for Occidental Chem Corp . U.S. EPA/OTS Public Files, Document Number: 88-920001208.



chose to utilize a NOEL of 3 ppm in its MADL calculation. However, further review of the Baeder and Hofmann study data shows that while the study noted slight reductions in consumption and fetal weight at 10 ppm these changes did not appear to be statistically different from the controls. Subsequently, according to the study text, mean fetal body weights and lengths did not differ significantly among groups.

ACC appreciates OEHHA's willingness to augment the record to include valuable study citations however; the Statement should be further revised to include the critical study details which support the MADL derivation and any study used as the basis for the MADL should be independently peer reviewed if it is not found in the published literature. Feel free to contact me if you would like to discuss these comments in more detail. I can be reached by email at Kimberly_Wise@americanchemistry.com or phone 202-249-6707.

Respectfully,

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