

INTERNATIONAL  
**Food  
Additives  
Council**

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June 25, 2012

Ms. Susan Luong  
Office of Environmental Health Hazard Assessment  
P. O. Box 4010. MS-19B  
Sacramento, California 95812-4010

Re: Proposed MADLs for Methanol as published in the California Regulatory Notice Register on March 16, 2012 (Register 2012, No. 11-Z)

Dear Ms. Luong:

The International Food Additives Council (IFAC) is an international association representing companies that produce high quality substances used worldwide as food ingredients, including food additives and GRAS substances. IFAC is responding to the request for comments on a notice of proposed rulemaking, published in the *California Regulatory Notice Register* on March 16, 2012 (Register 2012, No. 11-Z), announcing proposed maximum allowable dose levels (MADLs) for Methanol at 23,000 and 47,000 micrograms per day for oral and inhalation exposures, respectively. We appreciate the opportunity to comment on this matter, and are taking this opportunity to share a concern from numerous food additive and ingredient manufacturers regarding the methodology and data used to develop the proposed MADLs for Methanol.

We recognize that Proposition 65 requires the Office of Environment Health Hazard Assessment (OEHHA) to establish "safe harbor" levels (e.g. MADLs) for all chemicals listed on the Proposition 65 list of chemicals known to the state of California to cause cancer or reproductive toxicity. Under Proposition 65, a listing of methanol as a "developmental toxicant" became effective on March 16, 2012. Beginning in March 2013, products containing methanol above an OEHHA established "safe harbor" level will be required to display warning labels.

However, IFAC believes there are some serious problems with the data that has been used and methodology involved with the development of the proposed MADLs for methanol published by OEHHA in March 2012. According to OEHHA, the MADLs were developed based on data collected from studies with mice. However, evidence shows that relying on rodent data for methanol ignores the significant differences that exist in the way that humans and rodents process and metabolize methanol. Thus, IFAC strongly urges OEHHA to revise the MADL for methanol to a higher level and prevent the enactment of the unnecessarily burdensome proposed MADL that will have a significant impact on California businesses without adding any benefits to health and safety of the state's citizens.

Below, IFAC has outlined evidence to support the metabolic difference referenced above. We have also provided some general observations about the ubiquitous presence of methanol in the natural environment. We encourage you to review this information and use it to revise the propose MADL for methanol.

Primates and rodents metabolize methanol in vastly different ways. When exposed to methanol, rodents accumulate methanol in their blood at a faster rate than humans and primates. The OECD, in their 2004

summary of methanol, concluded that “At a higher inhalation exposure (6.5 mg/L), humans show the lowest blood methanol level (at 140 mg/L), followed by monkeys, rats, and mice, with the level in mice being more than 10 times higher than humans.<sup>i</sup> Similarly, the Dutch Expert Committee on Occupational Safety of the Department of Health, in their 2010 review of methanol, states that the methanol blood levels could be 13-to 18-fold higher in mice than in humans for comparable exposures.<sup>ii</sup> This is because, in rodents, the process for breaking down methanol into other compounds is overwhelmed at much lower levels of methanol than for humans and other primates. Consequently, rodents accumulate relatively high blood concentrations of methanol even at low exposure levels, compared to humans, who accumulate methanol in the blood at a much slower pace.

Humans are also less vulnerable than rodents to methanol’s developmental effects. OEHHA has determined that it is the internal level of methanol that results in developmental toxicity in rodents. Accordingly, the potential for developmental toxicity in humans is significantly lower than for rodents. The proposed “safe harbor” levels should be revised to recognize this difference and the MADL should be raised at least 3.5-fold based on the clearly dissimilar processing of methanol by primates and rodents. Thus, we propose that OEHHA raise the MADL for oral exposures from 23,000 to at least 80,000 micrograms per day.

Methanol (a.k.a., “wood alcohol”) is a natural substance. While methanol is generated naturally in many foods, it is also generated during food processing, from natural additives, and other food ingredients. Though IFAC members believe that in most cases the abovementioned sources of methanol will result in exposures at levels lower than the “safe harbor” levels, there is significant legal risk for companies with regard to compliance with Proposition 65. Therefore, making the “safe harbor” more reasonable, by recognizing the differences between humans and rodents, would have a significant positive impact on a wide array of California companies including many IFAC members who operate in your state, providing jobs to residents and driving the local economy.

Thank you again for the opportunity to comment. IFAC would like to reaffirm our commitment to assisting OEHHA in developing Proposition 65 guidelines and MADLs for foods that meet protect the health and safety of Californians without having unintended and burdensome consequences on the businesses of the state. We would welcome the opportunity to meet with you to discuss MADLs for methanol or any future Proposition 65 issue for which we can offer assistance.

Sincerely,



Haley Curtis Stevens, Ph.D.  
Executive Director

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<sup>i</sup> OECD SIDS. 2004. Methanol. Page 16.

<sup>ii</sup> Health Council of the Netherlands. 2010. Expert Committee on Occupational Safety. Methanol. Health-based recommended occupation exposure limit. Page 41 (citing conclusions by Perkins et al. 1995)