

March 10, 2015

Via Email - P65Public.Comments@oehha.ca.gov

Ms. Monet Vela
Office of Environmental Health Hazard Assessment
P.O. Box 4010, MS-25B
Sacramento, California 95812-4010

RE: No Significant Risk Level Determination for diisononyl phthalate

Dear Ms. Vela:

The Consumer Specialty Products Association¹ (CSPA) appreciates the opportunity to comment on the proposed No Significant Risk Level (NSRL) determination for diisononyl phthalate (DINP).

We have concerns with the underlying science used in establishing the NSRL and offer the following observations and recommendations. In our opinion, the MNCL tumor data should not be included in the dataset used for the derivation of the NSRL.

In the OEHHA assessment mononuclear cell leukemia (MNCL) tumor data from a Fisher 344 rat study was included in the derivation of the DINP NSRL. MNCL tumors are known to occur spontaneously at a high incidence in Fisher 344 rats. In addition, MNCL tumors are not observed in other species and there is no histologically comparable tumor in humans.² Therefore, MNCL tumors in Fisher 344 rats are of questionable relevance to humans. This finding has been noted in multiple articles^{2,3} as well as by the American Chemistry Council (ACC)⁴ and also CPSC CHAP^{5,6} reviews of the potential of DINP to cause carcinogenicity.

¹ The Consumer Specialty Products Association (CSPA) is the premier trade association representing the interests of companies engaged in the manufacture, formulation, distribution and sale of more than \$100 billion annually in the U.S. of familiar consumer products that help household and institutional customers create cleaner and healthier environments. CSPA member companies employ hundreds of thousands of people globally. Products CSPA represents include disinfectants that kill germs in homes, hospitals and restaurants; candles, and fragrances and air fresheners that eliminate odors; pest management products for home, garden and pets; cleaning products and polishes for use throughout the home and institutions; products used to protect and improve the performance and appearance of automobiles; aerosol products and a host of other products used every day. Through its product stewardship program, Product Care[®], and scientific and business-to-business endeavors, CSPA provides its members a platform to effectively address issues regarding the health, safety and sustainability of their products.

² Caldwell, DJ. Review of mononuclear cell leukemia in F-344 rat bioassays and its significance to human cancer risk: A case study using alkyl phthalates. Regul Toxicol Pharmacol 1999 Aug; 30 (1):45-53.

³ Thomas, J; et al. A review of large granular lymphocytic leukemia in Fischer 344 rats as an initial step toward evaluating the implication of the endpoint to human cancer risk assessment. Toxicological Sciences 2007 99(1): 3-19.

⁴ ACC letter to EPA Docket Center re: Docket ID Number TRI-2005-0004. October 12, 2005, <http://www.regulations.gov/contentStreamer?objectId=0900006480cbee67&disposition=attachment&contentType=pdf>.

⁵ US Consumer Product Safety Commission. June 2001. Report to the US Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Diisononyl phthalate (DINP), <https://www.cpsc.gov/PageFiles/98260/dinp.pdf>.

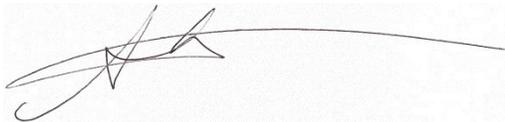
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We agree to the liver tumor-based approach for DINP, as OEHHA applied to DEHP. The scaling factor used for DEHP was not applied in the OEHHA proposed derivation of the NSRL for DINP. Liver adenoma and carcinomas were found in rats and mice following DINP exposure. Similar to other phthalates, the mechanism of action for these tumors is believed to result from peroxisome proliferation. Rodents are known to be much more sensitive to hepatocellular tumors caused by peroxisome proliferation than humans. This was acknowledged in the derivation by OEHHA of the NSRL for another phthalate, DEHP.⁷ Per OEHHA:

“Female mice were identified as the most sensitive sex and species to the tumorigenic effects of DEHP. Based on the relative expression levels of the PPAR- α in humans compared to mice, a ten-fold factor was applied to reduce the potency extrapolated from carcinogenicity studies in female mice to account for this assumed lower level of human cellular sensitivity. The application of this scaling factor to the extrapolated cancer potency derived from the experimental animal studies provides a reasonable basis for calculating a level posing no significant risk of cancer to humans.”

We believe it is reasonable to also apply this scaling factor accounting for this difference in species sensitivity since DINP is a similar phthalate that also causes hepatocellular tumors in rodents by peroxisome proliferation. Therefore we urge OEHHA to take into account known species differences in establishing the NSRL for DINP, applying a scaling factor to NSRL derived from liver tumors.

Sincerely,



Steven D. Bennett, Ph.D.
Senior Director, Scientific Affairs and Sustainability



Kristin Power
Vice President, State Affairs

cc: CSPA Scientific Affairs Committee Proposition 65 Task Force
Nicole Quinonez, Randlett Nelson Madden

⁶ US Consumer Product Safety Commission. July 2014. Report to the US Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Phthalates and Phthalates Alternatives, <http://www.cpsc.gov/PageFiles/169902/CHAP-REPORT-With-Appendices.pdf>.

⁷ Reproductive and Cancer Hazard Assessment Section Office of Environmental Health Hazard Assessment (OEHHA) California Environmental Protection Agency. June 2001. No Significant Risk Level (NSRL) for the Proposition 65 Carcinogen Di(2-ethylhexyl)phthalate.