Formaldehyde Council

May 12, 2008

Document Control Office (7407M)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C., 20460-0001

Re: Sierra Club TSCA Petition; Docket ID Number EPA-HQ-OPPT-2008-0267

Dear Sir or Madam:

On behalf of the Formaldehyde Council Institute (FCI),[1] I am responding to a notice regarding the petition submitted to the Environmental Protection Agency (EPA) under section 21 of the Toxic Substances Control Act (TSCA). 73 Fed. Reg. 22369 (April 25, 2008). By letter dated March 20, 2008,[2] the Sierra Club and other organizations and individuals asked the EPA to exercise its authority under TSCA § 6(a) to adopt and apply nationally the formaldehyde emissions regulation for composite wood products recently issued by the California Air Resources Board (CARB).[3]

FCI seeks to ensure that any decision involving formaldehyde or formaldehyde-based products is based on a common and correct understanding of the extensive toxicology and other scientific data on formaldehyde. The Sierra Club's Petition includes a statement that there is "no safe level of exposure" to formaldehyde. Petition at 2. This statement is demonstrably incorrect as explained below. Because the Petition asks that EPA promulgate a rule similar to that issued by CARB, FCI's comments on the CARB rulemaking are attached and incorporated by reference.

Since its founding, FCI has become recognized as an expert resource in the science of formaldehyde toxicology and applicable risk assessment models. FCI members manufacture the majority of the U.S. production volume of formaldehyde. FCI's mission is to encourage accurate scientific evaluation of formaldehyde and formaldehyde-containing products and to communicate sound scientific information relating to the uses, benefits and sustainability of these products.

---

[1] FCI is a trade association of leading producers and users of formaldehyde that is dedicated to promoting the responsible use and benefits of formaldehyde and ensuring its accurate scientific evaluation. For more information, please see http://www.formaldehydge.org.

[2] The letter was received by EPA on March 24, 2008. 73 Fed. Reg. 22369.

[3] CAL. CODE REGS. tit. 17, § 93120-93120.12 (2008). *See also* Comments of the Formaldehyde Council, Inc. on "Proposed Airborne Toxic Control Measure to Reduce Formaldehyde Emissions from Composite Wood Products;" Comments on Staff Report: Initial Statement of Reasons for Proposed Rulemaking (April 16, 2007) (attached).

FORMALDEHYDE COUNCIL, INC
1300 Wilson Blvd, Arlington, VA 22209 • 703-741-5750 • fax 703-741-5751
www.formaldehyde.org

FCI is committed to advancing the state of scientific understanding on potential toxicology, epidemiology, and environmental effects related to formaldehyde, as well as providing accurate technical and scientific information relating to potential exposures, uses and effects of formaldehyde or formaldehyde-based products.

A. Formaldehyde in Nature

Formaldehyde is naturally produced and is an important component of various metabolic processes in all living systems, from rodents to fish to humans. Because of its biological properties, highly efficient detoxification pathways have evolved specifically to maintain blood levels within a very narrow range. Consequently, formaldehyde needs to be assessed differently than an agent that has no role in normal metabolism and physiology. It is important to note that:

- Because of its importance in various metabolic processes, formaldehyde is naturally present in the human body with concentrations of approximately 1-2 parts per million (ppm) in the blood.
- As a result of normal metabolism and its innate volatility from the blood, formaldehyde is exhaled in human breath. In a study by Moser et al. (2005), the median level of formaldehyde in human breath was 0.004 ppm with levels of 0.006 ppm, 0.040 ppm and 0.073 ppm for the 75^{th}, 97.5^{th} and maximum, respectively.
- Due to the highly efficient activity of a variety of enzyme systems, formaldehyde is rapidly metabolized and does not accumulate in the body. For example, as discussed in ATSDR (1999) and OECD (2002), experiments analyzing formaldehyde blood levels in humans, primates and rodents, demonstrate that blood levels are unchanged even after exposure up to 15 ppm. Consequently, internal organs are protected from the effects of formaldehyde unless metabolic defense systems are simply overwhelmed by huge exposures (e.g., > 15 ppm).

FCI recognizes that the endogenous presence and role of a substance does not mean that we should ignore potential pathological responses from high exposure levels. Rather, it should be apparent that there are exposure levels that can be properly characterized as safe given formaldehyde's role in our basic metabolism, its natural presence in exhaled breath, and the fact that formaldehyde exposure does not increase formaldehyde levels in the blood stream, which is one indication of no systemic exposure from inhalation of exogenous formaldehyde.

B. Exposure Levels

Because Petitioners indicate that their request to EPA was prompted by the reported formaldehyde emission levels in the Federal Emergency Management Agency (FEMA) trailers used by Hurricane Katrina victims, we comment briefly on the preliminary test results published by the U.S. Centers for Disease Control and Prevention (CDC). While the average exposure levels reported by the CDC in the FEMA trailers (i.e., approximately 0.077 ppm) are marginally higher than levels found in a normal indoor environment, extensive scientific studies suggest they are not at levels that would typically trigger symptoms such as eye, nose and throat irritation. While exposure to formaldehyde at levels much higher than those reported by CDC can cause irritation, for most people that irritation is temporary and reversible. In fact, an indoor air quality survey was conducted in Southern Louisiana to determine levels of airborne

formaldehyde in conventional houses. Analyses of 419 air samples from 53 houses showed average formaldehyde levels of 0.37 ppm. Twenty-nine percent of samples had levels below 0.1 ppm, and approximately 71% exceeded this level. There were no formaldehyde-related irritation complaints from any of the occupants of the tested homes. (Lemus et al. 1998).

C. Sensory Irritation

With regard to sensory irritation concerns raised by the Petitioners, reviews of the formaldehyde literature have noted that the most sensitive endpoints reported are for eye and upper respiratory tract irritation. (USEPA/NAC 2003; Arts et. al. 2006). A concentration of 1 ppm appears to be the approximate threshold for complaints of symptoms ranging from none to mild to moderate with no clear concentration-response relationship or increase in complaints among exposed subjects compared with controls.

In the February 2007 ATSDR Health Consultation involving testing formaldehyde levels in FEMA temporary housing units, a target concentration of 0.3 ppm formaldehyde was selected because this level was "below the level of concern for sensitive individuals of 369 ug/m^3 (0.3 ppm)." This value was not arbitrary, but derived from ATSDR documents and supported by the scientific literature. Indeed, a sophisticated modeling of human data by NCEA (2005) showed a clear threshold at 0.5 ppm for moderate effects with an effective concentration at 1.5 ppm. The U.S. Environmental Protection Agency (EPA) and National Advisory Committee (2003) identified 0.9 ppm as the highest exposure concentration at which the responses of subjects whose eyes were sensitive to formaldehyde were not significantly different from controls. The weight of the evidence does not indicate that formaldehyde produces pathological changes to the mucous membranes or the eyes, especially at the exposure concentrations (0.4 – 3.0 ppm) used to evaluate sensory irritation and pulmonary changes. These findings are in line with the 0.4 ppm value established by the U.S. Department of Housing and Urban Development (HUD).

D. "No Safe Level of Exposure" to Formaldehyde

The Petitioners, relying on the CARB's statement that "there is not sufficient scientific evidence to support identification of a threshold level below which no significant adverse health effects are anticipated,"[4] claim there is no safe level of formaldehyde exposure. As previously noted, formaldehyde is emitted in human breath at levels up to 0.073 ppm; thus the assertion that there is no safe level is simply illogical. If this was correct, the various regulatory levels established by government agencies, including ATSDR, the Occupational Safety and Health Administration and HUD would all be wrong. Numerous expert panels have concluded that keeping levels of exposure under 0.3 ppm protects just about everyone from the temporary effects of sensory irritation. Within this scientific framework, it seems likely that CARB's statement was more reflective of science policy then the conclusions of a complete risk assessment.

E. Chronic Health Effects

---

[4] California Air Resources Board Resolution 07-14 (April 26, 2007) at www.arb.ca.gov/regact/2007/compwood07/res0714.pdf

Petitioners state that "formaldehyde is a known carcinogen . . . . " Petition at 2. As aptly summarized in OECD (2002):

> [C]ell proliferation and the induction of nasal cancer in rats provides a convincing scientific basis for aetiology of the carcinogenic response to be cytotoxicity driven. . . . .
>
> Formaldehyde causes toxic effects only in the tissues of direct contact after inhalation, oral or dermal exposure characterised by local cytotoxic destruction. Toxic effects in the target tissues are dependent upon concentration rather than cumulative dose, and are highly non-linear.

More simply stated, and consistent with other reviews, OECD (2002)(pages 5 and 19) concluded that cell death was a prerequisite to cancer. See also, NICNAS (2006). Thus levels lower than those responsible for sensory irritation would also be protective for cancer. Coggon et al. (2003); Duhayon et al.(2008); and Environment Canada and Health Canada (2001).

While The International Agency for Research on Cancer (IARC) raised formaldehyde to the category of a known human carcinogen based on nasopharyngeal (NPC) cancer in occupationally exposed workers, the empirical support for this has steadily eroded. IARC's findings were based primarily on an NCI study of more than 25,000 industrial workers at 10 U.S. industrial plants where formaldehyde was either produced or used in the production of other products. (Hauptmann et al. 2003). In this study, there were a total of 10 deaths from NPC. Six of the 10 cases came from only one plant and the remaining 4 cases occurred randomly in the other 9 plants. This is not the typical pattern one might expect if formaldehyde was actually the cause of NPC.

The recent publication of an analysis by Marsh et al. (2007) now provides further evidence that NPC may not be etiologically related to formaldehyde exposure at all. This analysis involved a careful investigation of the previous employment history of the 6 individuals at the plant who died from NPC. Five of the NPC cases had previously worked in occupations involving exposure to known risk factors for upper respiratory system cancers including sulfuric acid mists and metal dusts. Marsh et al. (2007) concluded that the large NPC mortality excess in the one plant was not likely due to formaldehyde but rather the previous exposures. If these 5 cases of NPC were not counted in the NCI study, the results would not have been statistically significant.

With respect to the ability of formaldehyde to cause cancer in rodents, it is well established that long-term inhalation exposures at concentrations of 6 ppm or more cause nasal cancers**.** The effective concentrations are over 1,000 times higher than typical environmental levels. The animal data have been used to construct a biologically based model to better predict the potential risks from exposure to formaldehyde (i.e., CIIT model). The validity of the CIIT model has now been further supported by the most recent genomics data involving formaldehyde-induced nasal tumors in rodents.

In the recently published genomics study (Andersen et al. 2008), rats were exposed to formaldehyde at the same doses (i.e., 0, 0.7, 2 and 6 ppm) as used in the definitive cancer study (i.e., Monticello et al. 1996) 5 days/week for three weeks. Epithelium from nasal tissues that had tumors in 2-year inhalation studies at 10 and 15 ppm was evaluated by histopathology and microarray analysis. In this study, no genes were statistically altered at 0.7 ppm at any time

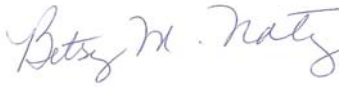
points indicating a clear threshold for formaldehyde-induced effects. At 2 ppm, 15 genes were significantly changed on day 5 and many more were changed at 6 ppm. Most importantly, no genes were significantly changed at 2 ppm at day 15. In other words, these data show that even at 2 ppm, nasal cells initially show some minor effects, but after a few days the nasal tissues rapidly adapt to formaldehyde at this concentration and return to a pattern of gene expression identical to 0 and 0.7 ppm. This study provides additional empirical support at the genomic level for the approach used in Conolly (2004), a widely accepted biologically based dose response model. In addition, these data in conjunction with the vast knowledge about the formaldehyde doses required to induce nasal tumors in rodents make it abundantly clear that a formaldehyde exposure level that is protective against sensory irritation would unequivocally also be protective for cancer.

It is evident from these comments and the attached materials that no unreasonable risk of injury to health or the environment is presented that warrants action under section 6(a) of the Toxic Substances Control Act, 15 U.S.C. § 2605.

* * * * *

We trust that the agency will find this discussion informative. We are available to meet with you and your staff to further discuss these points and to provide the most recent scientific literature on formaldehyde.

Sincerely,



Betsy Natz
Executive Director

Enclosures:

Comments of the Formaldehyde Council, Inc. on Proposed Airborne Toxic Control Measure to Reduce Formaldehyde Emissions from Composite Wood Products; Comments on Staff Report: Initial Statement of Reasons for Proposed Rulemaking

Sources:

Andersen, M.E., Clewell, H.J., Bermudez, E, Willson, G.A. and Thomas, R.S. (2008). Genomic Signatures and Dose Dependent Transitions in Nasal Epithelial Responses to Inhaled Formaldehyde in the Rat (in press).

Agency for Toxic Substances and Disease Registry (ATSDR). (1999). Toxicological Profile for Formaldehyde. U.S. Department Of Health And Human Services, Public Health Service.

Arts, J, Rennen, M, Heer, CD (2006a) Inhaled Formaldehyde: Evaluation Of Sensory Irritation In Relation To Carcinogenicity. Reg. Tox. & Pharm. 44:144-160.

Arts, J, de Heer, C and Woutersen, R (2006b) Local Effects In The Respiratory Tract: Relevance Of Subjectively Measured Irritation For Setting Occupational Exposure Limits. Int. Arch. Occup. Environ. Health 79, 2006, 286-2

Coggon D, Harris EC, Poole J, Palmer KT. (2003) Extended Follow-Up Of A Cohort Of British Chemical Workers Exposed To Formaldehyde. Journal of National Cancer Institute. 95:1608-1615.

Conolly, RB, Kimbell, JS, Janszen, D, Schlosser, PM, Kalisak, D, Preston, J, Miller, FJ (2004) Human respiratory tract cancer risks of inhaled formaldehyde: dose-response predictions derived from biologically-motivated computational modeling of a combined rodent and human dataset. Toxicol. Sci. 82(1):279-96.

Duhayon, S., Hoet, P., Maele-Fabry, G., and Lison, D. (2008) Carcinogenic potential of formaldehyde in occupational settings: a critical assessment and possible impact on occupational exposure levels, International Archives Of Occupational And Environmental Health, vol. 81, no. 6, pages 695-710.

Environment Canada and Health Canada (2001) Existing Substances Evaluation, Assessment Report – Formaldehyde (available at http://www.ec.gc.ca/substances/ese/eng/psap/final/formaldehyde.cfm).

Hauptmann M, Lubin JH, Stewart PA, Hayes RB, Blair A. Mortality From Lymphohematopoietic Malignancies Among Workers Employed In Formaldehyde Industries; J Natl Cancer Inst. 2003:1-5.

Lemus R, Abdelghani AA, Akers TG, and Horner WE. (1998). Potential Health Risks From Exposure To Indoor Formaldehyde. Rev Environ Health. Jan-Jun;13(1-2):91-8.

Marsh, G., Youk, A., Buchanich, J., Erdal, S., and Esmen, N., (2007). Work in the Metal Industry and Nasopharyngeal Cancer Mortality Among Formaldehyde-Exposed Workers. Reg. Tox. & Pharm. 48:308-319.

Monticello, T.M., Swenberg, J.A., and Gross, E.A., (1996). Correlation of regional and nonlinear formaldehyde-induced nasal cancer with proliferating populations of cells. Cancer Res. 56:1012-1022.

Moser, B, Bodroqi, F, Eibl, G, Lechner, M, Rieder, J, Lirk, P (2005) Mass spectrometric profile of exhaled breath -- field study by PTR-MS. Resp. Physiol. Neurobiol. 145(2-3):295-300.

NICNAS (2006) Australian Department of Health and Aging, National Industrial Chemicals Notification Assessment Scheme, Priority Existing Chemical Assessment Report No. 28. – Formaldehyde.

Organization for Economic Cooperation and Development (OECD) (2002) SIDS Initial Assessment Profile (UNEP Publications).

U.S. EPA/ National Advisory Committee (2003), Acute exposure guidelines levels (AEGLs) for Formaldehyde. Draft 1:02/2003. National Advisory Committee/ AEGL, U.S. EPA, Washington, DC.

U.S. EPA/ National Center for Environmental Assessment (2005), Controlled Exposure to Formaldehyde Via Inhalation: A Categorical Regression Analysis Of Human Exposure and Response, U.S. EPA, Washington DC.