
From: Karluss Thomas <kthomas@sehsc.com> To: "jdenton@oehha.ca.gov" <jdenton@oehha.ca.gov> CC: "galexeeef@oehha.ca.gov" <galexeeef@oehha.ca.gov>, "biomonitoring@oehha.ca.gov" <biomonitoring@oehha.ca.gov>, Howard Berman <Howard.Berman@dutkoworldwide.com> Date: Wednesday - December 3, 2008 7:10 PM
Subject: SEHSC Comments on California Biomonitoring Documents for CyclicSiloxanes

Dear Dr. Denton:

Please find attached comments on the draft documents provided by California that summarize technical information related to the cyclic siloxanes as potential candidates for the California biomonitoring program. Please consider these comments the Silicone Environmental, Health, and Safety Council's (SEHSC) formal response to the summary technical documents for the cyclic siloxanes. In addition, these comments also represent SEHSC's position on the potential inclusion of cyclic siloxanes on a list of candidate substances that could be considered for biomonitoring in California. We look forward to discussing these points further during the public meeting on December 5, 2008. Don't hesitate to contact me directly if you have any questions, comments, or concerns.

Best Regards,

Karluss Thomas

Karluss Thomas
Executive Director
Silicones Environmental, Health and Safety Council
2325 Dulles Corner Blvd., Suite 500
Herndon, VA 20171
(703) 788-6535 (direct line)
(703) 788-6545 (fax)
www.sehsc.com<<http://www.sehsc.com>>



Phone: 703.788.6570
Fax: 703.788.6545
www.sehec.com
2325 Dulles Corner Boulevard
Suite 500
Herndon, VA 20171

December 3, 2008

Joan E. Denton Ph.D.,
Director, Office of Environmental Health Hazard Assessment
1001 I Street
Sacramento, CA 95814

Dear Dr. Denton:

At a time when broader economic considerations are constraining the implementation of existing and new regulatory programs, it is increasingly important that newly funded programs, such as California's biological monitoring program, prioritize its efforts in a manner that recognizes the need to develop program priorities that are scientifically pragmatic and economically prudent. Accordingly, the available scientific data do not support biomonitoring for cyclic siloxanes as part of the California biological monitoring program.

The background document on cyclic siloxanes that was developed to support the inclusion of cyclic siloxanes in California's biomonitoring program and to be considered during the December 4-5, 2008 meeting of the California Environmental Contaminant Biomonitoring Program (CECBP) Scientific Guidance Panel (SGP) contains a number of factual errors that result in the adoption of inaccurate conclusions. Consequently, the Silicones Environmental Health and Safety Council (SEHSC) provides below some key corrections and explanations that should be made to the "Document on Cyclosiloxanes" [hereafter "the Document"] in order for the information therein to be complete and accurate.

Environmental Persistence

The Document generally mischaracterizes the environmental persistence of cyclic siloxanes, which creates an exaggerated impression of the potential for human exposure via the environment. This may be due to reliance on an earlier evaluation by OEHAA for D5, to which SEHSC has previously responded with corrections to the information used in that evaluation (OEHHA Memorandum to ARB September 13, 2007). The first page of the Document states:

"Certain siloxanes are persistent in the environment, resisting oxidation, reduction, and photodegradation. Varying information exists on the susceptibility of siloxanes to hydrolysis."

On the contrary, the available data would indicate that D4, D5, and D6 are *not persistent* in the environment due to degradation by a number of different pathways. The notion that environmental persistence is long, due to slow biodegradation, ignores incontrovertible data demonstrating rapid volatilization to air, where degradation half-lives are on the order of one week. When deposited to water, the fraction not volatilized to air hydrolyzes or partitions to sediments and is not readily available for uptake by aquatic organisms. Published data on D4 and D5, for example, demonstrate hydrolysis in surface water, clay-catalyzed degradation in soil, and atmospheric degradation (Durham et al., 2006; Xu et al., 1999a, 1999b; Lehmann et al., 1994, 1996; Atkinson et al., 1991; Latimer et al., 1998; and Chandramouli et al., 2001). Whereas the Document states "*Animal experiments have shown that unchanged D5 is persistent in a 'variety of tissues' for 'extended periods of time',*" available data on the *in vivo* metabolism of D4 and D5 in fish indicates both D4 and D5 are metabolized (Springer, 2007); this information should be incorporated into any assessment of bioaccumulation. In addition, current environmental monitoring data indicate that the cyclic siloxanes (D4, D5 and D6) do not biomagnify in the environment, but instead decrease in concentration at higher trophic levels in the food web with the lowest concentrations being found in the top predator fish that are consumed by humans.

Caveats Regarding Biomonitoring of Cyclic Siloxanes

SEHSC believes that credible biomonitoring for cyclic siloxanes requires careful attention to the physical-chemical characteristics of the materials as well as the analytical challenges inherent in measuring them accurately. It should be noted that these materials have a very low water solubility (D4; 56 ppb, D5; 17 ppb and D6: 5 ppb) as well as a high potential for accidental contamination of samples during collection due to their use in commonly used personal care products and laboratory equipment. The complex analytical challenges inherent in measuring these materials accurately will, significantly increase the cost and decrease the potential reliability of the results. For example some of the published data (e.g. Kaj et. al 2005) reported analytical results obtained from acidified breast milk samples taken from a sample bank) require a careful evaluation because they contradict intensely studied and well-understood properties of the cyclic siloxanes.

The Document creates the false impression that cyclic siloxanes have been found commonly in humans and are widely distributed to various tissues. The information cited, however, is based on routes of exposure relevant only to decades-old breast implant litigation. The studies conducted to support litigation claims measured cyclic siloxanes following administration of very high doses by subcutaneous, intraperitoneal, and intramuscular implantation, routes of exposure that bypass known metabolic and elimination pathways for cyclic siloxanes. In contrast, extensive animal and human pharmacokinetic data from dermal and inhalation pathways on D4 and D5 (Reddy et al., 2005a; 2007a; 2007b, Anderson et al., 2005; Jovanovic et al., 2000, 2004, 2007; Tobin et al., 2007) indicate rapid elimination in exhaled breath and extensive metabolism. These more extensive pharmacokinetic data are much more relevant for evaluating the relative importance of biomonitoring cyclic siloxanes than

The very weak dopaminergic activity of D5 (only at the highest doses achievable) does appear to decrease prolactin in a rat model with elevated prolactin, but even at this same dose there is a lack of effect on the nervous system or other endpoints other than uterine tumors in rats exposed to D5 for up to two years, an effect peculiar to the senescing rat reproductive tract. Thus, the data actually suggest that dopaminergic activity in humans is unlikely rather than indicating a basis for concern.

Utility of Biomonitoring to Determine Effects in Humans

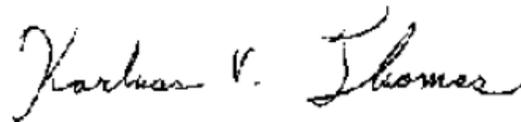
The Document's most fundamental mischaracterization concerns the concept that biomonitoring will help evaluate the safety of alternative chemistries. The Document states:

"It would be important to know if substitutes for existing chemicals are accumulating in the environment. Biomonitoring cyclosiloxanes could detect rising levels in humans, which would be of concern because of the evidence of biological effects associated with these chemicals. These measurements would be an important tool for evaluating the public health efficacy of substituting cyclosiloxanes as less toxic alternatives for other chemicals."

First, it should be noted that while cyclic siloxanes can be found in the environment as indicated above, the available data do not support the conclusion that they are accumulating in the environment. Second, biomonitoring would be unlikely to detect rising cyclic siloxane levels in humans who use consumer products containing them based on the extensive pharmacokinetic data already generated in animals and humans that demonstrated these materials do not bioaccumulate with continued exposure (Anderson, et al., 2008). Lastly it is not certain that those measurements can be made with sufficient precision to determine whether levels of cyclic siloxanes in humans are changing over time. For reliable, meaningful results to emerge, it would also be critical to control the myriad of factors that could arbitrarily alter individual cyclic siloxane measurements, thereby confounding the results. Even the high levels detected in women with ruptured breast implants failed to produce identifiable adverse effects. Thus, the public health efficacy of alternative chemistries cannot possibly be evaluated except by speculative extrapolation of effects observed in animals exposed to maximum achievable doses. Furthermore, because of an inability to control for the various factors that might produce disease within a biomonitored population, biomonitoring for cyclic siloxanes will also fail to provide interpretable new information about relationships between exposure and disease. The Centers for Disease Control and Prevention acknowledge this overarching limitation, stating in the preface to their biomonitoring reports: "Just because people have and environmental chemical in their blood or urine does not mean that the chemical causes disease." Therefore, the only reliable information that *might* be gleaned by biomonitoring for cyclic siloxanes is limited to the levels of these materials that may be present in humans, and possibly whether these levels are changing over time. The Document should describe these limitations clearly so that decisions are not based on a false impression of the information potentially gained from a biomonitoring program for cyclic siloxanes.

SEHSC respectfully requests that the background document be revised to more accurately reflect the currently available data. In addition, given the wealth of information and available scientific data that indicate that the cyclic siloxanes do not pose a risk to human health or the environment and the known technical difficulty of accurately biomonitoring these materials, SEHSC would also ask that California Environmental Contaminant Biomonitoring Program Scientific Guidance Panel and the State of California carefully consider the relative benefits and costs of including the cyclic siloxanes in the California Biomonitoring Program at this time. Please contact me if you have questions regarding the information we have provided.

Sincerely,

A handwritten signature in black ink that reads "Karluss V. Thomas". The signature is written in a cursive style with a large, stylized initial 'K'.

Karluss Thomas
Executive Director,
SEHSC

Cc: George Alexeeff
Howard Berman
OEHHA Science Guidance Panel

References

- Andersen, ME, Reddy, MB, Plotzke, KP (2008) *Are highly lipophilic volatile compounds expected to bioaccumulate with repeated exposures?* Toxicology Letters, 179, 85-92.
- Anderson, ME, Reddy MB, Plotzke KP. (2005) *Lack of Bioaccumulation with repeated, periodic exposures of cyclic siloxanes* (Abstract #855). Toxicol Sci. 84(S-1):175.
- Atkinson R, (1991) *Kinetics of the gas-phase reactions of a series of organosilicon compounds with hydroxyl and nitrate (NO₃) radicals and ozone at 297 ±2 K*. Environmental Science and Technology, 25, 863-866.
- Chandramouli, B. and R. Kamens. (2001) *The photochemical formation and gas-particle partitioning of oxidation products of decamethylcyclopentasiloxane and decamethyltetrasiloxane in the atmosphere*. Atmospheric Environment. 35:87-95.
- Durham, J. (2006) *Hydrolysis of Decamethylcyclopentasiloxane (D5)*. Silicones Environment, Health and Safety Council (SEHSC) Report.
- Kaj L., Andersson J, Palm Cousins A, Remberger M., Ekheden U., Dusan B., and Brorstrom-Lunden E., (2005) *Results from the Swedish National Screening Programme 2004: Subreport 4: Siloxanes. IVL*. Swedish Environmental Research Institute.
- Jovanovic, M.L, McMahon, J.M, McNett, D.A, Galavan, R.H., and Plotzke K.P (2000) *In vitro absorption of decamethylcyclopentasiloxane (D5) in human skin: a comparison to octamethylcyclotetrasiloxane (D4)*. Toxicologist, 54(S-1):14
- Jovanovic, M., J. McMahon, D. McNett, J. Tobin, R. Gallavan, and K. Plotzke. (2004). *In vivo percutaneous absorption of 14C-decamethylcyclopentasiloxane in fisher 344 rats*. *The Toxicologist*.
- Jovanovic, M., J. McMahon, D. McNett, J. Tobin, and K. Plotzke. (2007). *In Vitro and in Vivo Percutaneous Absorption of 14C-Octamethylcyclotetrasiloxane (14C-D4) and 14C-Decamethylcyclopentasiloxane (14C-D5)*. Accepted - Regulatory Toxicology and Pharmacology.
- Latimer, H., R. Kamens, and G. Chandra. (1998) *The atmospheric partitioning of decamethylcyclopentasiloxane and 1-hydroxynonamethylcyclopentasiloxane (DT4OH) on different types of atmospheric particles*. Chemosphere. 36(10):2401-2414.
- Lehmann, R. and J. Miller. (1996) *Volatilization and sorption of dimethylsilanediol in soil*. Environ. Toxicol. Chem. 15(9):1455-1460.

Lehmann, R., S. Varaparth, and C. Frye. (1994) *Fate of silicone degradation products (silanols) in soil*. Environ. Toxicol. Chem. 13:1753-1759.

Quinn AL, Regan JM, Tobin JM, Marinik BJ, McMahon JM, McNett DM, Sushynski, CM, Crofoot SD, Jean PA, and Plotzke KP. (2007) *In vitro and in vivo evaluation of the estrogenic, androgenic, and progestagenic potential of two cyclic siloxanes*. Toxicol Sci. 96(1):145-53.

Reddy, M., M. Utell, K. Plotzke, and M. Andersen. (2005) *Physiologically based pharmacokinetic modeling of decamethylcyclopentasiloxane (D5) in rats and humans*. "The Toxicologist". March, 2005.

Reddy, M., M. Utell, K. Plotzke, and M. Andersen. (2007a). *Physiologically based pharmacokinetic modeling of decamethylcyclopentasiloxane (D5) in rats and humans*. Toxicol Sci. Manuscript submitted.

Reddy, M.B., Looney, R.J., Utell, M.J., Plotzke, K.P., and Andersen, M.E. (2007b). *Modeling of Human Dermal Absorption of Octamethylcyclotetrasiloxane (D4) and Decamethylcyclopentasiloxane (D5)*. Toxicol Sci. 99(2):422-431.

Springer, T. (2007) *Decamethylcyclopentasiloxane (D5): A 96-hour study of the elimination and metabolism of orally gavaged ¹⁴C-D5 in Rainbow Trout (Oncorhynchus mykiss)*. Centre Europeen des Silicones. Draft report.

Tobin JM, McNett, DM, DurhamJ, and Plotzke KP. (2007). *Disposition of Decamethylcyclopentasiloxane in Fischer 344 Rats Following Single or Repeated Inhalation Exposure to ¹⁴C-Decamethylcyclopentasiloxane (¹⁴C-D5)*. Submitted. InhalationTox.

Xu, S. (1999a). *Fate of cyclic methylsiloxanes in soils. 1. The degradation pathway*. Environmental Science and Technology, 33, 603-608.

Xu, S and Chandra G, (1999b). *Fate of cyclic methylsiloxanes in soils 2. Rates of degradation and volatilization*. Environmental Science and Technology, 33:4034-4039.