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OEHHA
1515 Clay St, 16th Floor
Oakland, CA 94612

Re: Information Regarding Cyclic siloxanes Requested During December 5, 2008 CECBP Scientific Guidance Panel Meeting

Dear Dr. Roisman:

The Silicones Environmental, Health, and Safety Council of North America (SEHSC) is pleased to provide the accompanying information to address the request made by members of the Scientific Guidance Panel (SGP) of the California Environmental Contaminant Biomonitoring Program (CECBP) during its December 5, 2008 meeting. Based on the discussion between SEHSC and the SGP during that meeting, SGP members requested the information listed in the following table to help determine whether to recommend that cyclic siloxanes be added to the CECBP's list of designated chemicals for potential biomonitoring.

As we indicated in our letter dated December 3, 2008, the available data indicate the cyclic siloxanes are poor candidates for inclusion in the CECBP.These materials have not demonstrated significant health risk at the levels to which humans are typically exposed. While there is human exposure to cyclic siloxanes as a consequence of their use in consumer products, the physical-chemical properties of the materials, including their high volatility and low water solubility, minimize their bioavailability in human blood and plasma. Indeed, extensive animal and human pharmacokinetic data from dermal and inhalation exposure evaluations of D4 and D5 indicate rapid elimination in exhaled breath and extensive metabolism. In addition, the inherent difficulties associated with biological monitoring for these materials in blood and plasma will require extensive method validation, a comprehensive QC program during sample collection, transport, storage, and analysis, and carefully controlled laboratories to ensure accuracy, precision, sensitivity, specificity and speed.

The data and references included with our December 3 letter, as well as the additional information enclosed with this letter demonstrate that cyclic siloxanes should not be listed as

designated chemicals under the criteria prescribed in Section 105449(c) of the California Health and Safety Code (H&S Code).

Further, we note that the statutory criteria are by their nature broad, and indeed, would allow few, if any, substances in commerce to be excluded from the list of designated chemicals. An expansive portfolio of substances on the list of designated chemicals would be fundamentally inconsistent with the language and spirit of the statute. Prioritizing the chemicals for human biomonitoring would require a greater commitment of resources without providing any demonstrable public health benefits. We believe this warrants the SGP establishing an underlying rationale for determining the specific substances to be included on the list.

| Request Ref ID | Request Description |
|---|---|
| a. | Additional information on health hazards associated with cyclic siloxanes. |
| b. | Accurate persistence and bioaccumulation potential information. |
| c. | Information on uses and expected uses for cyclic siloxanes in California for all applications (GreenEarth agreed to provide data for dry cleaning.) |
| d. | Dermal absorption, pharmacokinetics, metabolism, and measurement data for cyclic siloxanes in human blood and plasma. |
| e. | Information on the feasibility of the development of breath biomarkers for cyclic siloxanes. |
| f. | QA / QC program data for measurement, handling, storage, and transport. |
| g. | Feasibility of finding cyclic siloxanes in blood. |

To address those requests, we are providing a number of reports and other data, as discussed further below, including the following. (Letter in brackets represents the request ID that data is intended to address):

1. Published studies on health effects, dermal absorption, pharmacokinetics and metabolism of cyclic siloxanes (a, d, e, g)
2. Octamethylcyclotetrasiloxane ($D_4$) Background and Environmental Fate Data (b)
3. Decamethylcyclopentasiloxane ($D_5$) Background and Environmental Fate Data (b)
4. Dodecamethylcyclohexasiloxane ($D_6$) Background and Environmental Fate Data (b)
5. SEHSC Comments on the CMP Preliminary assessments for all three materials (b, f)
6. QA/QC Program Data (f)
7. Octamethylcyclotetrasiloxane ($D_4$) Health Submission to Canada with exposure assessment (a, c, d, g)
8. Decamethylcyclopentasiloxane ($D_5$) Health Submission to Canada with exposure assessment (a, c, d, g)
9. Dodecamethylcyclohexasiloxane ($D_6$) Health Submission to Canada with exposure assessment (a, c, d, g)

## SUMMARY

A brief discussion of key information pertinent to each statutory criterion and a summary of additional information relevant to an assessment of the cyclic siloxanes materials follows:

### *Exposure to the Public [H&S Code § 105449(c)(1)]*

We have previously provided an exposure assessment to OEHHA for its use in advising the California Air Resources Board on the use of D5 in dry cleaning (ENVIRON 2006). That information is still relevant here. In addition, we have included comprehensive exposure assessments conducted by the silicone industry (and independently reviewed by Health Canada) in support of the Canadian Chemicals Management Plan (CMP) assessments for D4, D5 and D6. It is important to note that Health Canada just recently concluded that D4, D5 and D6 are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health (Environment and Health Canada 2008a, b, c) and that adequate margins of exposure are present for use in consumer products.

While there is human exposure to cyclic siloxanes as a consequence of their use in consumer products, the physical-chemical properties of the materials, including their high volatility and low water solubility minimize their bioavailability in human blood and plasma. Indeed, extensive animal and human pharmacokinetic data from dermal and inhalation exposure evaluations of D4 and D5 indicate rapid elimination in exhaled breath and extensive metabolism (Utell et al., 1998, 2000, 2004; Looney et al., 2000; Plotzke et al., 2000, 2002; Reddy et al., 2003, 2007, 2008, Anderson et al., 2001, 2008; Varaprath et al., 1999, 2003 ; Jovanovic et al., 2008; Sarangapani et al., 2003; Dobrev et al., 2008; Tobin et al., 2008). Consequently, statistically significant quantities of these materials in human blood or plasma would be difficult to detect following normal consumer exposure.

The information cited in the OEHHA summary indicating a long half life in humans is based on routes of exposure relevant only to decades-old breast implant litigation (Flassbeck et al., 2001)

and half lives based on total silicon levels. In a subsequent publication (Flassbeck et al., 2003), silicone-specific species were analyzed and compared to total silicon in tissues from women with implants. The authors acknowledged that siloxanes (D4–D6) comprise only a small portion of the total silicon and that the use of elemental silicon as an indicator for siloxanes in tissues is not appropriate. In addition, other studies conducted to support litigation claims (Kala et al., 1998; Lierberman et al., 1999) measured cyclic siloxanes following administration of very high doses by subcutaneous, intraperitoneal, and intramuscular implantation, routes of exposure for cyclic siloxanes that are not appropriate for understanding behavior in humans following consumer exposure because they bypass known metabolic and elimination pathways.

The concept 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., 2005; 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). Environment Canada recently acknowledged there is conflicting data on these materials concerning bioaccumulation and have not categorized these materials as bioaccumulative in their final risk assessments (Environment and Health Canada 2008a, b, c). 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 predatator fish that are consumed by humans (SEHSC 2008a).

***Known or Expected Health Effects [H&S Code § 105449(c)(2)]***

We are not aware of any reports in the peer-reviewed literature that document human risks for cyclic siloxanes at the levels to which humans are typically exposed (Environment and Health Canada 2008a, b, c). Further, as indicated above, Health Canada just recently concluded that D4, D5 and D6 are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health and that adequate margins of exposure are present for use in consumer products. Extensive safety testing has been completed on these materials and although some studies have identified effects in laboratory animals, these effects are seen at levels much higher than concentrations to which humans are exposed. (SEHSC 2007a, b, c, d; 2008a, b; Environment and Health Canada 2008a, b, c)

***Assess Efficacy of Public Health Actions to Reduce Exposure [H&S Code § 105449(c)(3)]***

As far as we are aware there are no state or federal regulatory programs designed to minimize exposure to these materials in humans. Consequently the application of these criteria would explicitly exclude cyclic siloxanes from the list. Certainly, their inclusion on the CECBP list of designated materials would have no measurable public health benefit.

***Availability of a Biomonitoring Analytical Method and Incremental Analytical Cost to Perform Analysis [H&S Code § 105449(c)(4), (6)]***

Cyclic siloxanes 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 presence 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 (Varaprath et al., 1998, 2000a, 2000b, 2006). For example, some of the published data (e.g., Kaj et. al., 2004, which reported analytical results obtained from acidified breast milk samples taken from a sample bank) require careful evaluation because they contradict well-understood properties of cyclic siloxanes. The authors acknowledged the samples were collected and prepared for analysis of another chemical and that this analysis required acidification of the sample prior to analysis. Acidification of the sample prior to analysis more than likely would have destroyed cyclic siloxanes.

The increased analytical challenges and decreased reliability of results can also be seen in much of the screening monitoring data that have been generated (TemaNord 2005, NILU 2007, Backus 2006). While these studies were designed as preliminary assessments of siloxane concentration in the environment, the reports do not provide sufficient quality control information to evaluate accuracy of the analytical results or identify any contamination that may have occurred because of sample collection, processing, and storage. Because many products and equipment commonly found in scientific laboratories contain silicone-based materials, the potential for background contamination and analytical artifacts must be controlled. Also, field crews must be careful not to introduce contamination during sample collection from such sources as lubricants commonly used on field equipment, storage containers, or even personal care products such as hand creams or sunscreens. All of these factors would generate results that overestimate actual concentrations, especially when attempting to measure trace level concentrations at or near the limits of the analytical method. Consequently, while the results show that cyclic siloxanes appear to be detectable in biota, with most concentrations being near the limit of quantitation (LOQ), there is insufficient quality control (QC) data to evaluate the accuracy of these results. The importance of a robust QC program in interpreting environmental monitoring data was also a conclusion of the 2008 Workshop on Organosilicon Compounds in the Environment (Canada Centre for Inland Waters, March 2008): "Overall, the prevalence of background cVMS necessitates the use of a thorough QC program. This should include a series of blanks, including field blanks for the environmental sampling, within each sample batch analyzed." Consequently, to better understand areas of potential contamination and variability in the processing and analysis of cVMS in biological matrices, the silicone industry is currently participating with the Norwegian Institute for Air Research and Environment Canada in an inter-laboratory exchange and analysis of control and cyclic siloxanes dosed fish samples to further validate the appropriate handling and processing techniques for these unique substances.

***Availability of Adequate Biospecimen Samples [H&S Code § 105449(c)(5)]***

The caveats outlined above with regard to the high potential for sample contamination and the need for extensive quality controls during sample collection, transport, storage, and analysis point to the inappropriateness of attempting to analyze for D4 and D5 in existing samples collected for other purposes. In addition, extensive animal and human pharmacokinetic data from dermal and inhalation exposure evaluations of D4 and D5 indicate rapid elimination in exhaled breath and extensive metabolism. (Utell et al., 1998, 2000, 2004; Looney et al., 2000; Plotzke et al., 2000, 2002; Reddy et al., 2003, 2007, 2008; Anderson et al., 2001, 2008, Varaprath et al., 1999, 2003; Jovanovic et al., 2008; Sarangapani et al., 2003; Dobrev et al., 2008; Tobin et al., 2008). Consequently, statistically significant quantities of these materials in human blood or plasma would be difficult to detect following normal consumer exposure.

Being added to the CECBP list of designated chemicals could have deleterious market impacts, the effects of which could be particularly devastating in the existing economic environment. Accordingly, it is vital that all decisions to designate chemicals for inclusion in the CECBP be grounded in sound science and a fair and reasoned application of the criteria articulated by the state legislature in H&S Code § 105449(c). Any action that inappropriately identifies cyclic siloxanes as materials requiring increased regulatory scrutiny that does not have sound science as its basis will ultimately create unfavorable market conditions for these materials while yielding no public health benefit. Therefore, we urge the SGP to carefully consider all of the available the data regarding cyclic siloxanes. We believe these data clearly indicate the cyclic siloxanes should not be added to the list of designated chemicals for potential biomonitoring.

SEHSC appreciates the opportunity to provide information regarding the safety of cyclic siloxanes. If you have any questions about any of the materials that have been provided, please do not hesitate to contact me directly at (703) 788-6570.

Sincerely,

Karluss V. Thomas

Karluss Thomas
Executive Director, SEHSC

cc: Joan Denton (OEHHA)

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