

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

December 8, 2000

TO: File for dimethyl silicones and siloxanes (CASRN 63148-62-9)

FROM: Mary Lee Hultin

SUBJECT: Initial Threshold Screening Level re-evaluation

The AQD-TU files on siloxanes and silicones were reviewed in FY2001 and updated as deemed appropriate. Previously, the ITSL for dimethyl silicones and siloxanes (CASRN 63148-62-9) was set at trace ($0.1 \mu\text{g}/\text{m}^3$) based on annual averaging. Following a review of the information available on this compound, the ITSL is now set at $2 \mu\text{g}/\text{m}^3$.

Dimethyl silicones and siloxanes are one of many organosilicon-based polymers used in emulsions, oils, and putties. These products are used in a diversity of settings: caulking, antifoam agents in food processing, anti-gas compounds in medicinal products, heat transfer fluids, rubber products, breast implants, and cosmetics.

The following references and databases were searched to identify data to determine the ITSL for dimethyl silicones and siloxanes: IRIS-online, ACGIH guide, NIOSH Pocket Guide, RTECS, CAS-online, NLM-online, and the MDEQ library. While many products were found that contained this compound, typically the products were mixtures. Not all reports indicated what proportion of the mixture was CASRN 63148-62-9. Only products for which that proportion was known were investigated. The majority of the product had to be the compound of interest in order to be considered when determining the ITSL.

The only inhalation studies found for dimethyl silicones and siloxanes were three acute studies. Two of the studies used products for which the percentage of CASRN 63148-62-9 was not indicated and therefore were disregarded. The remaining study (Dow Corning Corp., 1953) investigated the acute inhalation toxicity of Dow Corning 200 Fluid, a product manufactured in different viscosities, all formulations considered to be 100% CASRN 63148-62-9. Two dogs, 7 guinea pigs, and 7 rats (breeds and strains not identified) were exposed to 2.12 mg/L dimethyl silicones and siloxanes in an inhalation chamber for 6 hr. The chemical was relatively non-volatile and formed a dense cloud in the chamber. Three of the guinea pigs died during exposure. The remaining animals were sacrificed at the end of exposure, except for 1 dog allowed a 1-month recovery period. Clinical signs were minimal and included hyperventilation, excitability, muscular fasciculations, and salivation. Gross findings upon immediate sacrifice were hyperemic

lungs with hemorrhagic areas. The other organs appeared normal. Gross findings in the recovery dog showed small areas of dark coloration on the lung, with the other organs appearing normal. The only microscopic lesions seen for immediate and recovery animals were in the lung: edema, hemorrhage, and mild interstitial irritation.

Siddiqui and Stanton (1987) performed a subacute oral toxicity study on several products containing dimethyl silicones and siloxanes. Because they are non-absorbable and have physical characteristics similar to edible oils, several polydimethylsiloxane fluids were studied to determine whether silicone oils can be used as a low-calorie fat replacer. Doses of 2, 5, and 8 g/kg/day Dow Corning 1500 Silicone Antifoam (91% CASRN 63148-62-9), 8 g/kg/day Dow Corning 200 Fluid, 50 cs. (100% CASRN 63148-62-9) as a positive control, and 5 and 8 g/kg/day of a 50/50 mixture of Dow Corning 200 Fluid, 50 cs., and Dow Corning 112 Compound (a combined total of 92% CASRN 63148-62-9) were administered twice daily via gavage for 7 days to adult male rats (Sprague-Dawley strain, 5 males/group; body weight ~ 280g). Body weights and food consumption were measured on Days 0, 3, and 7. The degree of anal leakage of the test materials was determined by examining the perianal region of the rats twice a day. Observations were also made on haircoat changes, consistency of stool, and coating of oils around the fecal material. Gross necropsy was performed on all animals, with gross pathology being performed on the GI tracts of only the highest-dose animals. There were no treatment-related deaths, clinical signs or behavioral abnormalities. Although no statistically significant differences in either body weights or food consumption values were observed, a definite loss in body weight was observed in treated animals. The rats receiving the 1500 Antifoam (91%) showed no leaking, oily coats, or fecal consistency changes at a dose of 2 g/kg/day; none to slight leakage at 5 g/kg/day; and slight to moderate anal leakage, oily feces and oily haircoats at 8 g/kg/day. The rats receiving the positive control (100%) also showed slight to moderate anal leakage, oily feces and oily haircoats. The rats receiving the mixture showed only a mushy, light-green stool at either dose. Terminal sacrifice of rats showed gastric edema and slight intestinal irritation.

In a 28-day oral toxicity study of Dow Corning 200 Fluid, 350 cst. (100% CASRN 63148-62-9), dietary concentrations of 10,000, 25,000, 50,000, and 100,000 ppm of the compound were fed to groups of Fischer CDF rats (10/sex/group). The average calculated test article consumption was 950, 2428, 4986, and 10,615 mg/kg/d for males and 1013, 2562, 5286, and 11,325 mg/kg/d for females for the respective dietary groups. The only effects of note were an irritative ocular effect and matting of the fur. The ocular irritation, corneal opacities with microscopic lesions, was seen in all groups and was considered a local and not systemic effect. As well, this strain of rat is noted for having spontaneous corneal crystals. The matting of the fur was thought to be due to anal leakage and direct contact (when grooming). Cholesterol was monitored during the study but no effects were observed. (Dow Corning Corp., 1995d)

In a 13-week subchronic oral toxicity study of Dow Corning 200 Fluid, 350 cst., dietary concentrations of 5000, 10,000, 25,000, and 50,000 ppm of the compound were fed to groups of Fischer CDF rats (15/sex/group). The average calculated test article consumption of the dietary groups was 312, 618, 1590, and 3347 mg/kg/day for the males

and 352, 716, 1790, and 3824 mg/kg/day for the females for the respective groups. To compare the test article's potential to induce corneal opacities, it was also administered daily by gavage to 2 groups of rats (15/sex/group) for the same time period. The gavage doses were 500 mg/kg/day, corresponding to the 5000 ppm dietary group, and 2500 mg/kg/day, corresponding to the average amount consumed by the 25,000 ppm dietary group in the 28-day study (above). In this study, the irritative ocular effects were seen in both sets of rats, suggesting that a metabolite or the unchanged compound was in the feces and caused irritation as a result of grooming. Again there were no effects seen on cholesterol measures. (Dow Corning Corp., 1995b)

In a 28-day oral toxicity study of Dow Corning 200 Fluid, 10 cst. (100% CASRN 63148-62-9), groups of Fischer CDF rats (10/sex/group) were fed dietary concentrations of 10,000, 25,000, 50,000, and 100,000 ppm of the compound. The average calculated test article consumption was 978, 2545, 5244, and 11,228 mg/kg/day for males and 1043, 2706, 5623, and 12,058 mg/kg/day for females for the respective groups. Similar to the 2-day study for the 350 cst. viscosity (above), there were local irritative ocular effects and matting of the fur. In this study, there was a dose-dependent decrease in the average triglycerides, LDL cholesterol, and VLDL cholesterol observed in both sexes. (Dow Corning Corporation, 1995c)

In a 13-week subchronic toxicity study of Dow Corning 200 Fluid, 10 cst., groups of Fischer CDF rats (15/sex/group) were fed dietary concentrations of 5000, 10,000, 25,000, and 50,000 ppm of the compound. The average calculated test article consumption was 351, 718, 1780, and 3773 mg/kg/day for males and 395, 792, 2025, and 4348 mg/kg/day for females for the respective groups. Local effects (ocular irritation and matting of fur in the anogenital region) were seen, similar to the 28-day study and the studies with the 350 cst. viscosity. As well, there was a decrease in total cholesterol, HDL cholesterol, and phospholipids seen in the males. (Dow Corning Corp., 1995a)

In a 2-year chronic oral toxicity study with Dow Corning DB-100 Antifoam Compound (containing 88.3% CASRN 63148-62-9), albino Sprague-Dawley rats (45/sex/group) received the compound in the diet at 40 or 400 mg/kg/day for 23 months. (The researchers decided to terminate the study 1 month early due to increasing mortality in all groups. After the 15th month, mortality increased in all groups including control. Pathology results on expired animals revealed primarily kidney nephrosis and severe weight loss in the males and mammary masses in females. These, along with other postmortem results, indicated spontaneous disease, not related to treatment.) At 90 days, there was an interim sacrifice of 10/sex/group. This report covered only the results obtained from the animals taken through the entire study. Blood and urine samples were taken at 0, 1,3,6, and 18 months and upon termination and analyzed for hemoglobin, hematocrit, RBC, WBC, and differentials and albumin, glucose, pH, specific gravity, and occult blood, respectively. One week prior to termination, blood was taken for serum chemistry analysis. Upon sacrifice, the animals were subjected to extensive necropsy and histopathology. There were no differences in body weights or feed consumption. As well, no significant abnormalities were seen in hematological parameters and there were no significant differences in serum chemistry or urinalysis results. Spleen-to-body and

spleen-to-brain weight ratios were decreased in the high-dose females. (The number of females necropsied in the control, low-, and high-dose groups were 12, 12, and 11, respectively.) Histologically, extramedullary hematopoiesis of the spleen was seen in all groups of females, although not all females in each group were examined microscopically. Bone marrow analysis did not reveal any abnormalities. (Dow Corning Corp., 1973)

In reproduction and developmental toxicity studies, only 3 reports on Antifoam A (93% CASRN 63148-62-9), administered in the diet or via gavage, were found. No effects were observed in these studies. In metabolism studies, the common finding was that dimethyl silicones and siloxanes are excreted almost exclusively in the feces.

ITSL Calculation:

The studies from which an ITSL can be determined are the Dow Corning 1995c (28-day), 1995a (13-week), and 1973 (2-year) studies. When applying the absorption efficiency of the oral or inhalation route (b and a, respectively), while the Siddiqui and Stanton (1987) report stated that silicone oils are non-absorbable in the GI tract, there are no experimental data discussing the absorption efficiency of either route. Therefore, AQD default values will be applied.

Dow 1995c:

NOAEL = 10,000 ppm (978 mg/kg/d for males, 1043 mg/kg/d for females)

Body weight = 0.180 kg (male Fischer 344, subchronic study), 0.124 kg (female

Fischer 344, subchronic study)

Inhalation rate = 0.952 m³/kg (male Fischer 344 rat), 1.042 m³/kg (female Fischer 344 rat)

b = 1

a = 1

ITSL = NOAEL/(35 x 100) x W/I x b/a

= 0.0528 mg/m³ (male)

= 0.0355 mg/m³ (female) **FOR 100% CASRN 63148-62-9

Dow 1995a:

LOAEL = 5000 ppm for males (351 mg/kg/d)

Body weight = 0.180 kg (male Fischer 344, subchronic study)

Inhalation rate = 0.952 m³/kg (male Fischer 344 rat)

b = 1 = a

UF = 10

ITSL = LOAEL/(35 x 100 x UF) x W/I x b/a

= 0.001896 mg/m³

**FOR 100% CASRN 63148-62-9

Dow 1973:

LOAEL = 40 mg/kg/d for females

Body weight = 0.338 kg (female Sprague-Dawley, chronic study)

Inhalation rate = 0.972 (female Sprague-Dawley rat)

b = 1 = a

UF = 10

$$\begin{aligned} \text{ITSL} &= \text{LOAEL}/(35 \times 100 \times \text{UF}) \times \text{W/I} \times \text{b/a} \\ &= 0.000397 \text{ mg/m}^3 \quad \text{**FOR 88.3\% CASRN 63148-62-9)} \end{aligned}$$

While the most protective value above is that for the Dow 1973 study, it is possible that other components of DB-100 Antifoam may be contributing to the toxicity or that there may be interactions between components. Therefore, the ITSL calculated for the Dow 1995a study will be used.

$$\text{ITSL} = 0.001896 \text{ mg/m}^3 \times 1000 \text{ } \mu\text{g/mg} = 1.896 \text{ (2) } \mu\text{g/m}^3$$

The ITSL for dimethyl silicones and siloxanes (CASRN 63148-62-9) = 2 $\mu\text{g/m}^3$ based on annual averaging.

Reference:

Dow Corning Corporation. 1953 research. "Acute Inhalation Toxicity Masonry Water Repellents and Constituents." EPA Doc. # 86940001031, OTS0556485.

Dow Corning Corporation. 1973 research. "Two-Year Chronic Oral Toxicity Study with Dow Corning DB-100 Antifoam Compound in Albino Rats." EPA Doc. # 86940001184, OTS0572194.

Dow Corning Corporation. 1995a. "A 13-Week Subchronic Toxicity Study of Dow Corning 200 Fluid (Dimethyl Silicones and Siloxanes), 10 cst, in Rats." EPA Doc. # 86960000269, OTS0572930.

Dow Corning Corporation. 1995b. "A 13-Week Subchronic Toxicity Study of Dow Corning 200 Fluid (Dimethyl Silicones and Siloxanes), 350 cst, in Rats." EPA Doc. # 86960000270, OTS0572931.

Dow Corning Corporation. 1995c. "A 28-Day Oral Toxicity Study of Dow Corning 200 Fluid, 10 cst, in Rats." EPA Doc. # 86960000128, OTS0558268.

Dow Corning Corporation. 1995d. "Amendment to Final Report: A 28-Day Oral Toxicity Study of Dow Corning 200 Fluid, 350 cst, in Rats." EPA Doc. # 8696000130, OTS0558270.

Siddiqui, W. H., and E. Stanton. 1987 research, for Dow Corning Corporation. "Anal Leakage Potential of Polydimethylsiloxane Fluids in Rats." EPA Doc. # 86940001477, OTS0572724.