



8EHQ-0198-13585

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January 6, 1998

TSCA Document Processing Center (7407)  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
Attn: TSCA Section 8(e) Coordinator  
401 M Street S.W.  
Washington, D.C. 20460

PDCN: 889600000065

Re: Supplemental Submission to 8EHQ-0296-13585  
TSCA Section 8(e) Notification: Octamethylcyclotetrasiloxane

Dear Sir:

In accordance with the provisions of Section 8(e) of the Toxic Substances Control Act (TSCA), as interpreted in the Statement of Interpretation and Enforcement Policy (40 FR 11110, 16 March 1978), Dow Corning is submitting the following information as a supplemental submission to our TSCA Section 8(e) Notification of February 13, 1996 (8EHQ-0296-13585). The information presented in this supplemental submission was obtained from ongoing inhalation reproductive toxicity studies in Sprague-Dawley rats with octamethylcyclotetrasiloxane (OMCTS) that we are conducting as part of our Siloxane Research Program. This program was the subject of a Memorandum of Understanding, dated April 9, 1996, between Dow Corning and EPA.

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**Chemical Substance:**

556-67-2 Octamethylcyclotetrasiloxane



8EHQ-96-13585

**Manufacturer:**

Dow Corning Corporation  
2200 West Salzburg Road  
Midland, Michigan 48686-0994

**Contains No CBI**

**Ongoing Studies:**



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A TWO-GENERATION INHALATION REPRODUCTIVE TOXICITY  
AND DEVELOPMENTAL NEUROTOXICITY STUDY OF OCTAMETHYL-  
CYCLOTETRASIOXANE (D4) IN RATS

(Dow Corning Study No. 8713)

AN INHALATION REPRODUCTIVE TOXICITY STUDY OF OCTA-METHYLCYCLOTETRASILOXANE (D4) IN FEMALE RATS USING MULTIPLE EXPOSURE REGIMENS

(Dow Corning Study No. 8620)

AN INHALATION REPRODUCTIVE TOXICITY STUDY OF OCTA-METHYLCYCLOTETRASILOXANE (D4) IN FEMALE RATS USING MULTIPLE AND SINGLE DAY EXPOSURE REGIMENS

(Dow Corning Study No. 8864)

**Summary:**

In several earlier single generation reproductive toxicity studies, rats were exposed to high concentrations of octamethylcyclotetrasiloxane (OMCTS) for a prolonged pre-mating interval (at least 28 consecutive days). Exposures continued during the mating period, throughout gestation, and (in some studies) during lactation. In these studies, decreased litter sizes, decreased numbers of uterine implantations, and reduced numbers of corpora lutea were seen; these findings were previously communicated to EPA.

In an ongoing two generation inhalation reproductive toxicity study in rats with OMCTS, the reduction in mean live litter size was seen in litters produced by both the F0 and F1 animals. Among the F1 rats, mating and fertility indices were reduced, and some F1 female rats displayed signs of prolonged diestrus. It is well known that female rats in diestrus will not mate. The decreased mating and fertility indices are likely due, at least in part, to the increased number of female rats in diestrus.

In a separate series of ongoing studies, we have determined that the effects on litter size, uterine implantations, and corpora lutea are due to exposure of the female rats in the peri-coital interval. However, when female rats were subjected to prolonged exposures (at least 28 consecutive days) followed by a short recovery interval (three days), no reproductive impairment was evident. Hence, the effects appear to be readily reversible.

The effects we are reporting occurred only at exposure concentrations that greatly exceed typical occupational or consumer exposures. Consequently, we do not believe that the results of this study are necessarily indicative of a substantial risk to human health or the environment. Nevertheless, we are reporting these findings to EPA to ensure our compliance with both the letter and the spirit of TSCA Section 8(e).

## **Background:**

### Previous Findings

Previously, Dow Corning informed EPA of preliminary data from several single generation inhalation reproductive toxicity studies conducted with OMCTS in rats using exposure concentrations up to 700 ppm (see submissions to 8EHQ-0296-13585). Final reports from these studies have been forwarded to EPA. In these studies, decreases in mean live litter size, decreased numbers of uterine implantation sites, and reduced numbers of corpora lutea were noted. No effects were seen on the number of days elapsed between pairing and mating, on mating indices, or on fertility indices. In studies where the estrous cycle was evaluated, no effects on estrous cyclicity were detected.

### Exposures in an Ongoing Two Generation Study

In an ongoing two generation inhalation reproductive toxicity study in Sprague-Dawley rats, the F0 males and females were exposed to concentrations of 0, 70, 300, 500, and 700 ppm OMCTS for at least 70 consecutive days prior to mating. Exposures continued during the mating interval and throughout gestation until gestation day (GD) 20. Maternal exposures were suspended from GD 20 through postnatal day (PND) 4. F0 maternal exposures then resumed on PND 4 and continued through weaning on PND 21. Direct inhalation exposure of the F1 commenced on PND 22 and continued for at least 70 consecutive days prior to pairing and mating of the F1 to produce the F2. F1 exposures then continued throughout gestation and lactation (except for a scheduled interruption from GD 20 through PND 4) until weaning of the F2. The exposure concentrations for the F1 were the same as those used for the F0 (*i.e.*, 0, 70, 300, 500, and 700 ppm).

### New Findings

In the ongoing two generation inhalation reproductive toxicity with OMCTS in rats, no significant effects were seen among the F0 on the number of days between pairing and mating, on mating indices, or on fertility indices. Among the F1, statistically significant decreases were observed on both mating and fertility indices at 500 and 700 ppm. Decreases in the mating and fertility indices at 70 and 300 ppm were not statistically significant. The effects on mating and fertility indices were not accompanied by changes in the number of days elapsed between pairing and mating. We also noted that the F1 female rats showed signs of prolonged diestrus. It is well known that female rats in diestrus will not mate. It is possible that there is a causal relationship between the increase in diestrus and the decrease in mating and fertility.

A mating of the F1 males with females that had never been exposed to OMCTS did not result in reduced mating or fertility indices. This finding confirms our belief that male reproductive functions were not impaired.

In addition to the mating and fertility effects reported above, the F1 female rats in the 700 ppm group were observed to have statistically significantly increased pituitary weights. The significance of this finding is not yet known.

In a separate series of studies, we have determined that the sensitive period for the decreases in mean live litter size and reduced numbers of corpora lutea seen previously in several single generation studies is in the peri-coital interval. Female rats that received prolonged exposures (at least 28 continuous days) to 700 ppm OMCTS followed by a short recovery interval (three days) showed no signs of reproductive impairment. Hence, the effects appear to be readily reversible.

It is noteworthy to add that signs suggestive of prolonged diestrus were observed in a previous 90-day inhalation study. In that study, rats were exposed to nearly 1000 ppm OMCTS (nose-only exposure to a mixed vapor and aerosol). No reproductive parameters were assessed. However, histopathological analyses revealed an increased incidence of vaginal mucification. Although this finding is consistent with prolonged diestrus, interpretation of the data was confounded by the stress experienced by the animals as a result of the restraint that accompanied the nose-only exposure. Increased vaginal mucification was not seen at the next lower exposure concentration (400 ppm). It is possible that the vaginal mucification seen in this study as well as the estrous effects noted above for the F1 females in the two generation study were due to the high exposure to OMCTS.

#### **Actions:**

These findings from the aforementioned studies will be communicated to appropriate internal and external audiences. Dow Corning is now considering further studies to understand the potential relevance to humans for the reproductive effects seen in the earlier range-finding studies as well as in the ongoing two generation study. Dow Corning is also preparing an exposure assessment to provide support for an interim quantitative risk assessment.

Dow Corning will notify EPA of any further relevant information that may be developed concerning this material. Dow Corning will provide EPA with copies of the final reports from these studies when they are available.

If you have any questions with any of the aforementioned studies, please contact me at 517-496-4057 or at the address provided herein. If you require further general information regarding this supplemental submission, please contact Dr. Rhys G. Daniels, Regulatory Compliance Specialist, Product Stewardship and

Regulatory Compliance Department, at 517-496-4222 or at the address provided herein.

Sincerely,

Handwritten signature of Michael P. Hill in black ink, written over a horizontal line.

Michael P. Hill  
Americas Vice-President and Corporate Director  
Health and Environmental Sciences

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