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INITIAL SUBMISSION: LTR FR DOW CORNING CORP TO USEPA RE 24-MO COMBINED CHRONIC TOXICITY & ONCOGENICITY VAPOR INHALATION STUDY OF HEXAMETHYLDISILOXANE IN FISCHER RATS, DATED 110899		
Chemical Category		
HEXAMETHYLDISILOXANE		

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November 8, 1999

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

Re: TSCA Section 8(e) Notification of Substantial Risk:
A 24-Month Combined Chronic Toxicity and Oncogenicity Whole Body Vapor Inhalation Study of Hexamethyldisiloxane (HMDS) in Fischer 344 Rats

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 concerning an ongoing study.

Chemical Substance:

107-46-0 Hexamethyldisiloxane

Manufacturer:

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

Ongoing Study:

A 24-MONTH COMBINED CHRONIC TOXICITY AND ONCOGENICITY WHOLE BODY VAPOR INHALATION STUDY OF HEXAMETHYLDISILOXANE (HMDS) IN FISCHER 344 RATS

Dow Corning Study No. 8788

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Summary:

In an ongoing combined chronic/oncogenicity study, male and female Fischer 344 (F344) rats have been exposed by vapor inhalation to 0, 100, 400, 1600, and 5000

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ppm of hexamethyldisiloxane (HMDS) for six hours/day, five days/week. Histopathological evaluation performed on male rats following one year of exposure showed an increase in Leydig cell hyperplasia and Leydig cell tumors (LCTs). The Leydig cell hyperplasia occurred in 20/20 males in all exposure groups including controls (i.e., 0 ppm) and tended to increase in severity as the exposure concentration increased. The incidence of LCTs was 4/20, 10/20, 9/20, 12/20, and 15/20 in the 0, 100, 400, 1600, and 5000 ppm exposure groups respectively.

Discussion:

LCTs are commonly encountered in one year old F344 rats and become increasingly more frequent with age (Boorman, et. al. 1990). The incidence of spontaneous LCTs is generally greater than 90% in the F344 strain of rat at 2 years of age (Iwata, et. al. 1991).Virtually all plausible modes-of-action for the chemical induction of LCTs involve the elevation of serum luteinizing hormone (LH) and/or Leydig cell response to LH (Cook, et. al. 1999). There are several lines of evidence that suggest human Leydig cells are quantitatively less sensitive than rats in their proliferative response to LH and hence their sensitivity to chemically induced LCTs (Clegg, et. al. 1997; Quigley, et. al. 1995; Shenker, et. al. 1993). Further, epidemiology studies available on a number of compounds that induce LCTs in rats do not demonstrate an association between human exposure to these compounds and induction of Leydig cell hyperplasia or adenomas (Himmelstein, et. al. 1996; Longnecker, et. al., 1995; IARC, 1986; Preston-Martin, et. al. 1991; and Wilmer, et. al. 1994).

Because of the apparent differences in sensitivity of rodents and human Leydig cells to proliferative effects of LH and, therefore, differences in sensitivity to chemically induced LCTs, and because of the high spontaneous LC tumor incidence that occurs in F344 rats, and because potential human exposure to HMDS is low, we believe this material does not necessarily represent a risk to human males or the environment and we are reporting our findings to ensure compliance with both the letter and spirit of TSCA Section 8(e). However, full evaluation of the significance of this data should wait until the final report of this study is available.

Actions:

These findings from the aforementioned study will be communicated to appropriate internal and external audiences. Dow Corning will notify EPA of any further relevant information that may be developed concerning this material and will provide the Agency with a copy of the final report from this study when it is available.

If you have any questions concerning these studies, please contact me at 517-496-4057 or at the address provided herein. If you require further general information regarding this submission, please contact Dr. Rhys G. Daniels, Senior Regulatory Compliance Specialist, Regulatory Compliance Group, HERA Americas, at 517-496-4222 or at the address provided herein.

Sincerely,

Robert B. Meeks for Michael P. Hill

Michael P. Hill
Executive Director of
Environmental, Health and Safety
(517) 496-4057

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References

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