

DOW CORNING

TOXICOLOGICAL STUDIES CONDUCTED ON
DOW CORNING® 344 FLUID AND RELATED MATERIALS

SUMMARY OF DATA

BIOLOGICAL SERVICES DEPARTMENT

March 9, 1977

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1. Acute Oral Toxicity of a Mixture of Cyclic Polydimethylsiloxane¹

Ten albino laboratory rats received an undiluted acute oral dose of 34.6 gm/kg body weight. No deaths or untoward effects were observed. In view of the extremely large dose employed in this study, it is very unlikely any significant ingestion hazard would exist from acute exposure to this fluid.

2. 7-Day Subacute Oral Toxicity Test on Dow Corning 344 Fluid²

A 7-day subacute oral toxicity test was conducted on Dow Corning 344 fluid. Physiological saline was used as a treated control material. No adverse findings were noted in the parameters investigated, such as mortality, behavioral reactions, body weights, gross pathologic studies and seminal vesicle weights and ratios.

3. Acute Aerosol Inhalation Toxicity of Dow Corning 344 Fluid³

Albino rats were exposed to Dow Corning 344 fluid for a period of 7-1/2 hours. The aerosol concentration was approximately 90 mg/liter. The exposure consisted of an aerosol burst every 1/2 hour for a total of 15 exposures over the 7-1/2 hour period. Based on the parameters investigated such as body weight, mortality, behavioral reactions and gross pathologic examination, acute aerosol exposure to Dow Corning 344 fluid appears to present no apparent hazard.

4. 90-Day Subacute Aerosol Inhalation Toxicity of Dow Corning 344 Fluid⁴

A 90-day subacute aerosol inhalation toxicity study was conducted with TX-997 using cynomolgus monkeys as experimental animals. TX-1015 was used as treated control material. Twelve monkeys were divided equally into two groups designated treated control, T-I. T-I was exposed to the aerosol of Dow Corning 344 fluid and the treated control animals were exposed to the propellant. Each inhalation chamber (3.5 cubic meter Plexiglas®) received clean air from the top center of the chamber at a rate of 25 L/min. Each group was exposed to its respective aerosol twice daily, each exposure consisting of four 15-second sprays with five minute intervals between sprays, for 90 consecutive days. The average set of four aerosol releases from the treated control and T-I were 73.9 and 78.9 grams respectively. The average daily nominal concentrations were 147.2 and 158.3 mg/L air for treated control and T-I respectively. Filter samples taken daily from the T-I chamber revealed an average analytical concentration of 0.005 mg/L air.

During the course of the study, all animals were observed and data with respect to incidence of mortality, food consumption, reactions displayed, body weight, hematologic and clinical blood chemistry profiles, urinalyses, ophthalmic examinations, respiratory function tests, and neurological examinations were collected. All numerical data from the test group were compared to the treated control group, when statistically possible, by "t-tests." On day 91 of the investigation, all animals were given a complete gross and microscopic pathologic examination.

No deaths occurred during the experiment and no untoward behavioral reactions were observed. Growth, as indicated by body weight data, was unaffected by exposure to the test compounds. No changes in food or water consumption patterns of the animals were observed during the testing program. Ophthalmic examinations following the exposure periods revealed no treatment-induced ocular lesions (confirmed histologically). Neurological examinations, including evaluation of the righting, supporting, flexor, extensor thrust, and patella or knee jerk reflexes revealed no differences between test and control monkeys. Ten lead electrocardiograms conducted during the study revealed no abnormalities.

Hematologic studies, including total and differential leukocyte counts, erythrocyte counts, hemoglobin concentration, hematocrit, sedimentation rate, and calculated cell indices, revealed no differences between test and control monkeys. Clinical blood chemistry studies, including fasted blood glucose concentration, blood urea nitrogen concentration, serum alkaline phosphatase activity, serum glutamic-pyruvic transaminase activity, were unremarkable. Urinalyses (which included determinations for the presence of blood, ketones, glucose, reducing substances, proteins and microscopic formed elements) showed no treatment-related abnormalities.

Respiratory function studies, including air way resistance, dynamic compliance, respiratory rate, average tidal volume, minute volume, PO_2 , PCO_2 , pH, functional residual capacity, lung clearance index, fraction of CO_2 removed from respired air, diffusing capacity of CO_2 and of O_2 , peak flow and total plural pressure failed to reveal any treatment-related changes. No differences between test and control monkeys were apparent following gross pathologic examination and evaluation of organ weight data. Histopathologic studies revealed no lesions which could be attributed to inhalation of the test material.

5. The Results of Range Finding Toxicological Tests on Octamethylcyclotetrasiloxane⁵

Octamethylcyclotetrasiloxane has a low acute oral toxicity, ALD_{50} is >2 gm/kg. It is very slightly irritating to the eye and causes essentially no irritation to the skin upon repeated/prolonged contact. The vapor of this material at room temperature or when generated at $100^\circ C$ is without appreciable effects upon laboratory animals.

6. Chronic Eight Month Feeding Studies with Various Methylsiloxanes in Rabbits⁶

The effects of dietary administration to rabbits of a series of polymerized methylsiloxanes have been studied by a number of parameters of physiological status and tissue morphology. No significant differences were noted on hemograms, leukocytic data, blood chemical data, urine analytical findings, organ weights and gross or microscopic appearances of tissue from all organ systems among the groups. A scattered incidence of unusual findings seen throughout all groups were attributed to the type of respiratory infection or parasitic infestations often seen in comparable colonies of control animals of this species. It was concluded that ingestion of 0.05% of a 1-5 mixture of the trimer and tetramer, of 1% of the cyclic trimer or tetramer, or trimethyl endblocked DOW CORNING® 200 fluid 1.5 cs by rabbits for eight months produced no significant adverse effects.

7. Chronic One-Year Feeding Studies with Methylsiloxane Fluids in Rats⁷

A study comparing the effects of dietary administration to rats of 0.05% of a 1-5 mixture of dimethylcyclictrimer and dimethylcyclictetramer, 1% dimethylcyclictrimer, 1% dimethylcyclictetramer, or 1% trimethyl end-blocked Dow Corning 200 fluid 1.5 cs with those of an unsupplemented diet was conducted. Over a one year period no significant differences were noted in growth or in the physiological status of the rats receiving any of these methylsiloxanes in comparison to the base of the control group. Post mortem examinations showed no treatment-related differences in organ weights or gross and microscopic appearance of tissues. It was concluded that administration of methylsiloxanes in the diet of rats for more than one year did not have any adverse effects.

8. Human Repeated Insult Patch Test (HRIPT)⁸

Dow Corning 344 fluid failed to produce any evidence of primary skin irritation or skin sensitization following nine daily repeated applications to each of fifty human subjects.

9. A Publication Entitled, "Toxicological Studies on Certain Commercial Silicones" by Rowe, Spencer and Bass

This publication deals with single dose oral administration, repeated dose oral administration, intraperitoneal injection, subcutaneous injection, eye installation, skin application, single exposure vapor inhalation and repeated exposure vapor inhalation. In conclusion, these toxicological studies with laboratory animals have shown the subject methyl silicones ranging in viscosity from 0.65 centistoke to 12,500 centistokes to respond in a similar manner and to be low in toxicity and most likely present no significant handling problems.

10. A Publication Entitled "Health and Environmental Aspects of Polydimethylsiloxane Fluids" by Calandra, Keplinger, Hobbs, and Tyler

The reprint gives details on the acute, subacute, and chronic oral ingestion toxicity, effects upon injection, skin and eye response, acute and subacute inhalation studies, reproductive, teratologic, and mutagenic response. Environmental studies including the effects on various birds, aquatic and marine species, and biodegradation and bioaccumulation are detailed.

Human and animal metabolism of various cyclic and linear polydimethylsiloxanes are also outlined.

- ¹Dow Corning Internal Company Report No. 1723-2
- ²Dow Corning Internal Company Report No. 1547-80A
- ³Dow Corning Internal Company Report No. 1547-1
- ⁴Dow Corning Internal Company Report No. 2061-1
- ⁵Dow Corning Internal Company Report No. 1362-1
- ⁶Dow Corning Internal Company Report No. 1179-1
- ⁷Dow Corning Internal Company Report No. 1179-1
- ⁸Dow Corning Internal Company Report No. 2061-1

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