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Submitting Organization	WITCO ORGANOSILICONES GP		
Contractor			
Document Title	INITIAL SUBMISSION: LTR FR WITCO ORGANOSILICONES GP TO USEPA REPORTING PRELIMINARY RESULTS FROM MAMMALIAN ERYHROCYTE MICRONUCLEUS STUDY WITH SILQUEST A-187 SILANE, DATED 5/10/1999		
Chemical Category	GAMMA-GLYCIDOXYPROPYLTRIMETHOXSILANE		

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Witco

OrganoSilicones Group **Product Safety and Regulatory Affairs**

3500 South State Route 2
Friendly, WV 26146
Ph: (304) 652-8000
Fax: (304) 652-1478

Document Processing Center (TS-790)
Office of Toxic Substances
US Environmental Protection Agency
401 M Street SW
Washington, DC 20460
Attn: TSCA 8(e) Coordinator

May 10, 1999

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Dear Sir or Madam:

Witco Corporation, herewith submits the following information pursuant to TSCA Section 8(e) concerning preliminary audited information from a mammalian erythrocyte micronucleus study with mice on glycidoxyalkyltrimethoxysilane, Silquest A-187 silane.

Silquest A-187 silane is composed of the following:

% Maximum Concentration	Chemical Name	CA S #
99	gamma-Glycidoxypropyltrimethoxysilane	2530-83-8
0.1	Allyl Glycidol Ether	106-92-3
0.1	Methanol	67-56-1
0.01	Toluene	108-88-3

The information provided in this letter is based on the instructions regarding reportability of toxicity data stated in the EPA's TSCA Section 8(e) Reporting Guide. Witco Corporation received the information described and summarized herein on April 27, 1999.

A study of Silquest A-187 silane (A-187) in ICR mice was conducted to evaluate the clastogenic potential of A-187 as measured by its ability to induce micronucleated polychromatic erythrocytes in mouse bone marrow following intraperitoneal (i.p.) injection. The i.p. route was selected since this is an acceptable and standard method for administering test articles in this type of study. Injection is not a plausible route of exposure for humans. The information from this study indicates that under the conditions of this test, A-187 induced a significant increase in micronucleated polychromatic erythrocytes in male and female mice.

The test article in the vehicle (water) was administered i.p. at dosage levels of 500, 1000, and 2000 mg/kg. All animals in the 1000 and 2000 mg/kg dose groups showed signs of toxic effects (lethargy and piloerection). One high dose group animal died on the day of dosing. (This animal was part of the high dose replacement group and not required for analysis.) All other animals survived to the scheduled necropsy.

Bone marrow cells were collected 24 and 48 hours after treatment, and examined microscopically for micronucleated polychromatic erythrocytes. Moderate to severe reductions in the ratio of polychromatic erythrocytes to total erythrocytes were observed in all of the test article-treated groups relative to the respective vehicle controls. These reductions demonstrate bioavailability of the test article to the bone marrow. A significant increase in micronucleated polychromatic erythrocytes was observed in male and female mice 24 hours after treatment with 500, 1000 and 2000 mg/kg and in male and female mice 48 hours after treatment with 2000 mg/kg. There was evidence of a dose related increase in the number of micronucleated polychromatic erythrocytes observed in male and female mice over the three test article dose levels in the 24 hour sacrifice groups.

It should be noted that A-187 readily hydrolyzes to form a silane triol, and, based on the storage conditions and use of water as a vehicle, the actual test article was a mixture of A-187, methanol, and the silane triol. The relative concentrations of these species would have changed as the test solutions were allowed to age, and the other species may have been present as well.

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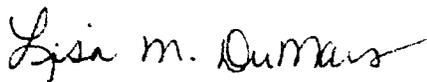
Considerable testing to investigate the tumorigenic and genotoxic potential of A-187 has been conducted. A-187 has been tested for its dermal tumorigenic potential by chronic application to the skin of mice. No tumors of the skin or subcutaneous tissues were observed in the A-187 treated group, although some animals had hyperkeratosis consistent with mild skin irritation. No local tumors were observed in the vehicle control group (treated with acetone). In the positive control group, 39 of the 40 animals developed skin tumors, with 33 being confirmed squamous cell carcinomas, indicating the test was sensitive and valid. A-187 is not considered to be tumorigenic for mouse skin under the specific conditions of this test.

Several standard *in vitro* studies, including the Ames test, mouse lymphoma assay, and a sister chromatid exchange test (SCE), have shown A-187 to be weakly mutagenic. The positive results were primarily found in the absence of metabolic activation; genotoxic activity was decreased in the presence of activation enzymes. *In vivo* mammalian studies have shown that repeated exposure of the intact animal to A-187, even at toxic doses, does not result in genotoxic effects. In rabbits injected i.p. (5 daily injections per week for two weeks) at A-187 doses of 30 or 100 mg/kg, there was no consistent, dose-dependent increase in SCE frequency in peripheral blood lymphocytes. In a second study, rats and rabbits were exposed 6 hrs/day for a total of nine exposure days, to aerosol concentrations of A-187 ranging from 73 to 734 mg/m³. The highest chamber concentration was lethal to 5 of 10 male rats and 4 of 5 rabbits after two days of exposure. There was no consistent, dose-related increase in SCEs in peripheral lymphocytes of either rats or rabbits, indicating a lack of genotoxic activity under these test conditions.

The results of these studies suggest that A-187 is capable of being converted by the intact animal to product(s) which are devoid of mutagenic potential, and thus the material should not present a significant *in vivo* genetic hazard. This finding accords with the observation that no tumors occurred locally in response to the chronic topical application of A-187.

A full copy of the audited report will be provided upon request. Please contact the undersigned with questions, if any, at (304) 652-8825.

Sincerely,



Lisa M. DuMars
Manager, Product Safety and Regulatory Affairs

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