



Great Lakes
Chemical Corporation

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Document Control Center (TS-790)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

Attention: Section 8(e) Coordinator

RE: Tetrahydrofurfuryl Alcohol TSCA 8(e) Notice
(When responding, please refer to JAB-95-2)



88950000099

Gentlemen:

Great Lakes Chemical Corporation is submitting a TSCA Section 8(e) substantial health risk notification concerning a 90-day dermal and a 90-day inhalation toxicity study with tetrahydrofurfuryl alcohol (THFA) in rats. The CAS Registry Number for this cycloaliphatic compound is 97-99-4. The studies, which are individually identified below, are being performed at WIL Research Laboratories, Inc., Ashland, Ohio. The following information was obtained from unaudited summary tables of available data.

90-Day Dermal Toxicity Study of THFA in Rats: The test material was administered dermally to the dorsal regions of male and female rats at the dosage level of either 100, 300, or 1000 mg/kg/day, five days a week for at least 65 applications. The study was designed whereby the number of animals being evaluated was 17 males and 12 females per group. A concurrent control group was represented with the same number of animals. After seven weeks on study, five (5) males from each group were randomly selected for termination as required by a specific section of the protocol for an interim evaluation of reproductive tissue. The remaining 24 animals per group were terminated after 13 weeks on study.

A review of the summary data (tables) that are currently available reveal no treatment-related effects with respect to survival, clinical observations, ophthalmic examinations, hematology values and serum chemistries, absolute and relative organ weights, or food consumption. However, statistically significant decreases in weekly body weights were noted beginning study week nine (9) in the high dose males (1000 mg/kg/day).

Significant difference from the control group was at $p \leq 0.05$ for weeks 9 through 12 and $p \leq 0.01$ for week 13.

90-Day Inhalation Toxicity Study of THFA in Rats: The test material administration is by inhalation using male and female rats. Concentrations being administered are at either 50, 150, or 500 ppm, 6 hours per day, five days a week for at least 65 exposures. The study was designed whereby the number of animals being evaluated was 14 males and 10 females per group. A concurrent control group was represented with the same number of animals. After six weeks on study, four (4) males from each group were randomly selected for termination as required by a specific section of the protocol for an interim evaluation of reproductive tissue. The remaining 20 animals per group will be terminated after 13 weeks on study.

A review of the summary data (tables) that are currently available reveal treatment-related effects during exposure in both sexes. The observations include hypoactivity and intermittent whole body spasms. The spasms are concentration-related. At one-hour post-exposure, hypoactivity ceases and intermittent whole body spasms become less noticeable. However, hyperactivity is noted instead and is concentration-related. Also wet yellow urogenital matting is being noted in both sexes at 500 ppm during the one-hour post-exposure observation period.

Statistically significant decreases in weekly body weights were noted beginning study week one (1) in the high concentration males (500 ppm). Significant difference from the control group was at $p \leq 0.01$ for weeks one through four and seven through 11. Significance decreased to $p \leq 0.05$ at week five and six. In the case of the high concentration females, statistically significant increases in weekly body weights were recorded during weeks three through nine. However, body weight gains, overall, did not reveal significant changes in either sex. Although statistically significant decreases in weekly food consumption were noted in the high concentration males, the decreases were minimal and sporadic.

At four (4) weeks into the study, the platelet count was statistically significantly decreased ($p \leq 0.01$) at 150 and 500 ppm in both sexes. This affect appears to be concentration related at this time in the study. The only serum chemistry parameters that may be test-related affects are the statistically significantly increased ($p \leq 0.05$) chloride and sodium values in males at 150 and 500 ppm.

Document Control Center (TS-790)
4 January 1995
Page Three

A follow-up notification will be submitted to the Agency concerning these two toxicology studies after additional data (collected at termination) has been tabulated and reviewed. In the meantime, any questions related to this submission can be directed to my attention at (317) 497-6223.

Sincerely,


John A. Bieseemeier
Regulatory Toxicologist
Regulatory Affairs

JAB/clw