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June 8, 2004

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Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460 – 0001

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2004 JUN 15 AM 8:3

CONTAINS NO CBI

Dear Sir or Madam,

Re: Preliminary Results from a Repeated Dose 28-Day Dermal Toxicity Study of Furfural [CASRN 98-01-1] in Rats

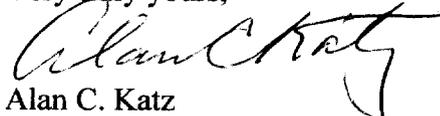
Dear Sir of Madam:

Pursuant to the guidance EPA has published for reporting information under the requirements of TSCA § 8(e), we wish to report the following results from a preliminary repeated dose 28-day dermal toxicity study of furfural [CASRN 98-01-1] in rats.

In this study, furfural was applied at dose levels of 0 (control), 25, 50 or 100 mg/kg/day. At the highest dose, transient neurotoxic signs were reported to have been observed in the majority of the female group immediately after dosing. These signs persisted for a period of 3 – 4 hours after dosing. Only drowsiness was observed for the male group at the same dose. The results are described in the attached summary.

The final report will be submitted to the Agency promptly after we receive it. Please contact the undersigned at (703) 335-5670 with questions, if any.

Very truly yours,


Alan C. Katz
President



Attachment



276010

SUMMARY REPORT

Repeated Dose 28-Day Dermal Toxicity Study of Furfural in Rats Followed By A 4-Week Recovery Period (JRF Study N° 4700)

Study Period

Acclimatisation	:	March 04, 2004 to March 09, 2004
Treatment	:	March 12, 2004 to April 08, 2004
Recovery group Sacrifice	:	May 07, 2004

Groups of Wistar rats, comprising of 10 animals per sex per group, were dermally applied with Furfural at dose levels high dose recovery (G6-100 mg/kg b. wt) and control recovery groups (G5) were treated for 28 days and kept under observation for another 28 days in order to find out the persistence, recovery or delayed effect of the test substance, if any. Animals were housed individually in pre-sterilized solid floor polypropylene rat cages (size: 410 mm x 282 mm x 180 mm). Each cage was fitted with a stainless steel top grill having provision for keeping pelleted feed and a polypropylene water bottle with stainless steel drinking nozzle. The bottom of the cage was layered with clean, sterile rice husk. The animals were provided *ad libitum* rat pellet feed and drinking water (filtered through Aquaguard water filter system). Fresh feed was supplied once a week and water bottles were refilled daily.

Approximately twenty-four hours before application, about 10 per cent of the body surface area was clipped for the application of test substance from the dorsal area of the trunk of test animal using a clipper. The test substance was applied neat without dilution with respect to animals' body weight. The test substance was applied uniformly using micropipette over the clipped area and held in contact with the skin using aluminum foil, which will in turn be covered by a porous gauze dressing and non-irritating tape. After 6 hours of exposure period, treated area was cleaned with cotton soaked in distilled water to remove residual test substance. Control group animals were handled similarly, except for the application of test substance, applied with distilled water only.

All the animals were observed daily for visible signs of clinical symptoms. Every day after removing the patch, skin of each animal was observed for the presence of erythema and edema, if any. Individual body weight and food consumption were monitored weekly. Detailed clinical examination (Neurobehavioral observations) was conducted weekly, whereas functional observation battery tests were performed during 4th week of recovery period for recovery group animals. Ophthalmological examination was conducted on all animals from main group prior to treatment and prior to sacrifice.

Mortality

No mortality was observed in animals from the high dose recovery as well as in the control recovery group during the experiment.

Clinical Signs

No local skin reaction/ irritation was observed in any of the animals from the high dose recovery as well as in the control recovery group during the experiment. All the male rats treated with Furfural at the dose level of 100 mg/kg body weight (G6) showed drowsiness after dosing during first week of treatment. No such symptoms were observed in males of these groups during subsequent weeks of exposure.

Majority of females from high dose recovery (G6) groups showed symptoms such as abdominal breathing, drowsiness, dyspnoea, clonic convulsion, hyperactivity, tremors, unprovoked vocalizations immediately after the dosing and these symptoms persisted for 3-4 hours post dosing. During recovery period, no clinical signs were observed in any of animals from G5 and G6.

Ophthalmological examination performed on all animals from recovery group prior to treatment and prior to sacrifice did not reveal any ocular abnormalities. Functional observation battery tests performed in recovery group animals revealed no treatment related neurological abnormalities.

Recovery group animals were sacrificed on May 7, 2004. The data processing is being performed. Clinical chemistry analysis of recovery group and histopathology of main and recovery group is in progress.

Dr. P.Y. Bhoite

Study Director