

ORIGINAL

TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

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8FHG-10-17816	89100000293	8/3/10

COMMENTS:

DOES NOT CONTAIN CBI

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DuPont Haskell Global Centers
for Health and Environmental Sciences
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August 02, 2010

Via Federal Express



Document Processing Center (Mail Code 7407M)
Room 6428
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency, ICC Building
1201 Constitution Ave., NW
Washington, DC 20004

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No CBI**

8EHQ-0810-17816B
DCN:89100000293



Dear 8(e) Coordinator:

Tetrahydrofuran (CAS Number 109-99-9)
8EHQ-10-17816

DuPont received information from a third party on the above-referenced substance. DuPont has reviewed the information for reportability under TSCA §8(e) and provides below a summary of the information that has been determined to meet EPA's TSCA §8(e) criteria for reporting. It is unknown whether the information reported below has been previously reported to EPA by any third party or is otherwise considered known to the Administrator under TSCA §8(e) guidance.

Test substance: Tetrahydrofuran (CAS Number 109-99-9)

- Ready Biodegradability Assay

A biodegradability assay was conducted in accordance with EU Method C.4-D (Manometric Respirometry Test). The test substance (100 mg/L) was added to activated sludge (30 mg/L) in a closed system. Aniline was used as the reference substance. The average BOD-degradation based on ThOD was 0% after 28 days. Therefore, the test substance was considered to be not readily biodegradable.

- Inhalation Hazard Test

An acute inhalation test was conducted with male and female rats exposed to the test substance as follows: 302.65 mg/L for 1 hour; 375.2 mg/L for 30 minutes; or 332.08 mg/L for 10 minutes (all concentrations were nominal). There were 3 rats/sex exposed for the 1 hour and the 30 minute exposures and 6 rats/sex for the 10 minute exposure.

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The rats were observed for 14-days after the exposure and body weights and clinical signs were recorded. Mortality was noted as follows: in the 10 minute exposure 0/12; in the 30 minute exposure 3/6; and in the 1 hour exposure 6/6. Clinical signs included attempts to escape, elevated respiration, staggering unsteady gait, a lack of pain reflex and respiratory irritation. Gross pathology observations included acute dilatation of the right ventricle of the heart, congestive heart failure, and distended lungs. The estimated LC50 for male and female rats was 375 mg/L for 30 minutes.

- Acute Oral Study in Dogs

The test substance was administered orally as a 15% aqueous solution at dose levels of 2 and 3 cm³/kg body weight (1 animal in the high dose group, 2 animals in the low dose group) to dogs. Animals were observed for 7 days, weighed daily, sulfobromophthaleine tested, and blood-urea determined. No deaths occurred. Slight narcosis, abdominal position, staggering, emesis, irritation of gastric mucosa were observed. Other observations included enhanced urine protein content in two animals of the highest dosing group on day 1.

- Acute Oral Study in Rabbits

The test substance was administered by oral gavage to rabbits as a 10-25% aqueous solution at dose levels of 1000 (1 animal), 2000 (2 animals), 2500 (2 animals) and 3000 (1 animal) mg/kg body weight. Animals were observed for at least 38 days. All animals dosed at 2500 mg/kg and above died. Staggering, and faint appearance were observed in the animal dosed at 1000 mg/kg. There were no findings at 6 hours after dosing. Staggering, reduced food uptake, body weight loss, and reduced activity were observed in the animals dosed at 2000 mg/kg. Liver and kidney effects were observed at necropsy.

- Acute Inhalation Study in Cats

The test substance was administered whole body as a vapor to cats as follows: 10 mg/l air, 3 hours: 1 cat; 10 mg/l air, 8 hours: 1 cat; 50 mg/l air, 3 hours: 1 cat; 100 mg/l air, 1 hour: 1 cat; 100 mg/l air, 8 hours: 2 cats; 200 mg/l air, 1 hour: 1 cat; 200 mg/l air, 8 hours: 2 cats; and 400 mg/l air, 3 hours; 1 cat. Animals were observed for at least 12 days. All animals survived the treatment procedures with 10 and 50 mg/l air. All animals exposed to 200 mg/l and higher died. Clinical signs observed frequently in all dosing groups and at all exposure intervals were: attempts to escape, salivation, lacrimation, muzzling, nasal discharge, dizziness and drowsiness, elevated blinking; at higher concentrations and/or elongated exposure: abdominal/lateral position, narcosis, flat muscle tone, irregular respiration.

- Subacute Inhalation Study in F344 Rats and B6C3F1 Mice

In a subacute inhalation study (OECD 412) male rats and mice were exposed to by inhalation to the test substance 6 hours/day, 5 days/week for up to 20 exposures. Dose levels were 0, 600, 1800, 5400 mg/ m³ (0, 200, 600, 1800 ppm). In male rats, test

substance induced alpha-2 μ globulin deposition in the cortex of kidneys accompanied by increased cell proliferation in cortical proximal tubules after exposure to concentrations of 1,800 and 5,400 mg/m³. These changes were accompanied by an increased apoptotic index. These effects in the target organ in male rats are considered to constitute the mechanisms of tumor formation. In the livers of female mice induction of P450 enzymes and persistently increased zonal liver cell proliferation in zones 2 and 3 occurred after exposure to 5,400 mg/m³. At 1,800 mg/m³ a transient increase in cell proliferation after 5 exposures was observed. These effects in the target organs in female mice are considered to constitute the mechanisms of tumor formation. No relevant influence of the test substance via inhalation was observed on the uterus of mice. The 'No Observed Adverse Effect Concentration' (NOAEC) under the condition of this study was 600 mg/m³ (200 ppm) for both rats and mice.

- Acute Inhalation Toxicity Study in Cats and Guinea Pigs

Two guinea pigs and 4 cats were exposed to the test substance by inhalation at a concentration of 10 mg/L, 8 hours/day for up to 20 days. Both guinea pigs survived the experiment with mucosal irritation as the main symptom. Slight narcosis was observed. Clinical chemistry (urinary system) was without findings. Gross pathology revealed slight kidney damages in one guinea pig and signs of mucosal irritation concerning the airways. One cat died after the third exposure, another one after the 6th exposure. The two other cats exposed for 12 and 20 days survived the treatment. Clinical signs included general signs of mucosal irritation (strong salivation, lacrimation, nasal discharge and winking); after 4 exposures enhanced urinary protein content; and slight narcosis.

Sincerely,


A. Michael Kaplan, Ph.D. (dwd)
Director - Regulatory Affairs

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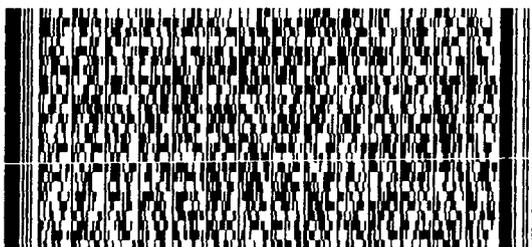
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