

BASF Corporation

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April 27, 1998



BEHQ-98-14172

Document Processing Center (TS-790)
Attention: (8e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Ladies and Gentlemen:

BEHQ - 0498 - 14172

Subject: Notice in Accordance to TSCA Section 8(e) - Results of a Dose Range-finding Prenatal Developmental and a 28-day Repeated Dose Oral Toxicity Study in Wistar with N,N'-Dimethylpropylene Urea.

BASF Corporation is submitting the results of two studies conducted by RCC Research & Consulting Company Ltd., CH-4452 Itingen, Switzerland on behalf of BASF Aktiengesellschaft, Ludwigshafen, Germany.

Amounts imported by BASF Corporation since 1993 are as follows: 200 kg in 1993; 100 kg in 1995 and 400 kg in 1998.

A. Dose Range-finding Prenatal Developmental Toxicity Study

The study was based on the EC Commission Directive 87/302/EEC of November 18, 1987; Official Journal of the European Communities; No. L 133 (1988) and the OECD Guidelines for Testing of Chemicals; Method No. 414 (May 1981). The test substance was administered to 5 mated female Wistar rats/group at doses of 0, 60, 120, and 180 mg/kg body weight on day 6 through day 20 post coitum by gavage.

The following is a summary of the most relevant results:

Clear, dose dependent signs of maternal toxicity occurred at all 3 doses levels; these were substantiated by lower mean food consumption, impaired body weight gains (with and without correction for uterus weight) and lowered mean gravid uterus weights.

Developmental toxicity occurred at the mid and the high dose level in the form statistically significant elevated postimplantation losses due to an increased resorption rate and clearly lowered mean fetal body weights. Borderline effects on resorption rate and fetal body weights were also recorded at 60 mg/kg. Fetal external examination did not yield indications of substance-induced teratogenicity up to and including the highest dose level.

Signs of developmental toxicity appeared in this range-finding study only in the presence of overt maternal toxicity.

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B. 28-Day Repeated Dose Oral Toxicity Study

The study was based on the EC Commission Directive 96/54/EEC of September 30, 1996; Official Journal of the European Communities; No. L 248 (1996) and the OECD Guidelines for Testing of Chemicals; Method No. 407 (July 1995) and Japan/MHW Guidelines for Toxicity Testing of Chemicals, MITI/MHW 1987.

The test substance was administered daily by oral gavage to Wistar rats of both sexes at dose levels of 0, 10, 50 and 250 mg/kg body weight/day for a period of 28 days. The control and high dose group consisted of 10 animals of each sex; low and mid dose group consisted of 5 animals of each sex. Five animals per sex of all groups were treated for 4 weeks and sacrificed thereafter (main groups); the remaining 5 animals per sex of control and high dose group were maintained for another 14 days without administration of the test substance (recovery groups).

The following is a summary of the most relevant results:

- The oral administration resulted in several effects on clinical signs, body weight, food consumption, clinical laboratory parameters and organ weights, mainly in animals of the high dose group. Morphological alterations were observed in the spleen and thymus of both sexes and in the kidneys and testes of males rats at 50 and 250 mg/kg/day.
- Findings in the spleen of both sexes at 250 mg/kg/day consisted of lymphoid atrophy, red pulp atrophy and increased hemosiderin. In females decreased hemopoiesis was also present. Red pulp and lymphoid atrophy underwent reversal during the recovery period, whereas hemopoiesis and hemosiderin were somewhat increased over control values.
- Thymic atrophy occurred in females at 50 mg/kg and in males and females at 250 mg/kg/day. At 250 mg/kg/day this finding was accompanied by slightly increased incidences of lymphocytolysis. After the recovery period, the incidence and severity of these findings were similar to those in the control group.
- A dose-related increase in findings indicative of alpha-2 μ -globulin nephropathy syndrome was present in male rats at 50 and 250 mg/kg/day. These findings underwent partial reversal during the recovery period.
- In the testes there was a dose-related increase in seminiferous tubular atrophy at 50 and 250 mg/kg/day. Although, some evidence of recovery was present following the recovery period, severe tubular atrophy was still in evidence.

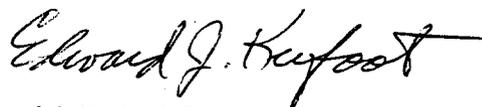
Based on the results of this study, the no observed effect level (NOEL) was 10 mg/kg/day.

Although BASF Corporation does not feel that this information presents a substantial risk to health or environment, it is being submitted under Section 8(e) of TSCA. Any reports or additional information that we receive will be forwarded to the Agency and Material Safety Data Sheets will be updated with this preliminary information.

If you have any questions, please feel free to call me at (734) 324-6207.

Very Truly Yours,

BASF Corporation



Edward J. Kerfoot, Ph.D.
Director, Toxicology and Product Regulations