UNITED STATES ENVIRONMENTAL PROTECTION AGENCY 000102

DATE: August 29, 1977

AUG 29, 1977

SUBJECT: EPA #201-401, Caswell No. 3?? 5 Azodrin, Water Miscible Air Formulating

FROM: Toxicology Branch, Spencer, H.W.

TO: Product Manager 15, Franklin D. R. Gee

Conclusion:

1. Do not register.
2. Provide the following data:
   (a) Primary eye irritation (5 Azodrin)
   (b) Primary skin irritation (5 Azodrin)
3. The Hen Demylinization Study as reviewed by W. Crecar DTD. March 22, 1977 was deemed inadequate due to controls exhibiting demyelination. Ref. EPA Acc. No. 091487.
4. The Three Generation Reproduction Study in Rats - submitted March 25, 1977 was reviewed by R. Conolly, Tox. Br. DTD. December 18, 1968 and was considered adequate at that time.

Review:

Chromosome Studies on Bone Marrow Cells - Mouse - Single Dose of Azodrin.

Test Procedure: Either 0, 2, or 4 mg/kg doses (approximately ¼ and ½ LD/50) of Azodrin in DMSO was given orally to 8 males and 8 females in each of 3 groups. A 0.4% Colcemid solution was injected ip. 90 minutes prior to harvest of femur marrow in 4 animals/sex/dosage at 8 and 24 hrs. Chromosome morphology of 100 marrow cells was analyzed from each animal.

Results: No demonstrable chromosome damage was induced by Azodrin in mice. Tox. Br. notes that times for collection and protocol were extrapolated to the mouse from data on the chinese hamster. It would have been more meaningful to have used data from the mouse, study by Tunstall Laboratory, TLGR 0014.73 DTD. June 1973.

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Teratology Study - Rabbit, Banded Dutch. Female were mated and treated with dosages of either 0,0.7,2.0mg/kg Azodrin or 37.5mg/kg thalidomide on days June 18 of gestation. The MTD was found to approximate 1.0mg/kg. Numbers & types of abnormalities seen in treated animal fetuses were not significantly different from control animal fetuses. Study by Tunstall Laboratory, TLGR 0031.72, Project No. T507521/69 DTD. October 1972. Tox. Br. considers this study to be core-minimum data.

Toxicity Studies on Azodrin: Dominant Lethal Assay in Male Mice - single dose of Azodrin. Male mice were orally dosed with 1,2, or 4 mg/kg of the test material, or with the vehicle, DMSO. Mating of control & treated males for 8 successive weeks occurred. Evidence was not found to substantiate dominant lethal mutations at 15 days following matings as would be represented by depressed fertility, reduced fetal implants or increased early fetal deaths. Study by Tunstall Laboratory, TLGR 0027.73, Experimental No. 321, dtd September 1973. Tox Br. considers this study as core minimum data.

Toxicity: Effect of Azodrin on Micro-organisms in the Host-Mediated Assay and in vitro Tests using Sac. cerevisiae, Ser. marcescens, and Sal. typhimurium.

Results: Azodrin, at (5-50 mg/ml) high concentrations, can produce lethal and mutagenic effects on Saccharomyces cerevisiae. However, Azodrin had no mutagenic effects on other bacterial systems tested. Tox. Br. agrees with study discussion in that Azodrin may be a weak mutagen detectable only at high concentrations in an extremely sensitive system. A core minimum study. Study by Tunstall Laboratory, TLGR .0030.74, dtd. July 19, 1974.

Further Reference: Dean, B.J. Arch. Toxicol. 30:67-74(1972)

H.W. Spencer
Toxicology Branch

9/22/77

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