

US EPA ARCHIVE DOCUMENT

BB-1357
TXR-0765



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

003765

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Botran 75W. Environmental Protection Agency
Registration No. 1023-36 Caswell No. 311

FROM: Alex Arce
Toxicology Branch (TS-769) *sup 4-5-84*

TO: Henry Jacoby
Registration Division PM 21 (TS-767)

THRU: William M. Butler, Section Head
Section III Toxicology Branch *William M Butler 4/20/84*
Hazard Evaluation Division (TS-769) *it/inf 4/20/84*

THRU: William L. Burnam, Chief
Toxicology Branch
Hazard Evaluation Division (TS-769)

THRU: Robert Coberly
Toxicology Branch (TS-769)

Request:

The registrat UPJOHN Co. has submitted safety information including a new teratology study. The registrant also refers to book III parts 1-111 section 12.07, a chronic feeding study-dogs. The registrant suggest that the NOEL will be closer to the 3000 ppm dose level than the 100 ppm approved by the Toxicology Branch and used for calculations of the ADI and TMRC.

RECOMENDATION

Toxicology Branch can not entertain any more suggestions regarding such matter. If the registrant desires, a new study can be performed using other dose levels than the 100 and 3000 ppm previously used. Thus, the NOEL is 100 ppm and will not be changed.

1/84

Toxicology Branch
Data Review

Study Type: Teratology." 4-2069 a Segment II Teratology in the rat."

Accession Number: 271567

MRID Number: Not Assigned

Sponsor: The UPJOHN Co.

Contracting Lab: The UPJOHN Co. Pharmaceutical Reserch

Date: July 26, 1982

Test Material: Botran Technical (U-2069)

PROTOCOL: GLP (CFR Title 21, Chapter/Part 58, 312, 314).

Abstract of the materials and methods employed in the conduct of the study. The product was administered to pregnant rats, by gastric intubation during the 6-15 day of gestation and at the 20 day cesarean section were performed. Dose levels 0.100-200- 400 mg/kg / day

Test substance and purity:

2, 6-dichloro-4-nitroaniline- 88.1 ± 5.3 %

Specie of animals: Rat Age: 8-10 Weeks Sex: females

Weight: 202-296 g

Number of subject per test level: 24/group

Route of administration: Oral intubation

Duration: 20 days

Observations

Behavior and appearance: One time a day

Necropsy: In all animals

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Tissue collected: uterus

Tissue examined: uterus for weight, live and dead fetuses and distribution, resorptions.

Other testing or observations:

Body weights: at the 0 day, at each dosing interval and at sacrifice day. Individual fetus weight. Malformations visceral and skeletal.

RESULTS:

Mortality: None

Clinical Observations: CNS depression observed at 200, 400 mg/kg symptoms are not mentioned

Appearance: Normal Behavior: Normal

Necropsy

Gross Pathology: No unusual tissues was found.

Maternal weight gain: Treated mothers weighted significantly less then the control. (P < 0.01)

Number of litters: Statistically significant difference at the high dose level, 50% less than controls

	00	100 mg/kg	200 mg/kg	400 mg/kg
	20	19	14	10

Number of implants: Reduced in relation to dose level. significant

	00	100 mg/kg	200 mg/kg	400 mg/kg
	254	234	176	129

Visceral or skeletal abnormalities (%)

Dose level:mg/kg	00	100	200	400	
Visceral Variations	3.3	6.4	2.4	16.7	(Fetus)
Skeletal Variations	70	63.2	71.4	100.00	(litter)

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Conclusion

Terata NOEL = 400 mg/kg

Maternal toxicity NOEL = 100 mg/kg

Embryo Toxicity NOEL = 100 mg/kg

Core Classification: Core Guideline