



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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 10182-97
PACLOBUTRAZOL TECHNICAL

FROM: William S. Woodrow WSW 1-30-89
Precautionary Review Section
Registration Support Branch
Registration Division (TS-767C) E 1/30/89
JB 1/30/89

TO: Robert J. Taylor (PM 25-)
Fungicide-Herbicide Branch
Registration Division (TS-767C)

APPLICANT: ICI Americas Inc.
Agricultural Chemicals Division
Wilmington, DE 19897

FORMULATION FROM LABEL:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
<u>Paclobutrazol</u>	
<u>(±)-(R*, R*)-β-[(4-chlorophenyl)methyl]</u>	
<u>-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-</u>	
<u>1-ethanol</u>	<u>90.0</u>
<u>Inert Ingredient(s):</u>	<u>10.0</u>
Total	100.0%

BACKGROUND:

Product Manager No. 25 requested review of an acute inhalation tox. study, and revised precautionary label statements. The inhalation study was submitted by ICI Americas, Inc., and conducted by ICI Central Tox Labs., Alderly Park, Macclesfield, Cheshire, UK. MRID No. was 407342-01.

RECOMMENDATION:

Reg. Support Branch finds the inhalation tox. study reviewed acceptable and does support registration of 10182-97 (Paclobutrazol Technical) herbicide.

LABELING:

Change the sentence "HARMFUL IF INHALED, ABSORBED THROUGH SKIN OR SWALLOWED" to read "HARMFUL IF INHALED OR SWALLOWED, MAY BE FATAL IF ABSORBED THROUGH SKIN."

The U.S. EPA proscribes a 2000 mg/kg Acute Dermal "limit" test in lieu of a minimum 3 dosage level acute dermal test. A toxicity category of II for acute dermal toxicity must be designated, since testing was performed using 1000mg/kg, e.g., 2200 thru 2000 mg/kg receives a Toxicity Category ^{of II}; consequently the statement "may be fatal if absorbed through skin"

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: (25)

MRID No.: 407342-01

Testing Laboratory: ICI Central Tox. Lab.

Author(s): P.M. Hext

Species: Rat (Wistar) 7 weeks old

Sex: M & F

Weight: M 235-261g, F 170-197g

Source: Alderly Park, Cheshire, UK

Test Material: Paracetamol 91.4% powder

Quality Assurance (40 CFR §160.12): satisfactory

Reviewer: W. Woodhouse
M. Waller

Report Date: 1-27-89

Report No. CTL/P/2072

Summary:

1. LC₅₀ (mg/kg): Males = 4.79 mg/L (95% C.L. 1.84 - 11.94); Females = 3.13 mg/L (95% C.L. 0.335 - 12.5 mg/L); Combined = 3.96 mg/L
2. The estimated LC₅₀ is 3.96 mg/L
3. Mean Concentration:
4. Tox. Category: III. Classification: Core minimum data

Procedure (~~Deviations From §81-2~~): Aerosol samples collected close to animal breathing zone, particulate concentrations measured gravimetrically, using differences in collecting filter weights. 91.4% respirable particles. 4 Brown animal exposure.

Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
0.54	0/5	0/5	0/10
1.84	0/5	1/5	1/10
3.70	1/5	4/5	5/10
5.19	3/5	3/5	6/10

Symptomology & Gross Necropsy Findings:

Principal findings included reduced response to sound, increased breathing depth, reduced breathing rate. Gasping in M & F at higher dose levels. Body weight gain in survivors similar to controls. Minor changes in lungs & liver of animals that died, or were killed in extremis: dark red areas.

→ behavior consistent with CNS depression

Median lethal concentration:

Tester states that his method of stating 95% C.L. is:
 Approximate lower and upper 95% C.L. are given by highest dose with no mortalities, and the lowest dose with 100% mortality, respectively.

Then, a lower 95% C.L. of 0.54 mg/L meets these requirements, however, at the highest dose tested, 100% mortality was not achieved (see table). So
 a Case Inhalation designation cannot be made.

Quoted from the tester's report:

Group	Particulate Concentration (mg/l)	Median Size (D ₅₀) (μm)	Geometric Standard Deviation	% by weight	
				'Respirable' ≤ 2.5 μm AED	'Inhalable' ≤ 15 μm AED
2	5.19	4.53	2.27	23.05	91.87
3	3.70	3.40	2.12	33.63	96.37
4	1.84	3.25	2.18	36.34	96.29
6	0.54	2.89	2.10	42.08	97.54

-AED = Aerodynamic Equivalent Diameter.

Ungulate

The table data above demonstrates clearly that a substantial amount of generated particulate aerosol was composed of 5 μm or less particles, and was therefore respirable immediately following exposure.

Distress and toxic signs: reduced breathing rate, increased depth, reduced response to sound, hunched posture, piloerection, stains around face, nose, and wet fur.

Tox Chem No. 628C

File Last Updated _____

Current Date 1-30-89

(Paclobutrazol)

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD50, LC50, PIS, NOEL, LEL	TOX. Cat.	CONF Grade/Doc. No.
Acute inhalation tox. study, Ret. ICI Central Tox. Lab. CTL/P/2072 - Jan. 26, 1988	Paclobutrazol Technical - 91.94% pure	407342-01	LC50 male 4.79 mg/L (95% C.L. - 1.84 - no upper limit) mg/L LC50 female 3.13 mg/L (95% C.L. - 0.835 - 12.5 mg/L) LC50 (M-F combined) = 3.96 mg/L	111	None