

Paclobutrazol ; CASRN 76738-62-0

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

STATUS OF DATA FOR Paclobutrazol

File First On-Line 03/31/1987

| Category (section) | Assessment Available? | Last Revised |
|---|-----------------------|--------------|
| Oral RfD (I.A.) | yes | 03/31/1987 |
| Inhalation RfC (I.B.) | not evaluated | |
| Carcinogenicity Assessment (II.) | not evaluated | |

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Paclobutrazol

CASRN — 76738-62-0

Last Revised — 03/31/1987

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of

information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.A.1. Oral RfD Summary

| Critical Effect | Experimental Doses* | UF | MF | RfD |
|---|--|------|----|---------------------|
| Elevated liver weights, serum cholesterol, hepatic aminopyrine N-demethylase activity, and alanine transaminase levels | NOEL: 250 ppm (diet) (12.5 mg/kg/day) | 1000 | 1 | 1.3E-2 mg/kg/day |
| | LEL: 1250 ppm (diet) (62.5 mg/kg/day) | | | |
| 90-Day Rat Feeding Study | | | | |
| ICI Americas, Inc., 1983a | | | | |

*Dose Conversion Factors & Assumptions: 1 ppm = 0.05 mg/kg/day (assumed rat food consumption)

I.A.2. Principal and Supporting Studies (Oral RfD)

ICI Americas, Inc. 1983a. MRID No. 00132689; HED Doc. No. 003813. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Four groups of Wistar rats (20/sex/dose level) were fed diets containing 0, 50, 250 or 1250 ppm of paclobutrazol for 90 days. At 1250 ppm liver weights were elevated in females along with serum cholesterol, hepatic aminopyrine N- demethylase activity, and alanine transaminase levels. The lowest dose tested was 50 ppm. No effects were seen in male rats.

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — Based on a subchronic exposure study, an uncertainty factor of 1000 was used to account for inter- and intraspecies differences and for the insufficient duration of the study to fully assess chronic effects.

MF — None

I.A.4. Additional Studies/Comments (Oral RfD)

None

Data Considered for Establishing the RfD:

- 1) 90-Day Feeding - Rat: Principal study - see previous description; core grade minimum
- 2) 1-Year Feeding - Dog: NOEL=15 mg/kg/day; LEL=75 mg/kg/day (increased liver weight, increased serum alkaline phosphatase and triglyceride levels, increased hepatic aminopyrine N-demethylase activity, and enlarged hepatocytes); core grade minimum (ICI Americas, Inc., 1984a)
- 3) 6-Week Oral Dosing - Dog: NOEL=15 mg/kg/day (LDT); LEL=75 mg/kg/day (at doses of 75 and 225 mg/kg dogs had increased liver weights and serum alkaline phosphatase levels, only one male and one female dog were tested at each dose); core grade supplementary (ICI Americas, Inc., 1983b)
- 4) Teratology - Rat: Maternal NOEL=40 mg/kg/day (LDT); Maternal LEL=100 mg/kg/day (slight decrease in body weight gain and food utilization efficiency; 250 mg/kg/day caused mortality (5/24), liver enlargement, and pallor of the liver); Fetotoxic NOEL not established; Fetotoxic LEL=40 mg/kg/day (LDT); (increased incidence of delayed ossification in fetuses; the 250 mg/kg/day dose induced cleft palate in three fetuses from two litters.); core grade supplementary (ICI Americas, Inc., 1983c)
- 5) Teratology - Rat: Maternal NOEL=100 mg/kg/day (HDT); Fetotoxic NOEL=10 mg/kg/day; Fetotoxic LEL=40 mg/kg/day (hydronephrosis, hydroureter, delayed ossification, minor skeletal defects); core grade minimum (ICI Americas, Inc., 1984b)
- 6) Teratology - Rabbit: Maternal NOEL=25 mg/kg/day; Maternal LEL=75 mg/kg/day (decreased body weight gain); Fetotoxic NOEL=125 mg/kg/day (HDT) (low fertility with only the mid- and low-dose groups having the minimum number of animals required); core grade supplementary

(ICI Americas, Inc. 1983c)

Data Gap(s): Chronic Rat Feeding Study; Rat Reproduction Study; Rabbit Teratology Study

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — Medium

RfD — Medium

The critical study is of good quality and is given a medium confidence rating. Additional studies are supportive, but the database on chronic toxicity is incomplete; therefore, confidence in the database can be considered medium to low. Confidence in the RfD can also be considered medium to low.

I.A.6. EPA Documentation and Review of the Oral RfD

Pesticide Registration Files

Agency Work Group Review — 09/02/1986

Verification Date — 09/02/1986

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for Paclobutrazol conducted in November 2001 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Paclobutrazol
CASRN — 76738-62-0

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Paclobutrazol
CASRN — 76738-62-0

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Paclobutrazol
CASRN — 76738-62-0

VI.A. Oral RfD References

ICI Americas, Inc. 1983a. MRID No. 00132689; HED Doc. No. 003813. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

ICI Americas, Inc. 1983b. MRID No. 00132690; HED Doc. No. 003813. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

ICI Americas, Inc. 1983c. MRID No. 00132693; HED Doc. No. 003813. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

ICI Americas, Inc. 1983d. MRID No. 00132692; HED Doc. No. 003813. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

ICI Americas, Inc. 1984a. MRID No. 00132691, 00143166; HED Doc. No. 003813, 004352. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

ICI Americas, Inc. 1984b. MRID No. 00143158; HED Doc. No. 004352. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Paclobutrazol
CASRN — 76738-62-0

| Date | Section | Description |
|------------|---------|--|
| 12/03/2002 | I.A.6. | Screening-Level Literature Review Findings message has been added. |

VIII. Synonyms

Substance Name — Paclobutrazol
CASRN — 76738-62-0
Last Revised — 03/31/1987

- 66346-04-1
- 76738-62-0
- 77108-06-6
- Cultar
- ICI-PP 333
- Paclobutrazol
- PP 333
- 1H-1,2,4-Triazole-1-ethanol-.beta.-((4-chlorophenyl)methyl)-.alpha.-(1,1-dimethylethyl)-