

Ethephon; CASRN 16672-87-0

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 Ethephon

File First On-Line 08/22/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	08/22/1988
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 — Ethephon

CASRN — 16672-87-0

Primary Synonym — 2-Chloroethylphosphonic acid

Last Revised — 08/22/1988

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
Plasma ChE inhibition	NOEL: None	100	1	5E-3 mg/kg/day
16-Day Human Study	LEL: 0.5 mg/kg/day			
Union Carbide, 1977a				

*Conversion Factors -- none

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

Union Carbide Agricultural Products Company, Inc. 1977a. MRID 00066931. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

In this human study, 10 humans/sex were orally dosed with ethephon at 0.5 mg/kg/day for 16 days, followed by a recovery period of 29 days. Dose related effects occurred in plasma cholinesterase activity, but not in red blood cell cholinesterase activity. The effect was reversible within 15 days. A statistically significant decrease in plasma cholinesterase activity also occurred in the control group (approximately 71 to 83% of initial control values) at the same periods of analysis reported for the test subjects, but the test subjects demonstrated a larger decrease (approximately 56 to 49% of paired initial values) than the control group. When the control group and test groups were compared by the Wilcoxon Rank Sum Test, the results were statistically significant (p<0.05). In addition, no dose related effects occurred in hematology, blood chemistry, or urine analyses.

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

UF — An uncertainty factor of 10 was used to account for the intraspecies differences. An additional UF of 10 was used to account for the lack of an established NOEL for plasma cholinesterase inhibition.

MF — None

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

Data Considered for Establishing the RfD

- 1) 16-Day Study - human: Principal study - see previous description; no core grade
- 2) 28-Day Study - human: NOEL=none; LEL=1.8 mg/kg/day (average of 2.2 mg/kg/day effect level in males and 1.5 mg/kg/day for females; dose related effects on diarrhea, urgency of bowel movements, urinary urgency, stomach cramps, and either loss or increase in appetite in the absence of plasma or RBC cholinesterase inhibition); no core grade (Union Carbide, 1972)
- 3) 104-Week Feeding (oncogenic) - rat: Systemic NOEL=300 ppm (15 mg/kg/day); Systemic LEL=3000 ppm (150 mg/kg/day) (HDT; plasma and RBC ChE inhibition); core grade supplementary (Union Carbide, 1978)
- 4) 2-Year Feeding - dog: NOEL=none; LEL=30 ppm (0.75 mg/kg/day; LDT) (plasma ChE inhibition); RBC ChE was inhibited at the MDT (300 ppm) and HDT (1000-3000 ppm, depending on day of administration; Smooth muscle hypertrophy was noted at the MDT and HDT; Body weight and efficiency of food consumption were reduced at HDT; core grade supplementary (Union Carbide, 1977b)
- 5) Teratology - rat: Embryo/fetal and Maternal NOEL=600 mg/kg/day; Embryo/fetal and Maternal LEL=1800 mg/kg/day (maternal death (56%) and equivocal teratogenicity); core grade minimum (Union Carbide, 1980)
- 6) Teratology - rabbit: Embryo/fetal NOEL=50 mg/kg/day; Embryo/fetal LEL=100 mg/kg/day (resorption); Maternal NOEL=100 mg/kg/day, Maternal LEL=250 mg/kg/day (decreased food consumption, and increased gut histopathology and mortality); core grade minimum (Union Carbide, 1981b)

Other Data Reviewed:

1) 78-Week Feeding/(oncogenic) - mouse: Systemic NOEL=30 ppm (4.5 mg/kg/day); Systemic LEL=300 ppm (45 mg/kg/day) (plasma ChE inhibition in males and females); Systemic NOEL=none; LEL=30 ppm (4.5 mg/kg/day for RBC ChE inhibition in females); core grade supplementary (Union Carbide, 1985)

Data Gap(s): Chronic Rat Feeding Study, Chronic Dog Feeding Study, Rat Reproduction Study

I.A.5. Confidence in the Oral RfD

Study — Low

Database — Medium

RfD — Low

The critical study is of low quality and is given a low confidence rating. The database is given a medium to low confidence rating due to the lack of adequate chronic studies. Low confidence in the RfD follows.

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

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — Pesticide Registration Standard, March 1988; Pesticide Registration Files

Agency Work Group Review — 03/23/1988

Verification Date — 03/23/1988

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 Ethephon conducted in September 2002 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to 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 — Ethephon

CASRN — 16672-87-0

Primary Synonym — 2-Chloroethylphosphonic acid

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Ethephon

CASRN — 16672-87-0

Primary Synonym — 2-Chloroethylphosphonic acid

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 — Ethephon

CASRN — 16672-87-0

Primary Synonym — 2-Chloroethylphosphonic acid

VI.A. Oral RfD References

Union Carbide Agricultural Products Company. 1972. MRID No. 00036510. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Agricultural Products Company. 1977a. MRID No. 00066931. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Agricultural Products Company. 1977b. MRID No. 00060359, 00147357.
Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Agricultural Products Company. 1978. MRID No. 00060358, 00144558.
Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Agricultural Products Company. 1980. MRID No. 00063745. Available from
EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Agricultural Products Company. 1981. MRID No. 00085755. Available from
EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Agricultural Products Company. 1985. MRID No. 00081634, 00165591.
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 — Ethephon

CASRN — 16672-87-0

Primary Synonym — 2-Chloroethylphosphonic acid

Date	Section	Description
08/22/1988	I.A.	Oral RfD summary on-line
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Ethephon

CASRN — 16672-87-0

Primary Synonym — 2-Chloroethylphosphonic acid

Last Revised — 08/22/1988

- 16672-87-0
- Amchem 68-250
- bromoflor
- camposan
- CEP
- 2-CEPA
- CEPHA
- CEPHA 10LS
- cerone
- 2-chloroethyl-phosphonsaeure
- chlorethephon
- 2-chloroethanephosphonic acid
- 2-Chloroethylphosphonic acid
- ethefon
- ethel
- Ethephon
- ethepon
- etheverse
- ethrel
- flordimex
- florel
- G 996
- kamposan
- phosphonic acid, (2-chloroethyl)-
- roll-fruct
- tomathrel