Tetraethyldithiopyrophosphate; CASRN 3689-24-5

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 Tetraethyldithiopyrophosphate

File First On-Line 09/07/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/07/1988
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 — Tetraethyldithiopyrophosphate
CASRN — 3689-24-5
Last Revised — 09/07/1988

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
Depressed RBC and plasma cholinesterase activity **Rat Subchronic Oral Study** **Kimmerle and Klimmer, 1974**	NOEL: 10 ppm diet (converted to 0.5 mg/kg/day) LOAEL: 20 ppm diet (1.0 mg/kg/day)	1000	1	5E-4 mg/kg/day

*Conversion Factors: Assumed rat food consumption = 5% body weight/day

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

Kimmerle, G. and O.R. Klimmer. 1974. Acute and subchronic toxicity of Sulfotep. Arch. Toxicol. 33(1): 1-16.

Groups of 20 male and 20 female SPF Wistar rats were fed 0, 5, 10, 20 or 50 ppm tetraethyldithiopyrophosphate (TEDP) in the diet for 3 months. The parameters examined were body weight, food consumption, hematology, urinalysis, and plasma and RBC cholinesterase activity. At the end of the experiment, the animals were sacrificed and necropsied; internal organs were examined macroscopically and histologically. The only parameter that differed from controls was cholinesterase activity. Plasma and erythrocyte cholinesterase activity of rats fed at 20 and 50 ppm TEDP were depressed in a dose-related manner. Depression of cholinesterase activity was more pronounced in erythrocytes. Therefore, 20 ppm is the LOAEL and 10 ppm, the NOEL.

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

UF — The UF of 1000 includes factors of 10 for interspecies extrapolation, 10 to extrapolate from a subchronic study and 10 to provide protection for sensitive individuals.

MF — None

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

Kimmerle and Klimmer (1974) determined the oral LD50 of TEDP in male and female NMRI mice, Wistar rats and white Leghorn hens, and male cats, New Zealand rabbits and beagle dogs. The LD50 ranged from 3-30 mg/kg bw with the most susceptible animals being cats and dogs. The symptoms involved depression of the cholinesterase activity of the peripheral and central nervous system. Hens exposed to oral doses up to 50 mg/kg body weight did not develop any neurotoxic effects. Lehman (1952a,b) fed rats TEDP in the diet at 60 or 180 ppm for 52 weeks. The only endpoints examined were histopathology and mortality. An increase in mortality was observed at 180 ppm (9 mg/kg/day) but not 60 ppm (3 mg/kg/day). No histopathological changes were reported. Pertinent data regarding the possible teratogenicity of TEDP were not located in the available literature.

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

The subchronic oral study in rats by Kimmerle and Klimmer (1974) uses a number of dosing levels, an adequate number of rats and examines a number of endpoints, with cholinesterase inhibition as the critical endpoint. There are no supporting studies so the study is ranked medium rather than high. TEDP has not been tested for chronic toxicity or teratogenicity so confidence in the database is low. Because of the incomplete database, confidence in the RfD is low.

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 — None

Agency Work Group Review — 02/24/1988

Verification Date — 02/24/1988

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 tetraethyldithiopyrophosphate conducted in August 2003 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 — Tetraethyldithiopyrophosphate
CASRN — 3689-24-5

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Tetraethyldithiopyrophosphate
CASRN — 3689-24-5

Not available at this time.

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Tetraethyldithiopyrophosphate
CASRN — 3689-24-5

VI.A. Oral RfD References

Kimmerle, G. and O.R. Klimmer. 1974. Acute and subchronic toxicity of sulfotep. Arch. Toxicol. 33(1): 1-16.

Lehman, A.J. 1952a. Chemicals in foods: A report to the Association of Food and Drug Officials on current developments. Part II. Pesticides. Section III. Subacute and chronic toxicity. Quart. Bull. Assoc. Food Drug Officials. U.S. 16: 47-53.

Lehman, A.J. 1952b. Chemicals in foods: A report to the Association of Food and Drug Officials on current developments. Part II. Pesticides. Section V. Pathology. Quart. Bull. Assoc. Food Drug Officials. U.S. 16: 126-132.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Tetraethyldithiopyrophosphate
CASRN — 3689-24-5

Date	Section	Description
09/07/1988	I.A.	Oral RfD summary on-line
10/28/2003	I.A.6	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Tetraethyldithiopyrophosphate
CASRN — 3689-24-5
Last Revised — 09/07/1988

- 3689-24-5
- TEDP
- Tetraethyldithiopyrophosphate