Ethyl p-nitrophenyl phenylphosphorothioate (EPN); CASRN 2104-64-5

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 EPN

File First On-Line 09/30/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/30/1987
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 — Ethyl p-nitrophenyl phenylphosphorothioate (EPN)
CASRN — 2104-64-5
Last Revised — 09/30/1987

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
Neurotoxicity **90-Day Hen Delayed Neurotoxicity Bioassay** **Morabani, Nissan, duPont and Velsicol, 1982**	NOEL: 0.01 mg/kg/day LEL: 0.1 mg/kg/day	1000	1	1E-5 mg/kg/day

*Conversion Factors and Assumptions — none

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

Morabani American Corp., Nissan Chemical Ind. Inc., duPont de Nemours & Co., and Velsicol Chemical Co. 1982. MRID No. 00158314. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Adult hens (20/group) were dosed orally at 0.01, 0.1, 0.5, 1.0, 2.5, or 5.0 mg/kg/day for 90 days. Animals were observed daily for signs of delayed neurotoxicity; histopathology was performed on nerves after study termination.

1) Signs of O-P type delayed neurotoxicity (ataxia) were seen at doses of 2.5 and 5.0 mg/kg/day. NOEL = 1.0 mg/kg/day

2) Histopathologically observed damage to nervous system was seen at doses of 0.1 and up. NOEL = 0.01 mg/kg/day

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

UF — An uncertainty factor of 1000 was used to account for inter- and intraspecies differences and for the fact that the NOEL was based on a subchronic exposure study.

MF — None

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

Data Considered for Establishing the RfD:

1) 90-Day Delayed Neurotoxicity - hen: Principal study - see previous description; core grade guideline

2) 90-Day Feeding - rat: ChE NOEL=5 ppm (0.25 mg/kg/day); ChE LEL=25 ppm (1.25 mg/kg/day) RBC ChE inhibition; The effects noted at 125 ppm included decreased plasma and brain ChE activity, decreased female growth and decreased RBC, hemoglobin, and hematocrit in both sexes; core grade guideline (Morabani American Corp.; Nissan Chemical Ind. Inc.; du Pont; and Velsicol Chemical Co., 1986a)

3) 90-Day Feeding - dog: ChE NOEL=0.3 mg/kg/day; ChE LEL=1.0 mg/kg/day (Plasma ChE inhibition); Systemic NOEL=1.0 mg/kg/day; Systemic LEL=3.0 mg/kg/day (decreased RBC and brain ChE activity, decreased RBC, hemoglobin, and hematocrit in both sexes and pancreatic aciner cell atrophy in two males); core grade guideline (Morabani American Corp.; Nissan Chemical Ind. Inc.; du Pont; and Velsicol Chemical Co., 1986b)

4) Recovery Study - hen: Following a single dose of 175 mg/kg all hens showed severe damage in the spinal cord but only 1/3 of the hens showed signs of neurotoxicity (ataxia). Recovery from cordal damage was minimal over a period of 90-days postdose. (Morabani American Corp.; Nissan Chemical Ind. Inc.; du Pont; and Velsicol Chemical Co., 1986c)

Data Gap(s): Chronic Dog Feeding Study; Rat Reproduction Study; Teratology (Rat & Rabbit) - These studies have been received and are not yet reviewed. They appear to be acceptable and negative for developmental toxicity.

I.A.5. Confidence in the Oral RfD

Study — High
Database — Medium
RfD — Medium

The principal study is of good quality and is given a high confidence rating. The subchronic data are supportive. However, since there are no data on chronic exposure toxicity, the database is given a medium confidence rating. Medium confidence in the RfD follows.

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

Pesticide Registration Files

Agency Work Group Review — 12/09/1986, 03/18/1987

Verification Date — 12/09/1986

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 Ethyl p-nitrophenyl phenylphosphorothioate (EPN) 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 — Ethyl p-nitrophenyl phenylphosphorothioate (EPN)
CASRN — 2104-64-5

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Ethyl p-nitrophenyl phenylphosphorothioate (EPN)
CASRN — 2104-64-5

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 — Ethyl p-nitrophenyl phenylphosphorothioate (EPN)
CASRN — 2104-64-5

VI.A. Oral RfD References

Morabani American Corporation, Nissan Chemical Ind., Inc., E.I. du Pont de Nemours & Company, and Velsicol Chemical Company. 1982. MRID No. 00158314. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Morabani American Corporation, Nissan Chemical Ind., Inc., E.I. du Pont de Nemours & Company, and Velsicol Chemical Company. 1986a. MRID No. 00157874. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Morabani American Corporation, Nissan Chemical Ind., Inc., E.I. du Pont de Nemours & Company, and Velsicol Chemical Company. 1986b. MRID No. 00158890. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Morabani American Corporation, Nissan Chemical Ind., Inc., E.I. du Pont de Nemours & Company, and Velsicol Chemical Company. 1986c. MRID No. 00159372. 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 — Ethyl p-nitrophenyl phenylphosphorothioate (EPN)
CASRN — 2104-64-5

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

VIII. Synonyms

Substance Name — Ethyl p-nitrophenyl phenylphosphorothioate (EPN)
CASRN — 2104-64-5
Last Revised — 09/30/1987

- 2104-64-5
- BENZENEPHOSPHONIC ACID, THIONO-, ETHYL-p-NITROPHENYL ESTER
- ENT 17,798
- EPN
- EPN 300
- ETHOXY-4-NITROPHENOXYPHENYLPHOSPHINE SULFIDE
- ETHYL p-NITROPHENYL BENZENETHIONOPHOSPHONATE
- ETHYL p-NITROPHENYL BENZENETHIOPHOSPHATE
- ETHYL p-NITROPHENYL BENZENETHIOPHOSPHONATE
- ETHYL p-NITROPHENYL PHENYLPHOSPHONOTHIOATE
- Ethyl p-nitrophenyl phenylphosphorothioate
- ETHYL p-NITROPHENYL THIONOBENZENEPHOSPHATE
- ETHYL p-NITROPHENYL THIONOBENZENEPHOSPHONATE
- O-AETHYL-O-(4-NITRO-PHENYL)-PHENYL-MONOTHIOPHOSPHONAT
- O-ETHYL-O-((4-NITRO-FENYL)-FENYL)-MONOTHIOFOSFONAAT
- O-ETHYL O-(4-NITROPHENYL)BENZENETHIONOPHOSPHONATE
- O-ETHYL O-(4-NITROPHENYL) PHENYLPHOSPHONOTHIOATE
- O-ETHYL O-p-NITROPHENYL PHENYLPHOSPHONOTHIOLATE
- O-ETHYL O-p-NITROPHENYL PHENYLPHOSPHOROTHIOATE

- O-ETHYL PHENYL p-NITROPHENYL THIOPHOSPHONATE
- O-ETIL-O-((4-NITRO-FENIL)-FENIL)-MONOTIOFOSFONATO
- O-(4-NITROPHENYL) O-ETHYL PHENYL THIOPHOSPHONATE
- PHENYLPHOSPHONOTHIOATE, O-ETHYL-O-p-NITROPHENYL-
- PHENYLPHOSPHONOTHIOIC ACID O-ETHYL O-p-NITROPHENYL ESTER
- PHENYLTHIOPHOSPHONATE DE O-ETHYLE ET O-4-NITROPHENYLE
- PIN
- SANTOX