Diethyl-p-nitrophenylphosphate; CASRN 311-45-5

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 Diethyl-p-nitrophenylphosphate

File First On-Line 10/01/1992

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	10/01/1992*

* A comprehensive review of toxicological studies was completed (August 7, 2006) - please see section II.D.2. for more information.

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Diethyl-p-nitrophenylphosphate
CASRN — 311-45-5
Primary Synonym — Paraoxon

Not available at this time.

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

Substance Name — Diethyl-p-nitrophenylphosphate
CASRN — 311-45-5
Primary Synonym — Paraoxon

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Diethyl-p-nitrophenylphosphate
CASRN — 311-45-5
Primary Synonym — Paraoxon
Last Revised — 10/01/1992

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-of-Evidence Characterization

Classification — D; not classifiable as to human carcinogenicity

Basis — No human data and no animal data available.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

None.

II.A.4. Supporting Data for Carcinogenicity

In an abstract, Quinto et al. (1981) reported that paraoxon exhibited a weak positive response in a reverse mutation asssay in Salmonella strains TA98 and TA1538 in the absence of metabolic activation. Paraoxon (10 mM) was positive in a forward mutation assay in Saccharomyces cerevisiae; when rat hepatic homogenate (S9) was added with the paraoxon, forward mutations were no longer induced (Gilot-Delhalle et a1., 1983). Nishio and Uyeki (1981) found positive results in a sister chromatid exchange assay in Chinese hamster ovary cells, but Singh et al. (1984) found negative results from tests of sister chromatid exchange, cell cycle kinetics, and chromosome breakage in human lymphocytes. After an intraperitoneal injection of 0.3 mg/kg paraoxon, no chromosome aberrations in bone marrow cells or on spermatogonia occurred in male mice (Degraeve and Moutschen, 1984). Paraoxon has been extensively used as a deacetylase inhibitor in the study of the mechanism of mutagenesis. Heflich et al. (1988) showed that 10 uM paraoxon completely inhibited the mutagenicity of 450 uM 2-acetylaminofluorene in CHO cells.

Paraoxon is the major metabolite of parathion, when administered to rats and dogs (Eigenberg et al., 1983). Parathion (the S analog of paraoxon) has been classified by the U.S. EPA (1987) as a Group C, possible human carcinogen.

II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

None.

II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

None.

II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1989

The 1989 Health and Environmental Effects Document for Diethyl-p- nitrophenylphosphate (Paraoxon) has received full review from the Office of Health and Environmental Assessment and from the Office of Pesticides and Toxic Substances.

II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review — 09/05/1991

Verification Date — 09/05/1991

A comprehensive review of toxicological studies published through August 2006 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing carcinogenicity assessment for Diethyl-p-nitrophenylphosphate and a change in the assessment is not warranted at this time. For more information, IRIS users may contact the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

II.D.3. EPA Contacts (Carcinogenicity Assessment)

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).

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

VI. Bibliography

Substance Name — Diethyl-p-nitrophenylphosphate
CASRN — 311-45-5
Primary Synonym — Paraoxon

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Degraeve, N. and J. Moutschen. 1984. Absence of genetic and cytogenetic effects in mice treated by the organophosphorus insecticide parathion, its methyl analogue, and paraoxon. Toxicology. 32(2): 177-183.

Eigenberg, D.A., T.L. Pazdernik and J. Doull. 1983. Hemoperfusion and pharmacokinetic studies with parathion and paraoxon in the rat and dog. Drug Metabol. Dispos. 11(4): 366-370.

Gilot-Delhalle, J., A. Colizzi, J. Moutschen and M. Moutschen-Dahmen. 1983. Mutagenicity of some organophosphorus compounds at the ade6 locus of Schizosaccharomyces pombe. Mutat. Res. 117(1-2): 139-148.

Heflich, R.H., Z. Djuric, Z. Zhou, N.F. Fullerton, D.A. Casciano and F.A. Beland. 1988. Metabolism of 2-acetylaminofluorene in the Chinese hamster ovary cell mutation assay. Environ. Mol. Mutagen. 11: 167-181.

Nishio, A. and E.M. Uyeki. 1981. Induction of sister chromatid exchange in Chinese hamster ovary cells by organophosphate insecticides and their oxygen analogs. J. Toxicol. Environ. Health. 8: 939-946.

Quinto, I., G. Martire and G. Vricella et al. 1981. Screening of 24 pesticides by Salmonella/microsome assay: Mutagenicity of benzolin, metoxuron and paraoxon. Mutat. Res. 85(4): 265.

Singh, S., B. Lehmann-Grube and H.W. Goedde. 1984. Cytogenetic effects of paraoxon and methyl-parathion on cultured lymphocytes: Sister-chromatid exchange, clastogenic activity and cell cycle delay. Int. Arch. Occ. Environ. Health. 54(3): 195-200.

U.S. EPA. 1987. Health Effects Assessment for Parathion. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC.

U.S. EPA. 1989. Health and Environmental Effects Document for Diethyl-p-nitrophenylphosphate (Paraoxon). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

VII. Revision History

Substance Name — Diethyl-p-nitrophenylphosphate
CASRN — 311-45-5
Primary Synonym — Paraoxon

Date	Section	Description
10/01/1992	II.	Carcinogenicity assessment on-line
12/03/2002	II.D.2.	Screening-Level Literature Review Findings message has been added.
09/28/2006	II.D.2.	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

VIII. Synonyms

Substance Name — Diethyl-p-nitrophenylphosphate
CASRN — 311-45-5
Primary Synonym — Paraoxon
Last Revised — 10/01/1992

- 311-45-5

- Phosphoric acid, diethyl 4-nitrophenyl ester
- Paraoxon