N-Nitrosodi-N-propylamine; CASRN 621-64-7

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 N-Nitrosodi-N-propylamine

File First On-Line 03/31/1987

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

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — N-Nitrosodi-N-propylamine
CASRN — 621-64-7

Not available at this time.

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

Substance Name — N-Nitrosodi-N-propylamine
CASRN — 621-64-7

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — N-Nitrosodi-N-propylamine
CASRN — 621-64-7
Last Revised — 03/31/1987

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 — B2; probable human carcinogen

Basis — Increased tumor incidence at multiple sites in two rodent species and in monkeys administered the compound by various routes

II.A.2. Human Carcinogenicity Data

Inadequate. Human exposure to nitrosamines results from contact with mixtures containing these compounds (e.g., cutting oils, tobacco products). Because of potential confounding by the other substances in these mixtures, data is of limited use in the evaluation of carcinogenicity of individual nitrosamines.

II.A.3. Animal Carcinogenicity Data

Sufficient. As part of a survey of 65 N-nitroso compounds, Druckrey et al. (1967) administered N-nitrosodi-n-propylamine in drinking water to BD rats of unspecified sex. A total of 48 rats was treated in groups inferred to number 16, 16, 15 and 1 at doses of 4, 8, 15 or 30 mg/kg/day, respectively, for life. Of 48 treated animals, 45 developed liver carcinomas; tumor induction time was dose-related. Tumors of the esophagus and tongue were also observed.

N-nitrosodi-N-propylamine administered to male Sprague-Dawley rats in drinking water at 1.8 mg/day, 5 days/week for 30 weeks resulted in liver carcinomas (9/15), esophageal papillomas (6/15) and carcinomas (8/15) and nasal adenocarcinomas (8/15) (Lijinsky and Taylor, 1978, 1979). F344 rats of both sexes treated in a similar fashion with 0.9 mg/day developed esophageal carcinomas (20/20) and forestomach tumors (12/20) (Lijinsky and Reuber, 1981).

Corn oil gavage of male and female F344 rats (2 times/week for 30 weeks) produced nasal and liver carcinomas, and esophageal tumors; tumors at these sites were not found in controls (Linjinsky and Reuber, 1983).

A high incidence of malignant tumors at distant sites, primarily nasal cavity, liver and lungs, was observed in Sprague-Dawley rats of both genders receiving lifetime weekly s.c. injections of 24.36, 48.72 or 97.44 mg/kg N-nitrosodi-n-propylamine (Reznik et al., 1975). Similar studies in hamsters reported increases in tumors of the nasal cavities, laryngobronchial tract and lungs (Pour et al., 1973, Althoff et al., 1973).

Macaque monkeys given weekly i.p. injections of 40 mg N-nitrosodi-n- propylamine for a total dose of 70 g had a higher incidence of hepatocellular carcinomas (6/6) compared with that of presumed historical controls (7/90) (Adamson and Sieber, 1979, 1983).

II.A.4. Supporting Data for Carcinogenicity

N-nitrosodi-n-propylamine is mutagenic for Salmonella typhimurium (IARC, 1978; Phillipson and Ioannides, 1985), E. coli (McMahon et al., 1979; Probst et al., 1981; Rao et al., 1981) and V79 cells and mouse lymphoma cells (Kuroki et al., 1977; Bartsch et al., 1980; Jones and

Huberman, 1980). Evidence of DNA damage by this compound includes unscheduled DNA synthesis in in vitro exposed rat hepatocytes and HeLa cells (Martin et al., 1978; Probst et al., 1981) DNA breakage in in vivo treated rat liver (Brambilla et al., 1981; Bradley et al., 1982) and chromosomal aberrations in Chinese hamster cells in vitro (Kaneko et al., 1978; Matsuoka et al., 1979; Ishidate et al., 1981).

Both presumed and documented metabolites of N-nitrosodi-n-propylamine have been shown to be carcinogenic for hamsters and rats (IARC, 1978).

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

II.B.1. Summary of Risk Estimates

Oral Slope Factor — 7.0E+0/mg/kg/day

Drinking Water Unit Risk — 2.0E-4/ug/L

Extrapolation Method — One-hit

Drinking Water Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	5E-1 ug/L
E-5 (1 in 100,000)	5E-2 ug/L
E-6 (1 in 1,000,000)	5E-3 ug/L

II.B.2. Dose-Response Data (Carcinogenicity, Oral Exposure)

Tumor Type: hepatocellular carcinomas
Test animals: Rat/BD, sex not specified
Route: drinking water
Reference: Druckrey, 1967; Druckrey et al., 1967

Information in the references cited was used in quantitation of risk using the following relationship:

Ck/(t50)** n = d

where: C = conversion between mmol and mg = 130.2 mg/mmol

k = empirically derived constant estimated to be 1.7E+4 mmol/kg/day

t50 = median time of tumor induction = 728

n = representative value for dialkylnitrosamines as published by Druckrey = 2.3

d = daily dose of test compound, calculated from the above to be 0.57831 mg/kg/day

The slope factor for rats (BA) was calculated from a rearrangement of the one- hit model:

BA = -ln (0.5/day) = 1.20/mg/kg/day

Adjusting this value by the cube root of the assumed human body weight (70 kg) to the assumed rat body weight (0.35 kg) gives the human slope factor 7.02/mg/kg/day.

II.B.3. Additional Comments (Carcinogenicity, Oral Exposure)

A reported value of n=2.2 for N-nitrosodi-n-propylamine was not used since a k for this value was not reported. The k used was estimated from a plot of k vs number of C-atoms for lower di-n-alkylnitrosamines.

The unit risk should not be used if the water concentration exceeds 5E+1 ug/L, since above this concentration the slope factor may differ from that stated.

II.B.4. Discussion of Confidence (Carcinogenicity, Oral Exposure)

Small numbers of rats were treated in groups of unspecified size. Sex of the animals was not reported nor were specific tumor incidences. There was no control group.

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

Not available.

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

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1986

The 1986 Health and Environmental Effects Profile has received Agency Review.

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

Agency Work Group Review — 02/11/1987

Verification Date — 02/11/1987

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for N-Nitrosodi-N-propylamine 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.

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 — N-Nitrosodi-N-propylamine
CASRN — 621-64-7

VI.A. Oral RfD References

None

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

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VII. Revision History

Substance Name — N-Nitrosodi-N-propylamine
CASRN — 621-64-7

Date	Section	Description
12/03/2002	II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — N-Nitrosodi-N-propylamine
CASRN — 621-64-7
Last Revised — 03/31/1987

- 621-64-7
- DIPROPYLAMINE, N-NITROSO-
- DIPROPYLNITROSAMINE
- DI-n-PROPYLNITROSAMINE
- DPN
- DPNA
- NDPA
- N-Nitrosodi-N-propylamine
- N-NITROSODIPROPYLAMINE
- N-NITROSODI-n-PROPYLAMINE
- N-NITROSO-N-PROPYL-1-PROPANAMINE
- PROPANAMINE, N-NITROSO-N-PROPYL-
- PROPYLAMINE, N-NITROSO-N-DI-
- RCRA WASTE NUMBER U111