

## N-Nitrosopyrrolidine; CASRN 930-55-2

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-Nitrosopyrrolidine

**File First On-Line 01/31/1987**

Category (section)	Assessment Available?	Last Revised
<b>Oral RfD (I.A.)</b>	not evaluated	
<b>Inhalation RfC (I.B.)</b>	not evaluated	
<b>Carcinogenicity Assessment (II.)</b>	yes	01/31/1987

## I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — N-Nitrosopyrrolidine  
CASRN — 930-55-2

Not available at this time.

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

Substance Name — N-Nitrosopyrrolidine  
CASRN — 930-55-2

Not available at this time.

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## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — N-Nitrosopyrrolidine  
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Last Revised — 01/31/1987

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  $\mu\text{g}/\text{cu.m}$  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 — Tumors at more than one site have been observed in two rodent species administered nitrosopyrrolidine orally.

## **II.A.2. Human Carcinogenicity Data**

None. 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 from these exposures is of limited use in the evaluation of the carcinogenicity of individual nitrosamines.

## **II.A.3. Animal Carcinogenicity Data**

There is a large database on the carcinogenicity of nitrosamines, most of which pertains to structure-activity relationships rather than to dose-response. Nitrosopyrrolidine produced a 100% incidence of liver carcinomas in MRC rats given an oral dose of 16 mg/kg/day. Male rats also developed papillary mesotheliomas of the testes (Greenblatt and Lijinsky, 1972a). Exposure in drinking water of 0.25 mg (7-8 mg/kg/day) induced a low incidence of lung adenomas in male and female Swiss mice (Greenblatt and Lijinsky, 1972b). Druckrey (1967) noted hepatocarcinogenicity in BD rats fed 10-20 mg/kg/day in the diet.

Equal numbers (12-31) of male and female Sprague-Dawley rats were maintained on water formulated to deliver 0, 0.3, 1, 3, or 10 mg/kg bw/day nitrosopyrrolidine (Preussmann et al., 1977). Animals remained on treatment until they died or became moribund. There was no statistically significant increase in numbers of tumors in the lowest dose group. Dose-related increases in hepatocellular carcinomas and adenomas were observed. Latency periods were also diminished with increasing dose.

## **II.A.4. Supporting Data for Carcinogenicity**

N-nitrosopyrrolidine is mutagenic for *Salmonella typhimurium* upon addition of mammalian metabolic enzymes (Montesano and Bartsch, 1976). It is structurally related to carcinogenic nitrosamines.

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

### **II.B.1. Summary of Risk Estimates**

Oral Slope Factor — 2.1E+0 per (mg/kg)/day

Drinking Water Unit Risk — 6.1E-5 per (ug/L)

Extrapolation Method — Linearized multistage procedure, extra risk

Drinking Water Concentrations at Specified Risk Levels:

<b>Risk Level</b>	<b>Concentration</b>
<b>E-4 (1 in 10,000)</b>	2E+0 ug/L
<b>E-5 (1 in 100,000)</b>	2E-1 ug/L
<b>E-6 (1 in 1,000,000)</b>	2E-2 ug/L

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

Tumor Type — hepatocellular carcinoma and adenoma

Test Animals — Rat/Sprague-Dawley, male and female

Route — diet

Reference — Preussmann et al., 1977

<b>Admin. Dose (mg/kg/day)</b>	<b>Human Equiv. Dose (mg/kg/day)</b>	<b>Tumor Incidence</b>
<b>0</b>	0	0/61
<b>0.3</b>	0.051	3/60
<b>1.0</b>	0.17	17/62
<b>3.0</b>	0.51	31/38
<b>10.0</b>	1.70	14/24

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

There was increased mortality because of pneumonia in the highest dose group. Preussmann et al. (1977) indicated that increased susceptibility to respiratory infection may have been due to cumulative nitrosopyrrolidine toxicity.

The unit risk should not be used if water concentrations exceed 200 ug/L, since above this concentration the unit risk may not be appropriate.

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

Tumor incidence was shown to be dependent on the nitrosopyrrolidine dose in the study above. Adequate numbers of animals were treated and observed for their normal lifetime at several lower doses. As incidences of benign and malignant growths were added, it is not possible to ascertain whether any animals were counted more than once.

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

#### **II.C.1. Summary of Risk Estimates**

Inhalation Unit Risk — 6.1E-4 per (µg/cu.m)

Extrapolation Method — Linearized multistage procedure, extra risk

Air Concentrations at Specified Risk Levels:

<b>Risk Level</b>	<b>Concentration</b>
<b>E-4 (1 in 10,000)</b>	2E-1 µg/cu.m
<b>E-5 (1 in 100,000)</b>	2E-2 µg/cu.m
<b>E-6 (1 in 1,000,000)</b>	2E-3 µg/cu.m

#### **II.C.2. Dose-Response Data for Carcinogenicity, Inhalation Exposure**

The inhalation risk estimates were calculated from the oral exposure data in Section II.B.2.

### **II.C.3. Additional Comments (Carcinogenicity, Inhalation Exposure)**

The unit risk should not be used if air concentrations exceed 20 µg/cu.m, since above this concentration the unit risk may not be appropriate.

### **II.C.4. Discussion of Confidence (Carcinogenicity, Inhalation Exposure)**

See II.B.4.

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

### **II.D.1. EPA Documentation**

Source Document — U.S. EPA, 1980, 1986

The values in the Ambient Water Quality Criteria Document for Nitrosamines (U.S. EPA, 1980) received extensive peer and public review.

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

Agency Work Group Review — 07/23/1986, 10/14/1986, 10/29/1986

Verification Date — 10/14/1986

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-Nitrosopyrrolidine conducted in November 2001 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at [hotline.iris@epa.gov](mailto: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](mailto:hotline.iris@epa.gov) (internet address).

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**III. [reserved]**

**IV. [reserved]**

**V. [reserved]**

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## **VI. Bibliography**

Substance Name — N-Nitrosopyrrolidine

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### **VI.A. Oral RfD References**

None

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### **VI.B. Inhalation RfC References**

None

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### **VI.C. Carcinogenicity Assessment References**

Druckrey, H., R. Preussmann, S. Ivankovic and D. Schmaehl. 1967. Organotropism and carcinogenic effects of 65 different N-nitroso compounds in BD-rats. *Z. Krebsforsch.* 69(2): 103-201.

Greenblatt, M. and W. Lijinsky. 1972a. Nitrosamine studies: Neoplasms of liver and genital mesothelium in nitrosopyrrolidine-treated MRC rats. *J. Natl. Cancer Inst.* 48(6): 1687-1696.

Greenblatt, M. and W. Lijinsky. 1972b. Failure to induce tumors in Swiss mice after concurrent administration of amino acids and sodium nitrite. *J. Natl. Cancer Inst.* 48(5): 1389-1392.

Montesano, R. and H. Bartsch. 1976. Mutagenic and carcinogenic N- nitroso compounds: Possible environmental Hazards. *Mutat. Res.* 32: 179-228.

Preussmann, R., D. Schmahl and G. Eisenbrand. 1977. Carcinogenicity of N-nitrosopyrrolidine: Dose-response study in rats. *Z. Krebsforsch.* 90: 161-166.

U.S. EPA. 1980. Ambient Water Quality Criteria Document for Nitrosamines. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC. EPA 440/5-80-064. NTIS PB 81- 117756.

U.S. EPA. 1986. Health and Environmental Effects Profile for Nitrosamines. 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.

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## VII. Revision History

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

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## VIII. Synonyms

Substance Name — N-Nitrosopyrrolidine

CASRN — 930-55-2

Last Revised — 01/31/1987

- 930-55-2
- 1-nitrosopyrrolidine
- Nitrosopyrrolidine, N-
- N-Nitrosopyrrolidine
- N-N-pyr
- NO-pyr
- NPYR
- Pyrrole, tetrahydro-N-nitroso-
- pyrrolidine, 1-nitroso-
- RCRA waste number U180