



# Integrated Risk Information System

You are here: EPA Home Human Health IRIS IRIS Summaries

## Nitrobenzene (CASRN 98-95-3)

view QuickView

MAIN CONTENTS



**Search IRIS by Keyword**

List of IRIS Substances

Full IRIS Summaries/Toxicological Reviews

Entire IRIS Website

Reference Dose for Chronic Oral Exposure (RfD)

0079

### Nitrobenzene; CASRN 98-95-3

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Nitrobenzene

File First On-Line 01/31/1987

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	01/01/1991
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	on-line	02/01/1995

### I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Nitrobenzene  
CASRN — 98-95-3  
Last Revised — 01/01/1991

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.

NOTE: The Oral RfD for nitrobenzene may change in the near future pending the outcome of a further review now being conducted by the Oral RfD Work Group.

#### I.A.1. Oral RfD Summary



<b>Critical Effect</b>	<b>Experimental Doses*</b>	<b>UF</b>	<b>MF</b>	<b>RfD</b>
Hematologic, adrenal, renal and hepatic lesions	NOAEL: none  LOAEL: 25 mg/cu.m (mice) converted to 4.6 mg/kg/day	10,000	1	5E-4 mg/kg/day
Rat/Mouse Subchronic Inhalation Study				
CIIT, 1984				

\*Conversion Factors: 6 hour/24 hour, 5 days/7 days, 0.039 cu.m/day/0.03 kg (mice breathing rate/body weight) and 0.8 absorption factor; thus, 25 mg/cu.m x 6 hour/24 hour x 5 days/7 days x 0.039 cu.m/day / 0.03 kg x 0.8 = 4.6 mg/kg/day

### **\_\_I.A.2. Principal and Supporting Studies (Oral RfD)**

CIIT (Chemical Industry Institute of Toxicology). 1984. Ninety-day inhalation toxicity study of nitrobenzene in F344 rats and B6C3F1 mice. Research Triangle Park, NC. FYI-OTS-0874-0333.

The CIIT 90-day inhalation study provides the most appropriate data currently available to derive an RfD. Ten animals/sex/species/dose group were administered nitrobenzene at 1 of 3 doses. Other than increased incidence of hemolytic anemia in rats at 25 mg/cu.m and vacuolization of adrenal cortical cells in female mice at 25 mg/cu.m and higher, adverse effects of nitrobenzene exposure in mice and rats were comparable to unexposed controls at this dose. Mice and rats exposed to nitrobenzene at 81 mg/cu.m showed increased incidence and severity of liver and kidney lesions.

Data regarding the effects of nitrobenzene in humans are limited to symptoms and observations in workers, including headaches, vertigo, and methemoglobinemia (ACGIH, 1980). The potential "safe" level derived from the TLV appears adequate to protect workers from such adverse effects; however, the effects of occupational exposure to nitrobenzene on the liver and/or kidneys have not been adequately evaluated. The CIIT (1984) study indicates that the liver and kidney may be target organs of chronic/subchronic nitrobenzene exposure, and an acceptable level based on the TLV may not be protective for the toxic effects of nitrobenzene on the liver and/or kidney. Therefore, until more definitive chronic data are available, the RfD of 0.0005 mg/kg/day is recommended to protect against adverse health effects of nitrobenzene.

### **\_\_I.A.3. Uncertainty and Modifying Factors (Oral RfD)**

UF — The uncertainty factor of 10,000 represents two 10-fold factors for both intra- and interspecies variability to the toxicity of this chemical in lieu of specific data, a 10-fold factor for estimating a chronic effect level, from its subchronic equivalent, and a 10-fold factor for estimating an RfD from a LOAEL rather than a NOAEL.

MF — None

### **\_\_I.A.4. Additional Studies/Comments (Oral RfD)**

None.

### **\_\_I.A.5. Confidence in the Oral RfD**

Study — Medium  
Database — Low  
RfD — Low

Medium to low confidence in the study is recommended because it is not an oral study, a limited number of animals/sex/dose were tested, and a NOAEL for the critical toxic effect (i.e., adrenal toxicity) was not determined, although two species were used and many parameters were measured. Low confidence in the database is recommended because chronic reproductive and teratology data are missing. Low confidence in the RfD follows.

### **\_\_I.A.6. EPA Documentation and Review of the Oral RfD**

Source Document — U.S. EPA, 1985

Other EPA Documentation — None

Agency Work Group Review — 06/24/1985, 07/08/1985, 11/06/1985

Verification Date — 07/08/1985

### **\_\_I.A.7. EPA Contacts (Oral RfD)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (301)345-2870 (phone), (301)345-2876 (FAX) or hotline.iris@epa.gov (internet address).

### **\_\_I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)**

Substance Name — Nitrobenzene  
CASRN — 98-95-3

Not available at this time.

## **\_\_II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — Nitrobenzene  
CASRN — 98-95-3  
Last Revised — 02/01/1995

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.

NOTE: The carcinogenicity assessment for nitrobenzene may change in the near future pending the outcome of a further review now being conducted by the Carcinogen Risk Assessment Verification Endeavor Work Group.

### **\_\_II.A. Evidence for Human Carcinogenicity**

#### **\_\_II.A.1. Weight-of-Evidence Characterization**

Classification — D; not classifiable as to human carcinogenicity

Basis — Based on no data concerning carcinogenicity in humans or animals.

#### **\_\_II.A.2. Human Carcinogenicity Data**

None.

#### **\_\_II.A.3. Animal Carcinogenicity Data**

None.

#### **\_\_II.A.4. Supporting Data for Carcinogenicity**

In Salmonella/microsomal mutagenicity assays with strains TA92, TA94, TA97, TA98, TA100, TA1535, TA1537 and TA1538, nitrobenzene was not positive (Garner and Nutman, 1977; Chiu et al., 1978; Shimizu et al., 1983; Ho et al., 1981; Haworth et al., 1983; Anderson and Styles, 1978; Miyata et al., 1981). These assays were conducted with and without liver homogenates by plate incorporation, spot test and in one study (Hughes et al., 1984), by the vapor exposure method.

Nitrobenzene was mutagenic in the presence of liver homogenate and norharman in *S. typhimurium* strain TA98 but not in strain TA100 (Suzuki et al., 1983). Nitrobenzene did not cause an increase in unscheduled DNA synthesis in hepatocytes isolated from gavage-treated rats (Mirsalis et al., 1982). Fel'dt (1985) reported that oral administration of nitrobenzene did not produce micronucleus or chromosome aberrations in bone marrow cells or dominant lethal mutations in mice.

#### **\_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**

U.S. EPA. 1985. Health and Environmental Effects Profile for Nitrobenzene. 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.

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

The 1985 Health and Environmental Effects Profile for Nitrobenzene and the 1987 Health Effects Assessment for Nitrobenzene have received OHEA review.

##### **\_\_II.D.2. EPA Review (Carcinogenicity Assessment)**

Agency Work Group Review — 11/08/1989, 12/07/1994

Verification Date — 11/08/1989

##### **\_\_II.D.3. EPA Contacts (Carcinogenicity Assessment)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (301)345-2870 (phone), (301)345-2876 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

**\_III. [reserved]**

**\_IV. [reserved]**

**\_V. [reserved]**

## **\_VI. Bibliography**

Substance Name — Nitrobenzene

CASRN — 98-95-3

Last Revised — 12/01/1990

### **\_VI.A. Oral RfD References**

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values. 4th ed. Cincinnati, OH. p. 303.

CIIT (Chemical Industry Institute of Toxicology). 1984. Ninety-day inhalation toxicity study of nitrobenzene in F344 rats, CD rats, and B6C3F1 mice. Research Triangle Park, NC. FYI-OTS-0784-0333.

U.S. EPA. 1985. Health and Environmental Effects Profile for Nitrobenzene. 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.

### **\_VI.B. Inhalation RfC References**

None

### **\_VI.C. Carcinogenicity Assessment References**

Anderson, D. and J.A. Styles. 1978. An evaluation of 6 short-term tests for detecting organic chemical carcinogens. Appendix II. The bacterial mutation test. *Br. J. Cancer*. 37: 924-930.

Chiu, C.W., L.H. Lee, C.Y. Wang and G.T. Bryan. 1978. Mutagenicity of some commercially available nitro compounds on *Salmonella typhimurium*. *Mutat. Res.* 58: 11-22.

Fel'dt, E.G. 1985. Evaluation of the mutagenic Hazards of benzene and some of its derivatives. *Gig. Sanit.* 7: 21-23.

Garner, R. and C.A. Nutman. 1977. Testing of some azo dyes and their reduction products for mutagenicity using *Salmonella typhimurium* TA1538. *Mutat. Res.* 44: 9-19.

Haworth, S., T. Lawlor, K. Mortelmans, W. Speck and E. Zeiger. 1983. *Salmonella* mutagenicity test results for 250 chemicals. *Environ. Mutagen.(Suppl.)* 1: 3-142.

Ho, C.H., B.R. Clark, M.R. Guerin, B.D. Barkenbus, T.K. Rao and J.L. Epler. 1981. Analytical and biological analyses of test materials from the synthetic fuel technologies. IV. Studies of chemical structure-mutagenic activity relationships of aromatic nitrogen compounds relevant to synfuels. *Mutat. Res.* 85(5): 335-345.

Hughes, T.J., C. Sparacino and S. Frazier. 1984. Validation of chemical and biological techniques for evaluation of vapors in ambient air/mutagenicity testing of twelve (12) vapor-phase compounds. EPA 600/1-84-005. NTIS PB 84-164219.

Mirsalis, J.C., C.K. Tyson and B.E. Butterworth. 1982. Detection of genotoxic carcinogens in the in vivo-in vitro hepatocyte DNA repair assay. *Environ. Mutagen.* 4: 553-562.

Miyata, R., T. Nomi, K. Yoshikawa and M. Ishidate. 1981. Metabolic activation of p- nitrotoluene and trichloroethylene by rat liver S9 or mouse liver S9 fractions in *Salmonella typhimurium* strains. *Eisei Shikensho Hokoku.* 99: 60-65.

Shimizu, M., Y. Yasui and N. Matsumoto. 1983. Structural specificity of aromatic compounds with special reference to mutagenic activity in *Salmonella typhimurium*: A series of chloro- or fluoro-nitrobenzene derivatives. *Mutat. Res.* 116: 217-238.

Suzuki, J., T. Koyami and S. Suzuki. 1983. Mutagenicities of mono-nitrobenzene derivatives in the presence of norharman. *Mutat. Res.* 120: 105-110.

U.S. EPA. 1985. Health and Environmental Effects Profile for Nitrobenzene. 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.

U.S. EPA. 1987. Health Effects Assessment for Nitrobenzene. 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 — Nitrobenzene  
CASRN — 98-95-3

<b>Date</b>	<b>Section</b>	<b>Description</b>
03/01/1988	I.A.2.	Text deleted
03/01/1988	I.A.4.	Text deleted
03/01/1988	I.A.5.	Confidence levels revised
03/01/1988	I.A.7.	Documentation corrected
06/30/1988	I.A.3.	UF corrected in text
07/01/1989	I.B.	Inhalation RfD now under review
08/01/1989	I.A.	Oral RfD summary noted as pending change
12/01/1989	II.	Carcinogen assessment now under review
06/01/1990	IV.F.1.	EPA contact changed
06/01/1990	VI.	Bibliography on-line
12/01/1990	II.	Carcinogen assessment on-line
12/01/1990	VI.C.	Carcinogen assessment references added
01/01/1991	I.A.	Text edited
01/01/1992	I.A.7.	Primary contact changed
01/01/1992	IV.	Regulatory actions updated
01/01/1995	II.D.2.	Work group review date added
02/01/1995	II.	Carcinogenicity assessment noted as pending change
08/01/1995	I.A., I.B., II., II.D.2.	EPA's RfD/RfC and CRAVE workgroups were discontinued in May, 1995. Chemical substance reviews that were not completed by September 1995 were taken out of IRIS review. The IRIS Pilot Program replaced the workgroup functions beginning in September, 1995.
04/01/1997	III., IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.
01/02/1998	I., II.	This chemical is being reassessed under the IRIS Program.

## **\_VIII. Synonyms**

Substance Name — Nitrobenzene

CASRN — 98-95-3

Last Revised — 01/31/1987

- 98-95-3
- Benzene, Nitro-
- Essence of Mirbane
- Essence of Myrbane
- Mirbane Oil
- NCI-C60082
- Nitrobenzene
- Nitrobenzol
- Oil of Mirbane
- Oil of Myrbane

### **IRIS Home**

#### **Chronic Health Hazards for Non-Carcinogenic Effects**

##### **Reference Dose for Chronic Oral Exposure (RfD)**

- Oral RfD Summary
- Principal and Supporting Studies
- Uncertainty and Modifying Factors
- Additional Studies/Comments
- Confidence in the Oral RfD
- EPA Documentation and Review

##### **Reference Concentration for Chronic Inhalation Exposure (RfC)**

- Inhalation RfC Summary
- Principal and Supporting Studies
- Uncertainty and Modifying Factors
- Additional Studies/Comments
- Confidence in the Inhalation RfC
- EPA Documentation and Review

##### **Carcinogenicity Assessment for Lifetime Exposure**

##### **Evidence for Human Carcinogenicity**

- Weight-of-Evidence Characterization
- Human Carcinogenicity

	Data
•	Animal Carcinogenicity Data
•	Supporting Data for Carcinogenicity
	<b>Quantitative Estimate of Carcinogenic Risk from Oral Exposure</b>
•	Summary of Risk Estimates
•	Dose-Response Data
•	Additional Comments
•	Discussion of Confidence
	<b>Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure</b>
•	Summary of Risk Estimates
•	Dose-Response Data
•	Additional Comments
•	Discussion of Confidence
•	EPA Documentation, Review and, Contacts
	<b>Bibliography</b>
	<b>Revision History</b>
	<b>Synonyms</b>