

o-Dinitrobenzene; CASRN 528-29-0

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 o-Dinitrobenzene

File First On-Line 09/01/1992

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	09/01/1992*

*A comprehensive review of toxicological studies was completed (07/22/05) - 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 — Substance Name — o-Dinitrobenzene
CASRN — 528-29-0

Not available at this time.

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

Substance Name — o-Dinitrobenzene
CASRN — 528-29-0

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — o-Dinitrobenzene
CASRN — 528-29-0
Last Revised — 09/01/1992

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 — Based on no data in humans and animals.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

None.

II.A.4. Supporting Data for Carcinogenicity

Data are not available regarding the carcinogenicity of any dinitrobenzene isomers (i.e., o-, m- or p-dinitrobenzene) in humans or animals by any route of exposure.

In the only available evaluation of o-dinitrobenzene mutagenicity, no reverse mutations were observed in *Salmonella typhimurium* strains TA1535, TA1538, TA98, TA100 or TA100NR3 with or without metabolic activation with rat liver S9 fractions (Spanggord et al., 1982). Spanggord et al. (1982) also reported that p-dinitrobenzene was not mutagenic in the same strains, but Probst et al. (1981) reported mutagenic activity in strains TA1535, TA1538 and TA98 following exposure to p-dinitrobenzene.

In contrast, m-dinitrobenzene was mutagenic with or without metabolic activation in strains TA1538, TA98 and TA100, but not in TA100NR3, TA1535 or TA1537 (Spanggord et al., 1982). Other tests have observed mutagenic responses to m-dinitrobenzene in *Salmonella typhimurium* (McGregor et al., 1980; Chiu et al., 1978; Garner and Nuttman, 1977; Matsuda, 1981; Probst et al., 1981). It has been suggested that the lack of mutagenicity in strain TA100NR3 (a nitro-reductase-deficient strain) indicates that nitro-reduction may be required for the expression of m-dinitrobenzene genotoxicity (Spanggord et al., 1982).

Qualitative and quantitative differences in the metabolic pathways of the dinitrobenzenes have been observed in rats (Nystrom and Rickert, 1987). Direct conjugation with glutathione appeared to be the most important pathway for o- dinitrobenzenes; pathways involving reduction of the nitro groups appeared to be of secondary importance. Radioactivity in urinary S-(2-nitrophenyl)-N- acetylcysteine accounted for 42% of administered radiolabeled o-dinitrobenzene in rats. In contrast, no evidence was observed for direct conjugation of m- dinitrobenzene with glutathione; the significant pathways for m-dinitrobenzene in rats involved initial reduction of the nitro groups followed by acetylation of the resulting amino groups. Analysis of urinary metabolites indicated that both pathways (i.e., reduction of nitro groups and direct conjugation with glutathione) operated in rats following exposure to p-dinitrobenzene (Nystrom and Rickert, 1987).

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, 1991

The 1991 Health and Environmental Effects Document for Dinitrobenzenes (draft) has received Agency Review.

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

Agency Work Group Review — 04/02/1992

Verification Date — 04/02/1992

A comprehensive review of toxicological studies published through July 2005 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing carcinogenicity assessment for o-Dinitrobenzene 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 — o-Dinitrobenzene
CASRN — 528-29-0

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

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

Garner, R.C. 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.

Matsuda, A. 1981. Studies on the mutagenicity of nitroaromatic compounds in environment. *Gifu Daigaku Igakubu Kiyō.* 29(2): 278-296.

McGregor, D.B., C.G. Riach, R.M. Hastwell and J.C. Dacre. 1980. Genotoxic activity in microorganisms of tetra-, 1,3-dinitrobenzene and 1,3,5-trinitrobenzene. *Environ. Mutagen.* 2(4): 531-541.

Nystrom, D.D. and D.E. Rickert. 1987. Metabolism and excretion of dinitrobenzenes by male Fischer-344 rats. *Drug Metab. Dispos.* 15(6): 821-825.

Probst, G.S., R.E. McMahon, L.E. Hill, C.Z. Thompson, J.K. Epp and S.B. Neal. 1981. Chemically-induced unscheduled DNA synthesis in primary rat hepatocyte cultures: A comparison with bacterial mutagenicity using 218 compounds. *Environ. Mutagen.* 3(1): 11-32.

Spangord, R.J., K.E. Mortelmans, A.F. Griffin and V.F. Simmon. 1982. Mutagenicity in Salmonella typhimurium and structure-activity relationships of waste water components emanating from the manufacture of trinitrotoluene. Environ. Mutagen. 4(2): 163-179.

U.S. EPA. 1991. Health and Environmental Effects Document on Dinitrobenzenes. 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. (Draft)

VII. Revision History

Substance Name — o-Dinitrobenzene
CASRN — 528-29-0

Date	Section	Description
09/01/1992	II.	Carcinogenicity assessment on-line
10/28/2003	II.D.2.	Screening-Level Literature Review Findings message has been added.
08/15/2005	II.D.2.	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

VIII. Synonyms

Substance Name — o-Dinitrobenzene
CASRN — 528-29-0
Last Revised — 06/01/1992

- 528-29-0
- Benzene, 1,2-dinitro-
- AI3-15338

- Benzene, o-dinitro-
- HSDB 4486
- o-dinitrobenzene
- 1,2-Dinitrobenzene