N-Nitroso-di-n-butylamine; CASRN 924-16-3

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-Nitroso-di-n-butylamine

File First On-Line 01/31/1987

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

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — N-Nitroso-di-n-butylamine
CASRN — 924-16-3
Primary Synonym — Dibutylnitrosamine

Not available at this time.

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

Substance Name — N-Nitroso-di-n-butylamine
CASRN — 924-16-3
Primary Synonym — Dibutylnitrosamine

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — N-Nitroso-di-n-butylamine
CASRN — 924-16-3
Primary Synonym — Dibutylnitrosamine
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 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 incidences of several tumor types in rats, mice, and hamsters exposed by various routes

II.A.2. Human Carcinogenicity Data

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 human exposure is of limited use in the evaluation of 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. Druckrey reported dibutylnitrosamine produced bladder rather than liver tumors in rats treated by s.c. injection. Dibutylnitrosamine also induces carcinoma of the bladder, lung, and trachea in Syrian hamsters and stomach carcinomas in Chinese hamsters treated by gavage. Liver tumors, lung adenomas, and forestomach carcinomas were observed in male CR mice fed this compound in the diet.

Druckrey et al. (1967) treated BD rats with dibutylnitrosamine in dietary concentrations providing doses of 10, 20, 37, or 75 mg/kg bw/day. Treatment was presumably lifetime. No control data were reported. All four of the surviving high-dose animals developed liver tumors as well as 13/16, 4/10, and 2/10 in the 37, 20, and 10 mg/kg bw/day groups. Esophageal tumors and bladder tumors were also observed in the lower dose groups. Average time-to-tumor was treatment dose-dependent.

Bertram and Craig (1970) exposed 50 each male and female C57Bl6 mice to either 60 mg or 240 mg dibutylnitrosamine/L in drinking water. The treatment solution was replaced by water for 50% of all animals in the high-dose group, as these animals showed hematuria. The remainder of the high-dose animals and all low-dose animals were maintained on the treatment solutions until they became moribund or died. Squamous-cell carcinomas of the bladder were found in 44/90 high-dose mice and 19/89 low-dose mice; they predominated in the males. Carcinomas and papillomas of the esophagus were also found.

II.A.4. Supporting Data for Carcinogenicity

Dibutylnitrosamine is mutagenic for E. coli and S. typhimurium and causes mitotic recombination in S. cerevisiae, recessive lethal mutations in D. melanogaster and chromosome aberrations in mammalian cells. Positive responses are dependent upon the presence of mammalian metabolic enzymes (Montesano and Bartsch, 1976).

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

II.B.1. Summary of Risk Estimates

Oral Slope Factor — 5.4E+0 per (mg/kg)/day

Drinking Water Unit Risk — 1.6E-4 per (ug/L)

Extrapolation Method — Linearized multistage procedure, extra risk

Drinking Water Concentrations at Specified Risk Levels:

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

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

Tumor Type — bladder and esophagus tumors
Test Animals — Mouse/C57Bl6, males
Route — drinking water
Reference — Bertram and Craig, 1970

Administered Dose (mg/L)	Tumor Incidence
0	not reported
60	46/47
240	45/45

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

Water consumption reported by the authors indicates that males received doses of 7.6 and 29.1 mg/kg/day. Specific tumor incidences were not reported for control animals. The authors stated that this strain has a very low spontaneous tumor incidence. A slope factor of 1.2 per (mg/kg)/day for dibutylnitrosamine was calculated from the data of Druckrey et al. (1967). The unit risk should not be used if the water concentration exceeds 60 ug/L, since above this concentration the unit risk may not be appropriate.

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

Although adequate numbers of animals were treated for their lifetime, control data were not reported. The risk estimate above is supported by an independent study (Druckrey et al., 1967); a slope factor of 1.9 per (mg/kg)/day was derived from these data using a one-hit model.

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

II.C.1. Summary of Risk Estimates

Inhalation Unit Risk — 1.6E-3 per (ug/cu.m)

Extrapolation Method — Linearized multistage procedure, extra risk

Air Concentrations at Specified Risk Levels:

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

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

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

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

The unit risk should not be used if air concentrations exceed 6 ug/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.

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

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1980

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

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

Agency Work Group Review — 07/23/1986, 08/13/1986, 10/29/1986

Verification Date — 10/29/1986

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-Nitroso-di-n-butylamine conducted in August 2003 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-Nitroso-di-n-butylamine
CASRN — 924-16-3
Primary Synonym — Dibutylnitrosamine

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Bertram, J.S. and A.W. Craig. 1970. Induction of bladder tumours in mice with dibutylnitrosamine. Br. J. Cancer. 24: 352-359.

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

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

U.S. EPA 1980. Ambient Water Quality Criteria 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.

VII. Revision History

Substance Name — N-Nitroso-di-n-butylamine
CASRN — 924-16-3
Primary Synonym — Dibutylnitrosamine

Date	Section	Description
10/28/2003	II.D.2	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — N-Nitroso-di-n-butylamine
CASRN — 924-16-3
Primary Synonym — Dibutylnitrosamine
Last Revised — 01/31/1987

- 924-16-3
- 1-butanamine, N-butyl-N-nitroso-
- butylamine, N-nitrosodi-
- DBN: DBNA
- Dibutylamine, N-nitroso
- Dibutylnitrosamine
- di-n-butylnitrosamine
- di-n-butylnitrosamin
- N-butyl-N-nitroso-1-butamine
- NDBA
- Nitroso-di-n-butylamine, N-
- N,N-di-n-butylnitrosamine
- N-nitrosobutylamine
- N-Nitroso-di-n-butylamine
- RCRA waste number U172