

N-Nitrosodiethanolamine; CASRN 1116-54-7

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-Nitrosodiethanolamine

File First On-Line 09/30/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	09/30/1987

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — N-Nitrosodiethanolamine
CASRN — 1116-54-7

Not available at this time.

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

Substance Name — N-Nitrosodiethanolamine
CASRN — 1116-54-7

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — N-Nitrosodiethanolamine
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Last Revised — 09/30/1987

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 incidence of liver tumors and tumors at other sites in three strains of rats and in hamsters

II.A.2. Human Carcinogenicity Data

Inadequate. Human exposure to nitrosamines results from contact with mixtures containing these compounds. Because of potential confounding by the other substances in these mixtures, human data are of limited use in the evaluation of carcinogenicity of individual nitrosamines. N-nitrosodiethanolamine occurs in cosmetics and cutting oils.

II.A.3. Animal Carcinogenicity Data

Lijinsky and Kovatch (1985) administered N-nitrosodiethanolamine in drinking water to a total of 126 F344 rats of both sexes at dose levels of 0, 28, and 64 mg/L for 100 weeks and at 64 and 160 mg/L for 50 weeks. The number of animals/sex/treatment group varied from 20 to 39. Animals were examined histologically at natural death or when moribund, or after 130 weeks. A statistically significant dose-response increase in the incidence of hepatocellular carcinomas and neoplastic nodules was seen in females, and a statistically significant increased incidence was seen in the higher dose treatment group in males. Low incidences of kidney tubular cell/adenoma which were not statistically significant were seen in most treatment groups.

Preussmann et al. (1982) administered N-nitrosodiethanolamine in drinking water to a total of 268 male Sprague-Dawley rats (100 days old) at 0, 1.5, 6, 25, 100, and 400 mg/kg/day for 5 days/week for life. A statistically significant increased incidence of liver and nasal cavity tumors was seen after adjustment for early death. The increase was dose-dependent for liver tumors.

Druckrey et al. (1967) administered N-nitrosodiethanolamine daily in the drinking water to groups of 4 and 16 BD rats at average concentrations of 600 and 1000 mg/kg, respectively, for life. A control group was not used. All 20 rats developed hepatocellular carcinomas and 4 (dose not specified) also had kidney adenomas.

Lijinsky et al. (1980) and Lijinsky and Reuber (1984) supplied N-nitrosodiethanolamine in the drinking water of F344 rats of both sexes at concentrations of 400, 1000, and 2500 ppm for 5-7 days/week for 34-75 weeks. The increased incidences of hepatocellular carcinomas and adenocarcinomas of the nasal cavity were statistically significant.

When N-nitrosodiethanolamine was administered to Syrian golden hamsters (for 27 weeks to lifetime) by a variety of routes (subcutaneous, oral swabbing, skin painting), carcinomas of the nasal cavity and papillomas of the trachea were primarily induced (Hilfrich et al., 1977; Schmeltz et al., 1978; Pour and Wallcave, 1981; Hoffmann et al., 1983).

II.A.4. Supporting Data for Carcinogenicity

N-nitrosodiethanolamine is mutagenic in *S. typhimurium* (Hesbert et al., 1979; McMahon et al., 1979) and *E. coli* (McMahon et al., 1979).

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

II.B.1. Summary of Risk Estimates

Oral Slope Factor — 2.8E+0/mg/kg/day

Drinking Water Unit Risk — 8.0E-5/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)	1E+0 ug/L
E-5 (1 in 100,000)	1E-1 ug/L
E-6 (1 in 1,000,000)	1E-2 ug/L

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

Tumor Type — hepatocellular carcinoma, cholangiocellular carcinoma and adenoma and neoplastic nodules

Test Animals — rat/F344, female

Route — drinking water

Reference — Lijinsky and Kovatch, 1985

Administered Dose (mg/kg/day)	Human Equivalent Dose (mg/kg/day)	Tumor Incidence
0	0	1/20
0.88	0.15	10/39
2.01	0.34	14/20

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

Only the incidences for the 100-week treatment groups in the Lijinsky and Kovatch (1985) study were used to calculate the slope factor, since these were closer to lifetime exposure. Daily animal doses were calculated using reported water consumption and corrected for less than 7 days/week exposure and for exposure that was less than lifetime (100/130). A slope factor of 9.7E-1/mg/kg/day was calculated from the incidence data in the Preussmann et al. (1982) study. The use of the higher slope factor derived from the Lijinsky and Kovatch (1985) study is preferred, since there are no substantial differences in quality between this study and that of Preussmann et al. (1982).

The unit risk should not be used if the water concentration exceeds 100 ug/L, since above this concentration the slope factor may differ.

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

An adequate number of animals were observed, and a statistically significant increase in incidence of liver tumors was seen in both sexes. The increase was dose-dependent in females. Treatment was for less than, but close to, normal lifetime. A slope factor derived from an independent study was within a factor of 3.

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 for Nitrosamines have received review within the Agency.

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

Agency Work Group Review — 01/28/1987

Verification Date — 01/28/1987

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-Nitrosodiethanolamine conducted in August 2003 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 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-Nitrosodiethanolamine
CASRN — 1116-54-7

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Druckrey, H., R. Preussmann, S. Ivankovic, and D. Schmahl. 1967. Organotropism and carcinogenic activities of 65 different N-nitroso compounds in rats. *Zeitschrift fur Krebsforschung*. 6a: 103-207.

Hesbert, A., M. Lemonnier and C. Cavalier. 1979. Mutagenicity of nitrosodiethanolamine on *Salmonella typhimurium*. *Mutat. Res.* 68(3): 207-210.

Hilfrich, J., I.Schmeltz and D. Hoffmann. 1977. Effects of N- nitrosodiethanolamine and 1,1-diethanolhydrazine in Syrian golden hamsters. *Cancer Lett.* 4(1): 55-60.

Hoffmann, D., A. Rivenson, J.D. Adams, A. Juchatz, N. Vinchkoski and S.S. Hecht. 1983. Effects of route of administration and dose on the carcinogenicity of N-nitrosodiethanolamine in the Syrian golden hamster. *Cancer Res.* 43(6): 2521-2524.

Lijinsky, W. and M.D. Reuber. 1984. Dose-response study with N-nitrosodiethanolamine in F344 rats. *Food Chem. Toxicol.* 22(1): 23-26.

Lijinsky, W. and R.M. Kovatch. 1985. Induction of liver tumors in rats by nitrosodiethanolamine at low doses. *Carcinogenesis*. 6(12): 1679-1681.

Lijinsky, W., M.D. Reuber and W.B. Manning. 1980. Potent carcinogenicity of nitrosodiethanolamine in rats. *Nature (Lond)*. 288(5791): 589-590.

McMahon, R.E., J.C. Cline and C.Z. Thompson. 1979. Assay of 855 test chemicals in ten tester strains using a new modification of the Ames test for bacterial mutagens. *Cancer Res.* 39(3): 682-693.

Pour, P. and L. Wallcave. 1981. The carcinogenicity of N- nitrosodiethanolamine, an environmental pollutant, in Syrian hamsters. *Cancer Lett.* 14(1): 23-28.

Preussmann, R., M. Habs, H. Habs and D. Schmahl. 1982. Carcinogenicity of N-nitrosodiethanolamine in rats at five different dose levels. *Cancer Res.* 42: 5167-5171.

Schmeltz, I., J. Hilfrich and D. Hoffmann. 1978. On the carcinogenic activity of nitrosodiethanolamine in the Syrian golden hamsters. *Toxicol. Appl. Pharmacol.* 45(1): 325.

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.

VII. Revision History

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

VIII. Synonyms

Substance Name — N-Nitrosodiethanolamine
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Last Revised — 09/30/1987

- 1116-54-7
- BIS(beta-HYDROXYAETHYL)NITROSAMIN
- BIS(beta-HYDROXYETHYL)NITROSAMINE
- DIAETHANOLNITROSAMIN
- DIETHANOLNITROSOAMINE
- DIETHYLAMINE, 2,2'-DIHYDROXY-N-NITROSO
- ETHANOL, N-NITROSOIMINODI-
- 2,2'-IMINODI-N-NITROSOETHANOL
- NCI-C55583
- NDELA
- Nitrosodiethanolamine, N-
- 2,2'-(NITROSOIMINO)BIETHANOL
- NITROSOIMINO DIETHANOL
- N-NITROSOAMINODIETHANOL
- N-NITROSOBIS(2-HYDROXYETHYL)AMINE
- N-NITROSODIAETHANOLAMIN
- N-Nitrosodiethanolamine
- RCRA WASTE NUMBER U173