

n-Butanol; CASRN 71-36-3

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-Butanol

File First On-Line 03/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	03/31/1987
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	03/01/1991

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

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Last Revised — 03/31/1987

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.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Hypoactivity and ataxia	NOAEL: 125 mg/kg/day	1000	1	1E-1 mg/kg/day
Rat Oral Subchronic Study	LOAEL: 500 mg/kg/day			
U.S. EPA, 1986				

*Conversion Factors: None

I.A.2. Principal and Supporting Studies (Oral RfD)

U.S. EPA. 1986. Butanol: Rat oral subchronic toxicity study. Office of Solid Waste, Washington, DC.

Four groups of male and female rats (30/sex/group) were dosed daily by gavage with 0, 30, 125 and 500 mg/kg/day of butanol for 13 weeks. Six weeks after the initiation of dosing, an interim sacrifice of 10 rats/sex was performed to evaluate clinical, biochemical and gross morphological changes. The remaining animals continued in the experiment until the day of the final sacrifice (day 92 or 93). Data generated from this study on body and organ weight changes, food consumption, moribundity, mortality, and ophthalmological, gross, and histopathologic examinations did not show any dose-related differences between control and treated animals. Slight but significant reductions in some hematologic parameters were observed in the mid- and high-dosed females at the interim, but not at final sacrifice. This effect was considered to be transitory rather than adverse. Ataxia and hypoactivity were consistently observed in high-dosed (500 mg/kg/day) males and females during the final 6 weeks of the dosing period. Thus, the 125 mg/kg/day dose of butanol is considered a NOAEL for central nervous system effects in rats. By application of an uncertainty factor of 1000, an RfD of 0.1 mg/kg/day or 9 mg/day for a 70 kg-person is derived.

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — An uncertainty factor of 1000 was applied: 10 for intraspecies variability, 10 for interspecies extrapolation, and 10 for expanding subchronic to long-term exposure.

MF — None

I.A.4. Additional Studies/Comments (Oral RfD)

Sterner et al. (1949) reported that occupational exposure to 100 ppm (300 mg/cu.m) butanol had no impact on workers' health. This 10-year study included hematological evaluations, test of liver function, urine analysis, chest X-rays, ophthalmological examinations, and comparison of absenteeism among butanol-exposed men vs. all men in the plant. Details of the experimental protocol of this study were not available for risk analysis. Several other human inhalation studies have reported irritations to eyes, nose, and throat, and mild headaches, at concentrations of 50 ppm (150 mg/cu.m) or higher; however, these effects were transitory in nature. An abstract of a rat inhalation study (4-month exposure) suggested a NOAEL of 0.8 mg/cu.m for reversible blood cholinesterase activity and increased thyroid activity.

I.A.5. Confidence in the Oral RfD

Study — High

Database — Low

RfD — Low

The oral subchronic study provided more than adequate toxicologic endpoints based on a very well-designed experimental protocol; therefore, a high confidence is recommended. The database does not provide pertinent information on oral chronic or reproductive studies; therefore, a low confidence is recommended. A low to medium confidence is recommended for the RfD.

I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — U.S. EPA, 1986

Agency Work Group Review — 05/14/1986

Verification Date — 05/14/1986

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for n-Butanol 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.

I.A.7. EPA Contacts (Oral RfD)

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).

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

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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — n-Butanol
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Last Revised — 03/01/1991

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 human and no animal cancer data.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

None.

II.A.4. Supporting Data for Carcinogenicity

1-Butanol was negative in reverse mutation and DNA damage tests in *Salmonella typhimurium* (McCann et al., 1975; Connor et al., 1985; Nakamura et al., 1987), but weakly positive for inhibition of DNA synthesis in *Escherichia coli* (Yoshiyama et al., 1973). Negative results were reported for sister chromatid exchanges in chick embryo and Chinese hamster cells and for micronucleus formation in Chinese hamster cells (Bloom, 1982; Obe and Ristowe, 1977; Lasne et al., 1984). 1-Butanol induced spindle disturbances in Chinese hamster V79 lung cells (Onfelt, 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, 1989

The 1989 Health and Environmental Effects Document for 1-Butanol has received Agency and external peer review.

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

Agency Work Group Review — 12/06/1990

Verification Date — 12/06/1990

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-Butanol 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-Butanol
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VI.A. Oral RfD References

Sterner, J.H., H.C. Crouch, H.F. Brockmyre and M. Cusak. 1949. A ten-year study of butyl alcohol exposure. *Am. Ind. Hyg. Assoc.* 10(3): 53-59.

U.S. EPA. 1986. Butanol: Rat oral subchronic toxicity study. Office of Solid Waste, Washington, DC.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Bloom, S.E. 1982. 6. Detection of sister chromatid exchanges in vivo using avian embryos. In: *Cytogen. Assays Environ. Mutagens.* p. 137-159.

Connor, T.H., J.C. Theiss, H.A. Hanna et al. 1985. Genotoxicity of organic chemicals frequently found in the air of mobile homes. *Toxicol. Lett.* 25(1): 33-40.

Lasne, C., Z.W. Gu, W. Venegas and I. Chouroulinkov. 1984. The in vitro micronucleus assay for detection of cytogenetic effects induced by mutagen- carcinogens: Comparison with the in vitro sister-chromatid exchange assay. *Mutat. Res.* 130(4): 273-282.

McCann, J., E. Choi, E. Yamasaki and B.N. Ames. 1975. Detection of carcinogens as mutagens in the Salmonella/microsome test: Assay of 300 chemicals. *Proc. Natl. Acad. Sci. USA.* 72(12): 5135-5139.

Nakamura, S., Y. Oda, T. Shimada et al. 1987. SOS-inducing activity of chemical carcinogens and mutagens in *Salmonella typhimurium* TA1535/pSK1002: Examination with 151 chemicals. *Mutat. Res.* 192(4): 239-246.

Obe, G. and H. Ristow. 1977. Acetaldehyde, but not ethanol, induces sister chromatid exchanges in Chinese hamster cells in vitro. *Mutat. Res.* 56(2): 211-213.

Onfelt, A. 1987. Spindle disturbances in mammalian cells. III. Toxicity, c- mitosis and aneuploidy with 22 different compounds. Specific and unspecific mechanisms. *Mutat. Res.* 182(3): 135-154.

U.S. EPA. 1989. Health and Environmental Effects Document for 1-Butanol. 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.

Yoshiyama, Y., K. Nagai, H. Some and G. Tamura. 1973. Selective inhibition by pantoyl lactone and butyl alcohol of the initiation of DNA replication in *E. coli*. *Agric. Biol. Chem.* 37(6): 1317-1320.

VII. Revision History

Substance Name — n-Butanol
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Date	Section	Description
03/01/1991	II.	Carcinogenicity assessment on-line
10/28/2003	I.A.6., II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

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Last Revised — 03/31/1987

- 71-36-3
- ALCOOL BUTYLIQUE
- BUTANOL
- 1-BUTANOL
- BUTANOLEN
- Butanol, n-
- BUTANOLO
- BUTYL ALCOHOL
- n-BUTYL ALCOHOL
- BUTYL HYDROXIDE
- BUTYLOWY ALKOHOL
- BUTYRIC ALCOHOL
- CCS 203
- 1-HYDROXYBUTANE
- METHYLOLPROPANE
- NA 1120
- PROPYLCARBINOL
- PROPYLMETHANOL
- RCRA WASTE NUMBER U031
- UN 1120