Dibutyl phthalate; CASRN 84-74-2

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 Dibutyl phthalate

File First On-Line 01/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	01/31/1987
Inhalation RfC (I.B.)	message	10/01/1990
Carcinogenicity Assessment (II.)	yes	09/07/1988

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Dibutyl phthalate
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Last Revised — 01/31/1987

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.

NOTE: The Oral RfD for dibutyl phthalate 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

Critical Effect	Experimental Doses*	UF	MF	RfD
Increased mortality **Rat Subchronic to Chronic, Oral** **BioassaySmith, 1953**	NOAEL: 0.25% of diet (125 mg/kg/day) LOAEL: 1.25% of diet (600 mg/kg bw/day)	1000	1	1E-1 mg/kg/day

*Conversion Factors: The values of 125 mg/kg/day for 0.25% dibutyl phthalate in the diet and 600 mg/kg/day for 1.25% were estimated from a figure depicting daily intake in mg/kg in Smith (1953).

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

Smith, C.C. 1953. Toxicity of butyl sterate, dibutyl sebacate, dibutyl phthalate and methoxyethyl oleate. Arch. Hyg. Occup. Med. 7: 310-318.

Male Sprague-Dawley rats in groups of 10 were fed diets containing 0, 0.01, 0.05, 0.25, and 1.25% dibutyl phthalate for a period of 1 year. One-half of all rats receiving the highest dibutyl phthalate concentration died during the first week of exposure. The remaining animals survived the study with no apparent ill effects. There was no effect of treatment on gross pathology or hematology. While it was stated that several organs were sectioned and stained, no histopathologic evaluation was reported.

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

UF — A factor of 10 was applied to account for interspecies variation, a factor of 10 for protection of sensitive human subpopulations, and an additional factor of 10 to account for both the less-than-chronic duration of the study and deficiencies in the study, such as the use of only male animals.

MF — None

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

Fetotoxicity was observed when mice were fed 2100 mg/kg/day dibutyl phthalate throughout gestation (Shiota and Nishimura, 1982). An increase in terata of borderline statistical significance was observed in progeny of this treatment group. Dibutyl phthalate produces degeneration of the seminiferous tubules, probably as a result of increased urinary excretion of zinc (Gangolli, 1982).

I.A.5. Confidence in the Oral RfD

Study — Low
Database — Low
RfD — Low

The study by Smith (1953) used few animals of one sex only. It was not indicated in the paper whether the 50% mortality observed early in the study was considered treatment-related, nor was the cause of death indicated. This is the only subchronic bioassay of dibutyl phthalate reported in the literature. Confidence in the study, database, and RfD are all rated low.

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

Source Document — U.S. EPA, 1980

The RfD in the 1980 Ambient Water Quality Criteria document received extensive peer and public review.

Other EPA Documentation — None

Agency Work Group Review — 01/22/1986

Verification Date — 01/22/1986

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 Dibutyl phthalate conducted in November 2001 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.

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)

Substance Name — Dibutyl phthalate
CASRN — 84-74-2

The health effects data for dibutyl phthalate were reviewed by the U.S. EPA RfD/RfC Work Group and determined to be inadequate for derivation of an inhalation RfC. For additional information on health effects of this chemical interested parties are referred to the EPA documentation listed below.

U.S. EPA. 1987. Drinking Water Criteria Document for Phthalic Acid Esters Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. (External Review Draft)

Agency Work Group Review — 07/26/1990

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfC for Dibutyl phthalate conducted in November 2001 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.

EPA Contacts:

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).

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Dibutyl phthalate
CASRN — 84-74-2
Last Revised — 09/07/1988

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.

Basis — Pertinent data regarding carcinogenicity was not located in the available literature.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

None.

II.A.4. Supporting Data for Carcinogenicity

DBP did not induce mutations in a modified reverse mutation plate incorporation assay in Salmonella strains TA100 and TA98 at concentrations up to 1000 ug/plate in the presence or the absence of S9 hepatic homogenate (Kozumbo et al., 1982). It was a weak direct-acting mutagen in a forward mutation assay in Salmonella typhimurium (Seed, 1982). DBP was mutagenic in the mouse lymphoma forward mutation assay only in the presence of metabolic activation (CMA, 1986). In addition, DBP showed some evidence of clastogenic activity in Chinese hamster fibroblasts (Ishidate and Odashima, 1977) but was negative in human leukocytes (Tsuchiya and Hattori, 1977). Research indicates that DBP is hydrolyzed to monoesters (Kluwe, 1982; Rowland et al., 1977; Albro and Moore, 1974). There is evidence that DBP induces peroxisome proliferation (U.S. EPA, 1987).

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

Not available.

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, 1987

The Drinking Water Criteria Document for Phthalic Acid Esters has received OHEA review.

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

Agency Work Group Review — 08/26/1987

Verification Date — 08/26/1987

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 Dibutyl

phthalate conducted in November 2001 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 — Dibutyl phthalate
CASRN — 84-74-2

VI.A. Oral RfD References

Gangolli, S.D. 1982. Testicular effects of phthalate esters. Environ. Health Perspect. 45: 77-84.

Shiota, K. and H. Nishimura. 1982. Teratogenicity of di-2-ethylhexyl phthalate and di-n-butyl phthalate in mice. Environ. Health Perspect. 45(0): 65-70.

Smith C.C. 1953. Toxicity of butyl sterate, dibutyl sebacate, dibutyl phthalate and methoxyethyl oleate. Arch. Hyg. Occup. Med. 7: 310-318.

U.S. EPA. 1980. Ambient Water Quality Criteria for Phthalate Esters. 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 440/5-80-067. NTIS PB 81- 117780.

VI.B. Inhalation RfC References

U.S. EPA. 1987. Drinking Water Criteria Document for Phthalic Acid Esters Prepared by the Office of Health and Environmental Assessement, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. (External Review Draft)

VI.C. Carcinogenicity Assessment References

Albro, P.W. and B. Moore. 1974. Identification of the metabolites of simple phthalate diesters in rat urine. J. Chromatogr. 94: 209-218.

CMA (Chemical Manufacturers Association). 1986. Mutagenicity of 1C (di-n- butyl phthalate) in a mouse lymphoma mutation assay. Final report. Submitted to Hazleton Biotechnologies Company. HB Project No. 20989. September, 1986.

Ishidate, M., Jr. and S. Odashima. 1977. Chromosome tests with 134 compounds on Chinese hamster cells in vitro -- A screening test for chemical carcinogens. Mutat. Res. 48: 337-354.

Kluwe, W.M. 1982. Overview of phthalate ester pharmacokinetics in mammalian species. Environ. Health Perspect. 45: 3-10.

Kozumbo, W.J., R. Kroll and R.J. Rubin. 1982. Assessment of the mutagenicity of phthalate esters. Environ. Health Perspect. 45: 103-109.

Rowland, I.R., R.C. Cottrell and J.C. Phillips. 1977. Hydrolysis of phthalate esters by the gastro-intestinal contents of the rat. Food Cosmet. Toxicol. 15: 17-21.

Seed, J.L. 1982. Mutagenic activity of phthalate esters in bacterial liquid suspension assays. Environ. Health Perspect. 45: 111-114.

Tsuchiya, K. and K. Hattori. 1977. Chromosomal study on human leukocyte cultures treated with phthalic acid ester. Hokkaidoritus Eisei Kenkyusho Ho. 26: 114. (Abstract)

U.S. EPA. 1987. Drinking Water Criteria Document for Phthalic Acid Esters. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. External Review Draft.

VII. Revision History

Substance Name — Dibutyl phthalate
CASRN — 84-74-2

Date	Section	Description
09/07/1988	II.	Carcinogen summary on-line
10/01/1990	I.B.	Inhalation RfC message on-line
12/03/2002	I.A.6., I.B., II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Dibutyl phthalate
CASRN — 84-74-2
Last Revised — 01/31/1987

- 84-74-2
- 1,2-Benzenedicarboxylic Acid Dibutyl Ester
- o-Benzenedicarboxylic Acid, Dibutyl Ester
- Benzene-o-Dicarboxylic Acid Di-n-Butyl Ester
- Butylphthalate
- Celluflex DPB
- Dibutyl 1,2-Benzene dicarboxylate
- Dibutyl phthalate
- Di-n-Butylphthalate
- Dibutyl-o-Phthalate
- DPB
- Elaol
- Ergoplast FDB
- Genoplast B
- Hexaplast M/B

- N-Butylphthalate
- Palatinol C
- Phthalic Acid Dibutyl Ester
- Polycizer DBP
- PX 104
- RC Plasticizer DBP