

Bisphenol A; CASRN 80-05-7

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 Bisphenol A.

File First On-Line 09/26/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/26/1988
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Bisphenol A.

CASRN — 80-05-7

Last Revised — 09/26/1988

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
Reduced mean body weight	NOEL: None	1000	1	5E-2 mg/kg/day
Rat Chronic Oral Bioassay	LOAEL: 1000 ppm diet (50 mg/kg/day)			
NTP, 1982				

*Conversion Factors: Assumed food consumption equivalent to 5% of body weight/day

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

NTP (National Toxicology Program). 1982. NTP Technical report on the carcinogenesis bioassay of bisphenol A (CAS No. 80-05-7) in F344 rats and B6C3F1 mice (feed study). NTP-80-35. NIH Publ. No. 82-1771.

In this 103-week dietary study, groups of 50 rats/sex were fed diets containing 0, 1000, or 2000 ppm bisphenol A. All treated groups of rats had reduced body weights, compared with controls, evident from the 5th week of exposure. Food consumption was also reduced, compared with controls, but this effect was not observed until the 12th week of treatment. Reduced body weights in rats, therefore, was considered a direct adverse effect of exposure to bisphenol A.

In the same study (NTP, 1982), male mice (50/group) were fed diets containing 0, 1000, or 5000 ppm bisphenol A and female mice (50/group) were fed 0, 5000, or 10,000 ppm bisphenol A. Male mice at 5000 ppm and female mice at 5000 and 10,000 had reduced body weights. At 1000 and 5000 ppm, there was an increase in the number of multinucleated giant hepatocytes in male mice. This effect was not considered to be adverse, and this level is a NOAEL in mice.

Assuming a food factor for mice of 0.13, this dietary concentration corresponds to a dosage of 130 mg/kg/day. Because the LOAEL of 50 mg/kg/day in rats is less than the NOAEL of 130 mg/kg/day in mice, the NOAEL in mice cannot be chosen as a basis for the RfD. The LOAEL of

50 mg/kg/day in rats, the lowest dosage used in either species in the chronic studies, is chosen as the basis for a chronic oral RfD.

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

UF — The UF of 1000 includes 10 for uncertainty in the extrapolation of dose levels for animals to humans, 10 for uncertainty in the threshold for sensitive humans, and 10 for uncertainty in the effects of duration on toxicity when extrapolating for subchronic to chronic exposure.

MF — None

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

Three subchronic oral toxicity studies of bisphenol A have been considered using dogs, rats and mice (U.S. EPA, 1984a,b,c; NTP, 1982). The only toxic effect seen in beagle dogs fed 1000-9000 ppm bisphenol A in the diet for 90 days was an increase in group mean liver weight in the high-dose group (U.S. EPA, 1984a). The only effect seen in 2-generation bisphenol A feeding studies (100-9000 ppm) conducted with Charles River rats (U.S. EPA, 1984b,c) were decreases in body weight in the F0 generation at 9000 ppm and F1 generation at greater than or equal to 1000 ppm. Rats and mice of both sexes were fed bisphenol A (250 to 4000 ppm rats; 5000 to 25,000 ppm mice) in the diet for 90 days (NTP, 1982). Doses >1000 ppm produced decreased body weight in both sexes of rats with no alteration in food consumption. Male mice receiving >15,000 ppm and all treated females had decreased body weight gain compared with controls. A dose-related increase in severity of multinucleated giant hepatocytes was found in the treated male mice.

In mice, a dosage of 1250 mg/kg/day was associated with fetotoxicity and maternal toxicity, but did not cause a significant increase in the incidence of malformations at any dose level (NTP, 1985a). In rats, dosages of less than or equal to 1280 mg/kg/day were not toxic and did not cause malformations to the fetus (NTP, 1985b).

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — High

RfD — High

Confidence in the key study is medium because this study, although well controlled and performed, failed to identify a chronic NOAEL for reduced body weight, the critical effect, in rats, the most sensitive species. Confidence in the database is high, however, because the

subchronic studies in rats indicate that the NOAEL for reduced body weight in rats is probably not far below the LOAEL of 1000 ppm of the diet and the uncertainty factor of 10 to estimate a NOAEL from the LOAEL is probably conservative. The developmental toxicity of bisphenol A has been adequately investigated. Confidence in the RfD, therefore, is high.

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

Source Document — U.S. EPA, 1987

Other EPA Documentation — U.S. EPA, 1984a,b,c

Agency Work Group Review — 09/16/1987, 03/24/1988, 04/20/1988

Verification Date — 04/20/1988

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 Bisphenol A. conducted in September 2002 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 — Bisphenol A.

CASRN — 80-05-7

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Bisphenol A.
CASRN — 80-05-7

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Bisphenol A.
CASRN — 80-05-7

VI.A. Oral RfD References

NTP (National Toxicology Program). 1982. NTP Technical Report on the carcinogenesis bioassay of bisphenol A (CAS No. 80-05-7) in F344 rats and B6C3F1 mice (feed study). NTP-80-35. NIH Publ. No. 82-1771.

NTP (National Toxicology Program). 1985a. Teratologic evaluation of bisphenol A (CAS No. 80-05-7) administered to CD-1 mice on gestational days 6-15. NTP, NIEHS, Research Triangle Park, NC.

NTP (National Toxicology Program). 1986a. Teratologic evaluation of bisphenol A (CAS No. 80-05-7) administered to CD(R) rats on gestational days 6-15. NTP, NIEHS, Research Triangle Park, NC.

U.S. EPA. 1984a. Ninety-day oral toxicity study in dogs. Office of Pesticides and Toxic Substances. Fiche No. OTS0509954.

U.S. EPA. 1984b. Reproduction and ninety-day oral toxicity study in rats. Office of Pesticides and Toxic Substances. Fiche No. OTS0509954.

U.S. EPA. 1984c. Fourteen-day range finding study in rats. Office of Pesticides and Toxic Substances. Fiche No. OTS0509954.

U.S. EPA. 1987. Health and Environmental Effects Document on Bisphenol A. 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.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Bisphenol A
CASRN — 80-05-7

Date	Section	Description
09/26/1988	I.A.	Oral RfD summary on-line
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Bisphenol A.

CASRN — 80-05-7

Last Revised — 09/26/1988

- 80-05-7
- bisferol A
- Bishpenol A.
- 2,2-bis-4'-hydroxyfenylpropan
- bis(4-hydroxyphenyl) dimethylmethane
- 2,2-bis(4-hydroxyphenyl)propane
- 2,2-bis(p-hydroxyphenyl)propane
- bis(4-hydroxyphenyl)propane
- bisphenol
- bisphenol A
- Bisphenol A.
- 4,4'-bisphenol A
- dian
- 4,4'-dihydroxydiphenyldimethylmethane
- p,p'-dihydroxydiphenyldimethylmethane
- 2,2-(4,4'-dihydroxydiphenyl)propane
- 4,4'-dihydroxydiphenylpropane
- 4,4'-dihydroxydiphenyl-2,2-propane
- p,p'-dihydroxydiphenylpropane
- 2,2-di(4-hydroxyphenyl)propane
- beta-di-p-hydroxyphenylpropane
- dimethyl bis(p-hydroxyphenyl)methane
- dimethylmethylene-p,p'-diphenol
- diphenylolpropane
- 2,2-di(4-phenylol)propane
- 4,4'-isopropylidenebisphenol
- p,p'-isopropylidenebisphenol
- p,p'-isopropylidenediphenol
- NCI-C50635
- phenol, 4,4'-dimethylmethylenedi-
- phenol, 4,4'-isopropylidenedi-
- propane, 2,2-bis(p-hydroxyphenyl)-