1,2,4-Tribromobenzene; CASRN 615-54-3

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 1,2,4-Tribromobenzene

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.)	not evaluated	

*A comprehensive review of toxicological studies was completed (2004) - please see section I.A.6 for more information.

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — 1,2,4-Tribromobenzene
CASRN — 615-54-3
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
Increased liver-to-body weight ratio and hepatic microsomal enzyme induction **Rat Oral Subchronic Study** **Carlson and Tardiff, 1977**	NOAEL: 5 mg/kg/day LOAEL: 10 mg/kg/day	1000	1	5E-3 mg/kg/day

*Conversion Factor and Assumptions -- None

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

Carlson, G.P. and R.G. Tardiff. 1977. Effect of 1,4-dibromobenzene and 1,2,4-tribromobenzene on xenobiotic metabolism. Toxicol. Appl. Pharmacol. 42: 189-196.

Six male rats/group were dosed daily with 0, 2.5, 5 or 10 mg 1,2,4- tribromobenzene (TBB)/kg bw for 45 or 90 days. TBB was administered in corn oil p.o. as 0.1% of body weight. Controls received corn oil only. Animals were sacrificed at 45 or 90 days or after an additional 30-day recovery period after 90 days of treatment. Body weight, liver weight, and hepatic microsomal enzyme activity were measured. Liver-to-body weight ratios were increased 12- 16% over controls for the rats treated at 10 mg/kg/day. Liver enzyme activities were 1.4- to 3-fold that of controls for the same group. Full recovery to baseline enzyme activity was observed after the 30-day recovery period; liver-to-body weight ratios were only 7% greater than the control values. Similar results were reported by Carlson (1979) in a follow-up study.

Although no overt liver toxicity was demonstrated for TBB, bromobenzene mixtures at higher doses cause acute hepatic necrosis. The mechanism of bromobenzene toxicity has been studied in detail and involves conversion of the parent compound to toxic intermediates by hepatic microsomal enzymes. Induction of these enzymes can potentiate the toxicity of bromobenzenes and other similarly-activated compounds.

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

UF — The uncertainty factor includes factors for interspecies variability, subchronic-to-chronic exposure duration extrapolation, and intrahuman variability.

MF — None

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

None.

I.A.5. Confidence in the Oral RfD

Study — Low
Database — Low
RfD — Low

Low confidence levels were assigned to both the study and the database because of the lack of adequate toxicity parameters in the critical study, the lack of chronic toxicity data in general, and a degree of uncertainty about the significance of the effects. Low confidence in the RfD follows.

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

Source Document — U.S. EPA, 1984

Other EPA Documentation — None

Agency Work Group Review — 10/09/1985, 05/15/1986

Verification Date — 05/15/1986

A comprehensive review of toxicological studies published prior to 2004 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing RfD for 1,2,4-Tribromobenzene and a change in the RfD is not warranted at this time.

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 — 1,2,4-Tribromobenzene
CASRN — 615-54-3

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 1,2,4-Tribromobenzene
CASRN — 615-54-3

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 — 1,2,4-Tribromobenzene
CASRN — 615-54-3

VI.A. Oral RfD References

Carlson, G.P. 1979. Brominated benzene induction of hepatic porphyria. Experimentia. 35(4): 513-514.

Carlson, G.P. and R.G. Tardiff. 1977. Effect of 1,4-dibromobenzene and 1,2,4-tribromobenzene on xenobiotic metabolism. Toxicol. Appl. Pharmacol. 42: 189-196.

U.S. EPA. 1984. Health and Environmental Effects Profile for Bromobenzene. Prepared by the Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC. NTIS PB88-137757/AS.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — 1,2,4-Tribromobenzene
CASRN — 615-54-3

Date	Section	Description
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.
09/29/2004	I.A.6.	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

VIII. Synonyms

Substance Name — 1,2,4-Tribromobenzene
CASRN — 615-54-3
Last Revised — 03/31/1987

- 615-54-3
- Benzene, 1,2,4-tribromo- (8CI)(9CI)
- 1,2,4-Tribromobenzene
- Tribromobenzene, 1,2,4-