m-Phenylenediamine; CASRN 108-45-2

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 m-Phenylenediamine

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.)	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 — m-Phenylenediamine
CASRN — 108-45-2
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.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Increased relative and absolute liver weights and degenerative liver lesions **Rat Oral Subchronic Study** **Hofer et al., 1982**	NOEL: 6.0 mg/kg/day LOAEL: 18.0 mg/kg/day	1000	1	6E-3 mg/kg/day

*Conversion Factor: none

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

Hofer, H., R. Hruby, E Hruby, et al. 1982. Ninety-day toxicity study with m- phenylenediamine on rats. Oestrr. Forschungszent. Seibersdorf (Ber.) OEFZS Ber. No. 4155. p. 1-46.

In the Hofer et al. (1982) study, groups of rats (20/sex/dose) were treated with 0, 2, 6, or 18.0 mg/kg/day m-phenylenediamine. The compound was administered orally as an aqueous solution for 90 days. No effect was observed on body weight, food consumption, ophthalmology, hematology, or blood and urine biochemistry of treated rats. A significant increase in relative and absolute liver weight, accompanied by an increased incidence of degenerative liver lesions occurred in rats treated with 18.0 mg/kg/day m- phenylenediamine. Female rats treated at the 18 mg/kg/day dose also had significantly increased relative kidney weights. Based on these findings, a NOEL of 6.0 mg/kg/day and a LOAEL of 18.0 mg/kg/day were established and an RfD of 0.006 mg/kg/day was derived.

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

UF — An uncertainty factor of 1000 was applied: 10 for interspecies variability, 10 for intraspecies variability and 10 for the use of subchronic data.

MF — None

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

Teratogenic studies of m-phenylenediamine in mice and rats have been conducted by a number of investigators (Bumett et al., 1976; Hruby et al., 1981; Picciano et al., 1983) with equivocal results.

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

The principal study was well designed and established a clear NOEL and LOAEL; however, testing was done in only one species for a subchronic period of time. Thus, the study was assigned a medium level of confidence. The database contains no other subchronic or chronic oral toxicity studies and no epidemiologic data and, therefore, a low confidence was assigned to the database. Until further chronic/reproductive studies are conducted, a low confidence in the RfD is recommended.

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

Source Document — U.S. EPA, 1985

The Health and Environmental Effects Profile has received extensive Agency- wide and external review.

Other EPA Documentation — None

Agency Work Group Review — 02/26/1986

Verification Date — 02/26/1986

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 m-Phenylenediamine 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 — m-Phenylenediamine
CASRN — 108-45-2

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — m-Phenylenediamine
CASRN — 108-45-2

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 — m-Phenylenediamine
CASRN — 108-45-2

VI.A. Oral RfD References

Burnett, C., E.I. Goldenthal and S.B. Harris, et al. 1976. Teratology and percutaneous toxicity studies on hair dyes. J. Toxicol. Environ. Health. 1(6): 1027-1040.

Hofer, H., R. Hruby, E. Hruby, et al. 1982. Ninety-day toxicity study with m-phenylenediamine on rats. Oestrr. Forschungszent. Seibersdorf (Ber.) OEFZS Ber. No. 4155. p. 1-46.

Hruby, E., R. Paar, K. Lippl, B. Schwarzinger and H. Hofer. 1981. Teratological studies with m-phenylenediamine on rats. Oesterr. Forschungszent. Seibersdorf. No. 4132. p. 1-36.

Picciano, J.C., W.E. Morris, S. Kwan and B.A. Wolf. 1983. Evaluation of teratogenic and mutagenic potential of the oxidative dyes, 4-chlororesorcinol, m-phenylenediamine and pyrogallol. J. Am. Coll. Toxicol. 2(4): 325-333.

U.S. EPA. 1985. Health and Environmental Effects Profile for Phenylenediamine. 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 — m-Phenylenediamine
CASRN — 108-45-2

Date	Section	Description
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — m-Phenylenediamine
CASRN — 108-45-2
Last Revised — 01/31/1987

- 108-45-2
- m-AMINOALINE
- 3-AMINOANILINE
- APCO 2330
- 1,3-BENZENEDIAMINE
- m-BENZENEDIAMINE
- C.I. 76025
- 1,3-DIAMINOBENZENE
- m-DIAMINOBENZENE
- DIRECT BROWN BR
- DIRECT BROWN GG
- m-FENYLENDIAMIN
- METAPHENYLENEDIAMINE
- 1,3-PHENYLENEDIAMINE
- Phenylenediamine, m-
- PHENYLENEDIAMINE, META, solid
- UN 1673