3,4-Dimethylphenol; CASRN 95-65-8

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 3,4-Dimethylphenol

File First On-Line 09/07/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/07/1988*
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

*A comprehensive review of toxicological studies was completed 01/05/05 - 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 — 3,4-Dimethylphenol
CASRN — 95-65-8
Last Revised — 09/07/1988

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
Changes in blood pressure and body weight; histo-pathological changes in liver, kidney and spleen **Rat Oral 1-Year Study** **Veldre and Janes, 1979**	NOEL: 1.4 mg/kg/day LOAEL: 14 mg/kg/day	1000	1	1E-3 mg/kg/day

*Conversion Factors -- none

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

Veldre. I.A. and H.J. Janes. 1979. Toxicological studies of shale oils, some of their components and commercial products. Environ. Health Perspect. 30: 141-146.

Veldre and Janes (1979) reported a study where 3,4-dimethylphenol was administered orally to white rats for an 8-month period. No toxic effects were seen at 1.4 mg/kg/day (NOEL) but a dose of 14 mg/kg/day resulted in body weight, blood pressure and histopathological changes in internal organs (LOAEL). Applying an uncertainty factor of 1000 to the NOEL of 1.4 mg/kg/day results in the RfD of 1E-3 mg/kg/day.

A LOAEL of 14 mg/kg/day was also identified from a study reported by Maazik (1967, 1968, 1970). In this study, male albino rats were given 3,4- dimethylphenol orally at doses of 0.14 and 14 mg/kg/day for 8 months. No effects were observed at the 0.14 mg/kg/day dose (NOEL). The

toxic symptoms reported at the higher or LOAEL dose were similar to those reported by Veldre and Janes (1979).

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

UF — 10 for interspecies extrapolation, 10 for the range of sensitivities within a population and 10 for the use of subchronic exposure data.

MF — None

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

Pertinent data regarding teratogenicity or reproductive effects of 3,4- dimethylphenol were not located in the literature. No chronic toxicity studies were located on 3,4-dimethylphenol. All the available subchronic studies were from the Russian literature and few details were reported.

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

The study reported by Veldre and Janes (1979) represents a subchronic oral animal study which not only supported the adverse effects (LOAEL) reported by Maazik (1968), but also provided an intermediate NOEL not tested by Maazik (1968). Therefore, the confidence in the study is considered medium. The database is considered low, since no studies were available other than those reported by Maazik (1967, 1968, 1970) to provide support for the RfD. Chronic and reproductive studies are needed to support a higher level of confidence in the RfD.

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

Source Document — U.S. EPA, 1986

Limited Peer Review and Extensive Agency-Wide Review, 1986.

Other EPA Documentation — None

Agency Work Group Review — 01/22/1986

Verification Date — 01/22/1986

A comprehensive review of toxicological studies published through 2004 was conducted. No new health effects data were identified that would be directly useful in the revision of the existing RfD for 3,4-Dimethylphenol and a change in the RfD is not warranted at this time. For more information, IRIS users may contact 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 — 3,4-Dimethylphenol
CASRN — 95-65-8

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 3,4-Dimethylphenol
CASRN — 95-65-8

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 — 3,4-Dimethylphenol
CASRN — 95-65-8

VI.A. Oral RfD References

Maazik, I.Kh. 1967. Standards for dimethylphenol isomers in water bodies. Gig Sanit. (Hygiene and Sanitation) 11: 28-35. (Rus.)

Maazik, I.Kh. 1968. Dimethylphenol (xylenol) isomers and their standard contents in water reservoirs. Gig Sanit. (Hygiene and Sanitation) 33(9): 18-22. (Rus.)

Maazik, I.Kh. 1970. Toxicity of small dimethylphenol doses in chronic experiments. Vop. Gig. Tr. Prof. Patol. Est. SSR. 2: 171-176. (Rus.)

Veldre, I.A. and H.J. Janes. 1979. Toxicological studies of shale oils, some of their components, and commercial products. Environ. Health Perspect. 30: 141-146.

U.S. EPA. 1986. Health and Environmental Effects Profile for 3,4- Dimethylphenol. 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 — 3,4-Dimethylphenol
CASRN — 95-65-8

Date	Section	Description
09/07/1988	I.A.	Oral RfD summary on-line
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.
03/03/2005	I.A.6.	Screening-Level Literature Review Findings message has been removed and replaced by comprehensive literature review conclusions.

VIII. Synonyms

Substance Name — 3,4-Dimethylphenol
CASRN — 95-65-8
Last Revised — 09/07/1988

- 95-65-8
- 3,4-Dimethylphenol
- Dimethylphenol, 3,4-
- 4,5-DIMETHYLPHENOL
- 3,4-DMP
- PHOSPHONOTHIOIC ACID, PHENYL-, O-ETHYL O-(p-NITROPHENYL)ESTER
- 1,3,4-XYLENOL