2,4-Dimethylphenol; CASRN 105-67-9

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 2,4-Dimethylphenol

File First On-Line 11/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	11/01/1990
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 — 2,4-Dimethylphenol
CASRN — 105-67-9
Last Revised — 11/01/1990

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
Clinical signs (lethargy, prostration, and ataxia) and hematological changes **Mouse Subchronic Oral Gavage** **U.S. EPA, 1989**	NOAEL: 50 mg/kg/day LOAEL: 250 mg/kg/day	3000	1	2E-2 mg/kg/day

* Conversion Factors: None

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

U.S. EPA. 1989. Ninety-day gavage study in Albino mice using 2,4- dimethylphenol. Study No. 410-2831, prepared by Dynamac Corporation, Rockville, MD, for the Office of Solid Waste and Emergency Response, Washington, DC.

2,4-Dimethylphenol was administered daily to male and female albino mice by gavage. The animals (30/sex/group) were dosed for 90 days with 5.0, 50.0, or 250 mg 2,4-dimethylphenol/kg/day. Two control groups, untreated and vehicle (corn oil), of similar size were also established. Effects examined included mortality, clinical signs, body weights, food consumption, opthalmology, hematology and clinical chemistry, organ weights, and gross histopathology. Although 15 deaths occurred during this study (mostly because of errors in technical procedure), only one was considered as possibly treatment-related: a male in the 5 mg/kg/day-dose group died during the first 30 days of the experiment. No significant differences were found between treated and vehicle control groups in mean body weight, body weight gains, food consumption, or eye examinations at any dosage. Toxicologically relevant clinical signs observed only after week 6 in the high-dose groups of both genders included: squinting, lethargy, prostration, and ataxia, with onset shortly after dosing. Statistically significant hematological

changes ($p<0.05$) included lower mean corpuscular volume and mean corpuscular hemoglobin concentration in females at terminal, but not interim, sacrifice.

At interim sacrifice in female mid- and high-dose groups, blood urea nitrogen (BUN) levels were significantly below vehicle controls; whereas at final sacrifice in the female mid-dose group, BUN levels were significantly higher than vehicle controls. Low-dose males at interim sacrifice had significantly higher cholesterol levels. Significant differences were not found in gross necropsy or histopathological evaluations, or in organ weights, except for an increase in adrenal weights of low-dose females. The LOAEL and NOAEL for this study were 250 and 50 mg/kg/day, respectively.

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

UF — An uncertainty factor of 3000 was established: 10 each for inter- and intraspecies variability and 30 for lack of chronic toxicity data, data in a second species and reproductive/developmental studies.

MF — None

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

A 14-day gavage study with 2,4-dimethylphenol conducted by the same laboratory that conducted the principal study, revealed lethargy, prostration, and ataxia in males and females in the 250 mg/kg/day-dose group, the same dose at which effects were found in the principal study (U.S. EPA, 1987).

No other long-term toxicity, reproductive, or developmental studies of 2,4- dimethylphenol were found in the databases searched. Literature concerning 2,6-dimethylphenol was identified, but an SAR-based RfD is considered inappropriate when a valid long-term toxicity study for 2,4-dimethylphenol is available.

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

Confidence in the study is medium, since it examined appropriate endpoints and identified both a LOAEL and a NOAEL. The results of this study are consistent with those of a 14-day gavage

study. The database provides no information on chronic and reproductive studies. Low confidence in both the database and oral RfD follows.

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

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — None

Agency Work Group Review — 02/21/1990

Verification Date — 02/21/1990

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 2,4-Dimethylphenol 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 — 2,4-Dimethylphenol
CASRN — 105-67-9

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 2,4-Dimethylphenol
CASRN — 105-67-9

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 — 2,4-Dimethylphenol
CASRN — 105-67-9

VI.A. Oral RfD References

U.S. EPA. 1987. Fourteen-day gavage study in Albino mice using 2,4- dimethylphenol. Study No. 410-2830, prepared by Dynamac Corporation, Rockville, MD for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1989. Ninety-day gavage study in Albino mice using 2,4- dimethylphenol. Study No. 410-2831, prepared by Dynamac Corporation, Rockville, MD, 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 — 2,4-Dimethylphenol
CASRN — 105-67-9

Date	Section	Description
11/01/1990	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 — 2,4-Dimethylphenol
CASRN — 105-67-9
Last Revised — 11/01/1990

- 105-67-9
- Phenol, 2,4-dimethyl-
- Caswell No. 907A
- EPA Pesticide Chemical Code 086804
- HSDB 4253
- m-XYLENOL
- NSC 3829
- RCRA WASTE NUMBER U101
- 1-HYDROXY-2,4-DIMETHYLBENZENE
- 2,4-dimethylphenol
- 2,4-Xylenol
- 4-HYDROXY-1,3-DIMETHYLBENZENE
- 4,6-DIMETHYLPHENOL