Dimethyl sulfate; CASRN 77-78-1

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 Dimethyl sulfate

File First On-Line 09/07/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	message	01/01/1992
Carcinogenicity Assessment (II.)	yes	09/07/1988

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Dimethyl sulfate
CASRN — 77-78-1

Not available at this time.

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Dimethyl sulfate
CASRN — 77-78-1

The health effects data for dimethyl sulfate were reviewed by the U.S. EPA RfD/RfC Work Group and determined to be inadequate for derivation of an inhalation RfC. For additional information on the health effects of this chemical, interested parties are referred to the EPA documentation listed below.

U.S. EPA. 1985. Health and Environmental Effects Profile for Dimethyl Sulfate. 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. NTIS/PB88-173620.

Agency Work Group Review — 09/12/1991

EPA Contacts:

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).

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfC for Dimethyl sulfate conducted in August 2003 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.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Dimethyl sulfate
CASRN — 77-78-1
Last Revised — 09/07/1988

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day.

The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-of-Evidence Characterization

Classification — B2; probable human carcinogen

Basis — Classification is based on induction of local carcinomas following inhalation and subcutaneous exposures in rats, tumor induction in rats following prenatal exposure, and evidence suggestive of carcinogenicity in hamsters and mice by inhalation. Dimethyl sulfate alkylates cellular macromolecules and is genotoxic.

II.A.2. Human Carcinogenicity Data

Inadequate. IARC (1979) reviewed an unpublished epidemiologic study by Pell (n.d.). Among workers occupationally exposed to dimethyl sulfate (number unspecified), six cancer deaths were reported vs. the expected mortality of 2.4. Respiratory tract cancer was responsible for three of the deaths (1.02 expected). Neither the increased incidence of respiratory tract cancer nor the increased rate of cancer at all sites was statistically significant. Four cases of bronchial carcinomas were reported in a group of 7 to 11 workers occupationally exposed to dimethyl sulfate (Druckrey et al., 1966). Although occasional dimethyl sulfate intoxication was noted in all of the workers, additional information regarding the exposures is not available.

II.A.3. Animal Carcinogenicity Data

Sufficient. Druckrey et al. (1970) treated 27 and 20 BD rats with 10 or 3 ppm dimethyl sulfate vapor, respectively, for 1 hour/day, 5 days/week for 130 days. After 643 days, one rat in the high-dose group was observed to have a cerebellar tumor and two low-dose group rats had nervous system tumors. These types of tumors are very rare and were observed distant from the exposure site. Although no concurrent control group was reported, in a later report Druckrey (1973) stated that the spontaneous rate of neurological tumors in BD rats was <1 per 1000.

Additional tumors were observed at 3 ppm (one squamous cell carcinoma of the nasal epithelium) and at 10 ppm (three squamous cell carcinomas of the nasal epithelium and one lymphosarcoma of the thorax with multiple metastases to the lung).

Druckrey et al. (1966) injected 17 and 8 BD rats subcutaneously with 8 and 16 mg/kg/week, respectively, dimethyl sulfate for 394 and 343 days, respectively. Injection-site sarcomas were reported in 7/11 of the surviving low-dose rats and 4/6 of the surviving high-dose rats, with occasional metastases to the lung. One hepatic carcinoma was reported in the rats exposed to 8 mg/kg/week dimethyl sulfate. Although the duration of the study was not reported, the mean tumor induction time was 500 days. Rats treated with a single subcutaneous injection of 50 mg/kg developed local sarcomas of the connective tissue in 7/15 rats within 740 days of treatment, with multiple metastases to the lungs in three cases (Druckrey et al., 1970).

In the same experiment, Druckrey injected 12 BD rats intravenously once a week with 2 or 4 mg/kg dimethyl sulfate for 800 days. No tumors were reported. A single intravenous dose of 20 mg/kg dimethyl sulfate given to eight pregnant BD rats on day 15 of gestation induced malignant tumors in 7/59 offspring observed for over 1 year (Druckrey et al., 1970). However, according to a review of this study by Druckrey (1973), 4/59 offspring had malignant tumors of the nervous system while 2/59 offspring had malignant hepatic tumors. No control data were reported.

Schlogel and Bannasch (1970) treated groups of 10 Golden hamsters, Wistar rats, and NMRI mice of each sex with 0.5 or 2.0 ppm dimethyl sulfate vapor, 6 hours/day, 2 days/week for 15 months. The animals were followed for an additional 15-month period. Tumors were observed in the lungs, thorax and nasal passages. The meaning of these results is unclear because control data were not reported nor were tumor incidences tabulated by species or dose.

II.A.4. Supporting Data for Carcinogenicity

Hoffman (1980) extensively reviewed the genetic effects of dimethyl sulfate, which does not require metabolic activation to elicit its mutagenicity. Dimethyl sulfate was positive in reverse mutation assays in S. typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 (Skopek et al., 1978). Positive results were observed in Bacillus subtilis (Bresler et al., 1968; Zamenhof and Arikawa, 1970), in S. cerevisiae (Prakash and Sherman, 1973), in Neurospora crassa (Kolmark, 1956), and in Ophiostoma multiannulation (Zetterberg, 1960). Mutagenicity was reported in Aspergillus nidulans (Moura Duarte, 1971), Chinese hamster ovary cells (Couch et al., 1978) and in sex-linked recessive lethal mutation assays in Drosophilia (Rapoport, 1947; Kolmark, 1956; Alderson, 1964). Dimethyl sulfate produces chromatid aberrations in mouse ascites tumor cells (Schoneich et al., 1970), and sister chromatid exchange (Wolff et al., 1977) and DNA damage (Cleaver, 1977) in human fibroblasts and cultured rat hepatocytes (Probst et al., 1981). Dimethyl sulfate is a potent alkylating agent for cellular macromolecules.

II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

Not available.

II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

Not available.

II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1985, 1986

The 1985 Health and Environmental Effects Profile for Dimethyl Sulfate has received Agency Review.

II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review — 05/13/1987

Verification Date — 05/13/1987

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for Dimethyl sulfate conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

II.D.3. EPA Contacts (Carcinogenicity Assessment)

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).

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Dimethyl sulfate
CASRN — 77-78-1

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

U.S. EPA. 1985. Health and Environmental Effects Profile for Dimethyl Sulfate. 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. NTIS/PB88-173620.

VI.C. Carcinogenicity Assessment References

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U.S. EPA. 1986. Evaluation of the Potential Carcinogenicity of Dimethyl Sulfate. Prepared by the Office of Health and Environmental Assessment, Carcinogen Assessment Group, Washington, DC for the Office of Emergency and Remedial Response and the Office of Solid Waste and Emergency Response, Washington, DC. (Review Draft).

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VII. Revision History

Substance Name — Dimethyl sulfate
CASRN — 77-78-1

Date	Section	Description
09/07/1988	II.	Carcinogen summary on-line
01/01/1992	I.B.	Inhalation RfC message on-line
10/28/2003	I.B., II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Dimethyl sulfate
CASRN — 77-78-1
Last Revised — 09/07/1988

- 77-78-1
- dimethyl monosulfate
- Dimethyl Sulfate
- DMS
- methyl sulfate