SCREENING-LEVEL HAZARD CHARACTERIZATION

Dimethyl Sulfoxide (CASRN 67-68-5)

The High Production Volume (HPV) Challenge Program[1] was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to "SIDS" (Screening Information Data Set[1,2]) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency's Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance[2,3] and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor's responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT's focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

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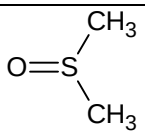
[1] U.S. EPA. High Production Volume (HPV) Challenge Program; http://www.epa.gov/chemrtk/index.htm.
[2] U.S. EPA. HPV Challenge Program – Information Sources; http://www.epa.gov/chemrtk/pubs/general/guidocs.htm.
[3] U.S. EPA. Risk Assessment Guidelines; http://cfpub.epa.gov/ncea/raf/rafguid.cfm.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public.

Chemical Abstract Service Registry Number (CASRN)	**67-68-5**
Chemical Abstract Index Name	**Methane, 1,1'-sulfinylbis-**
Structural Formula	

Summary

This chemical is a liquid with high water solubility and moderate vapor pressure. It is expected to have high mobility in soil. Volatilization of this chemical from water and moist soil is considered low based on its Henry's Law constant. The rate of hydrolysis is considered negligible to low. The rate of atmospheric photooxidation is considered moderate. This chemical is expected to have low persistence (P1) and low bioaccumulation potential (B1).

The acute oral toxicity of this chemical in rats and mice is low, and the acute inhalation toxicity in rats in low. It is mildly irritating to rabbit skin and eyes. This chemical is not a skin sensitizer in guinea pigs and mice. Repeated-dose studies showed a NOAEC at 2800 mg/m3 (highest dose tested) via the inhalation route in rats and a NOAEL of 1,000 mg/kg-bw/day in monkeys via the oral and dermal routes. In a combined reproductive/developmental toxicity screening study in rats via the oral route, the NOAELs for reproductive and developmental toxicity were 1,000 mg/kg-bw/day (no effects seen at highest dose tested). Prenatal developmental toxicity studies in rats and rabbits via the oral route showed a NOAEL of 1,000 mg/kg-bw/day and 300 mg/kg-bw/day for maternal toxicity in rats and rabbits, respectively. The NOAELs for developmental toxicity in both species were 1,000 mg/kg-bw/day. This chemical did not induce gene mutations or chromosomal aberrations *in vitro* or *in vivo*.

The acute hazard to fish and aquatic invertebrates is based on measured toxicity values for DMSO of 32,300 mg/L and 24,600 mg/L, and to aquatic plants is based on estimated toxicity values of 400 mg/L.

No data gaps were identified under the HPV Challenge Program.

The sponsor, Dimethyl Sulfoxide (DMSO) Producers Association, submitted a Test Plan and Robust Summaries to EPA for Dimethyl sulfoxide (Dimethyl sulfoxide, CASRN 67-68-5) on August 12, 2003. EPA posted the submission on the ChemRTK HPV Challenge website on October 15, 2003 (http://www.epa.gov/chemrtk/pubs/summaries/dimthslf/c14721tc.htm). EPA comments on the original submission were posted to the website on February 19, 2004. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on June 15, 2005 and August 30, 2005, which were posted to the ChemRTK website on July 5, 2005 and September 20, 2005, respectively. OECD SIDS Initial Assessment Profiles (SIAP) and SIDS Initial Assessment Reports (SIAR) are publicly available at

http://www.oecd.org/document/63/0,3343,en_2649_34379_1897983_1_1_1_1,00.html through the United Nations Environmental Programme website. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. The U.S. EPA is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments for the purpose of the U.S. HPV Challenge qualitative risk characterization process.

1. Chemical Identity

1.1 Identification and Purity

A typical commercial sample of dimethyl sulfide has a purity > 99.5% (w/w). The specific impurities depend on the production process.

1.2 Physical-Chemical Properties

The physical-chemical properties of dimethyl sulfoxide are summarized in Table 1. Dimethyl sulfoxide is a liquid with high water solubility and moderate vapor pressure.

Table 1. Physical-Chemical Properties of Dimethyl Sulfoxide[1]

Property	**Value**
CASRN	67-68-5
Molecular Weight	78.13
Physical State	Liquid
Melting Point	18.5°C (measured)
Boiling Point	Decomposes >190ºC (measured) 85-87°C at 25 mm Hg (measured) [2] 83°C at 17 mm Hg [3] 56.6°C at 5.11 mm Hg [3] 47.4°C at 2.82 mm Hg [3] 30°C at 0.79 mm Hg [3] 20°C at 0.37 mm Hg [3]
Vapor Pressure	0.61 mm Hg at 25°C (measured) 0.417 mm Hg at 20°C [2] 3.07 mm Hg at 50°C [2]
Water Solubility	1×10^{6} mg/L at 25°C (measured) (completely soluble in water)
Dissociation Constant (pK_a)	Not applicable
Henry's Law Constant	7.79×10^{-9} atm-m^3/mole at 15°C (measured)
Log K_{ow}	-1.35 (measured)

[1]ATOFINA, Inc. August 30, 2005. Revised Robust Summary for Dimethyl Sulfoxide. http://www.epa.gov/hpv/pubs/summaries/dimthslf/c14721tc.htm.
[2] Beilstein E3, Volume 1, part 2, page 1217.
[3] The Merck Index, 12 edition, 1996, page 551.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

Dimethyl sulfoxide had an aggregated production and/or import volume in the United States between 10 million and 50 million pounds during calendar year 2005.

Non-confidential information in the IUR indicates that the industrial processing and uses of the chemical include solvents and intermediates in the manufacture of various chemicals. Non-confidential information in the IUR indicates that the commercial and consumer products containing the chemical include electrical and electronic products, paints and coatings, wood and wood furniture. The HSDB for this chemical states that it is primarily used as a solvent for many organic compounds and for various chemical reactions; it is also used in industrial cleaners, pesticides, analytical reagent, in the preservation of cells at low temperatures, in plant pathology and nutrition, in spinning polyacrylonitrile and other synthetic fibers and in hydraulic fluids.

2.2 Environmental Exposure and Fate

No quantitative information is available on releases of this chemical to the environment.

The environmental fate properties are provided in Table 2. Dimethyl sulfoxide is expected to have high mobility in soil. Conflicting results were provided regarding the rate of biodegradation. Dimethyl sulfoxide was not readily biodegradable using a modified MITI (OECD 301C) test; however, 99% degradation was observed using the modified OECD (OECD 301E) test. In addition 90% biodegradation was observed using a domestic sewage simulation test (OECD 303A). The rate of volatilization of dimethyl sulfoxide from water and moist soil is considered low based on its estimated Henry's Law constant. The rate of hydrolysis is considered negligible to slow under environmental conditions. Dimethyl sulfoxide is expected to have low persistence (P1) and low bioaccumulation potential (B1).

Table 2. Environmental Fate Characteristics of Dimethyl Sulfoxide[1]	
Property	**Value**
Photodegradation Half-life	3 hours (estimated) (does not absorb light above 290 nm)
Hydrolysis Half-life	53 hours to 732 days (measured)
Biodegradation	98% after 27 days (measured , readily biodegradable); 3.1% after 14 days (measured , not readily biodegradable); 90.4% after 32 days (measured in adapted inoculum, simulation test) (good potential for biodegradation); <20% degradation in aerobic, batch degradation (measured); No biodegradation observed in aerobic test using adapted, activated sludge (measured); Not significantly reduced to dimethyl sulfide by a variety of pure cultured microorganisms (measured)
Bioconcentration	BCF = <4 (measured)
Log K_{oc}	0.645 (estimated)[2]
Fugacity (Level III Model)	Air = 0.0458% Water = 45.9% Soil = 53.9% Sediment = 0.0766%
Persistence[3]	P1 (low)
Bioaccumulation[3]	B1 (low)

[1]ATOFINA, Inc. August 30, 2005. Revised Robust Summary for Dimethyl Sulfoxide. http://www.epa.gov/hpv/pubs/summaries/dimthslf/c14721tc.htm.
[2]U.S. EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. United States Environmental Protection Agency, Washington, DC, USA. http://www.epa.gov/opptintr/exposure/pubs/episuite.htm.
[3]Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

3. Human Health & Hazard to the Environment

The human health and aquatic toxicity information is taken from the OECD SIDS Initial Assessment Profiles (SIAP) and SIDS Initial Assessment Reports (SIAR) which are publicly available at http://www.oecd.org/document/63/0,3343,en_2649_34379_1897983_1_1_1_1,00.html through the United Nations Environmental Programme website. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. The U.S. EPA is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments for the purpose of the U.S. HPV Challenge qualitative risk characterization process.

Conclusions:

The acute oral toxicity of this chemical in rats and mice is low, and the acute inhalation toxicity in rats in low. It is mildly irritating to rabbit skin and eyes. This chemical is not a skin sensitizer in guinea pigs and mice. Repeated-dose studies showed a NOAEC at 2800 mg/m3 (highest dose tested) via the inhalation route in rats and a NOAEL of 1,000 mg/kg-bw/day in monkeys via the oral and dermal routes. In a combined reproductive/developmental toxicity screening study in rats via the oral route, the NOAELs for reproductive and developmental toxicity were 1,000 mg/kg-bw/day (no effects seen at highest dose tested). Prenatal developmental toxicity studies in rats and rabbits via the oral route showed a NOAEL of 1,000 mg/kg-bw/day and 300 mg/kg-bw/day for maternal toxicity in rats and rabbits, respectively. The NOAELs for developmental toxicity in both species were 1,000 mg/kg-bw/day. This chemical did not induce gene mutations or chromosomal aberrations *in vitro* or *in vivo*.

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