

201-15002A

Sulfuric Acid, Diethyl Ester

(Diethyl Sulfate; CAS RN 64-67-5)

**High Production Volume (HPV) Chemical
Challenge Test Plan and Data Review**

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December 19, 2003

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Test Plan

Sulfuric Acid, Diethyl Ester (Diethyl Sulfate; CAS RN: 64-67-5)		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	Testing Required
STUDY		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL AND CHEMICAL DATA								
2.1	Melting Point	Y	N	N	Y	N	Y	N
2.2	Boiling Point	Y	N	N	Y	N	Y	N
2.4	Vapor Pressure	Y	N	N	Y	N	Y	N
2.5	Partition Coefficient	Y	N	N	N	Y	Y	N
2.6	Water Solubility	Y	N	N	Y	N	Y	N
ENVIRONMENTAL FATE AND PATHWAY								
3.1.1	Photodegradation	Y	N	N	N	Y	Y	N
3.1.2	Stability in Water	Y	N	N	N	N	N	Y
3.3	Transport and Distribution	Y	N	N	N	Y	Y	N
3.5	Biodegradation	Y	N	N	Y	N	Y	N
ECOTOXICITY								
4.1	Acute Toxicity to Fish	Y	N	N	Y	N	a	a
4.2	Toxicity to Daphnia	Y	N	N	N	Y	a	a
4.3	Acute Toxicity to Algae	Y	N	N	N	Y	a	a
TOXICITY								
5.1	Acute Toxicity	Y	N	N	Y	N	Y	N
5.4	Repeated Dose Toxicity	N	N	N	N	N	N	N ^b
5.5	Genotoxicity <i>In Vitro</i> (Bacterial Test)	Y	N	N	Y	N	Y	N
5.5	Genotoxicity <i>In Vitro</i> (Mammalian Cells)	Y	N	Y	Y	N	Y	N
5.8	Reproductive Toxicity	N	N	N	N	N	N	N ^b
5.9	Development Toxicity / Teratogenicity	N	N	N	N	N	N	N ^b

a See text for discussion of ecotoxicity approach.

b DES is classified by IARC (2A; “Probably carcinogenic to humans”) and NTP (“Anticipated carcinogen”) as a carcinogen. The production, labeling and handling of DES are specifically designed to minimize exposure to carcinogenic chemicals, and are therefore considered adequate for other potential toxic hazards. See text for discussion.

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1.0 Introduction

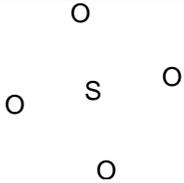
This document reviews the data availability for the High Production Volume (HPV) Chemical Challenge endpoints and provides a Test Plan for Sulfuric Acid, Diethyl Ester, hereafter called Diethyl Sulfate [DES; CAS RN 64-67-5]. DES is sponsored by The Dow Chemical Company. DES is classified as a carcinogen by IARC (2A; "Probably carcinogenic to humans") and NTP ("Anticipated carcinogen"). As a suspect human carcinogen, exposure is strictly controlled thus eliminating the need for fulfilling some HPV endpoints (i.e. no additional precautions are required regardless of the outcome of the study). The exposure-limited testing needs are defined herein.

2.0 General Use and Exposure

Diethyl sulfate is a versatile alkylating agent for producing ethyl derivatives of many compounds such as amines, phenols, and thiols. It is used in the preparation of a wide variety of intermediates and products in surfactants, dyes, agricultural chemicals, and pharmaceuticals. The major use of diethyl sulfate is in the manufacture of quaternary ammonium salts or that are used in: textile applications for fabric softeners in detergents and for dye operations to increase the affinity of the dye for the fiber; hair care applications for shampoos, conditioners and hair spray; germicides for disinfectants and sanitizers in a broad range of products including cleaners, drilling fluids, and cooling water applications; and production of organoclays for viscosity modifiers in drilling fluids, greases, lubricants, and oil based paints, phase transfer catalysts, electroplating, emulsifying agents including asphalt additives, and corrosion inhibitors. Other uses include production of ethers from alcohols; to produce fatty acid ethyl esters for plasticizers and to alkylate substituted aniline for dyes; and as a pharmaceutical intermediate. Production in the U.S. was in the range of 0.5 to 1 million pounds in 2002.

Approximately 194 full-shift samples were collected from 1978 to 1996 at a US production site. All results ranged between none-detected (limit of detection 0.01 ppm) and 0.7 ppm. There were no results greater than the established internal exposure guideline of 1 ppm as an 8-hr TWA. Samples were collected from a variety of tasks including drumming activities, work at a loading rack, and other routine tasks. Thirty short-term samples were collected from 1975 to 1987. Results ranged from one-detected (limit of detection 0.01) to 1.8 ppm. Samples were collected during drumming operations, filter changes, and connecting and disconnecting hoses. Therefore, exposure in the workplace is considered to be of no concern and appropriate measures are taken to avoid worker contact. In addition, based on its use as a chemical intermediate and the rapid hydrolysis of any residual DES from production, no significant exposure to consumers is anticipated to occur.

3.0 General Substance Information (Identity)

Chemical Name	Sulfuric Acid, Diethyl Ester
Synonyms	Diethyl Sulfate Diaethylsulfat [German] Diethyl sulphate Diethyl tetraoxosulfate Diethylester kyseliny sirove [Czech] Ethyl sulfate
CAS Number	64-67-5
Structure	
Molecular Weight	154.18
Substance Type	Organic
Physical State	Colorless liquid
Odor	Mild
Purity	>99%

4.0 Physical/Chemical Properties

A data summary for DES is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

4.1 Melting Point

The melting point for DES is listed as -24.5 °C (CRC Press, 1975). The Material Safety Data Sheet indicates the freezing point to be -24.4 °C. These data are considered adequate to meet the HPV Chemical Challenge requirements.

4.2 Boiling Point

The boiling point for DES is listed as 208 °C (CRC Press, 1975). The Material Safety Data Sheet indicates that DES decomposes at high temperatures. These data are considered adequate to meet the HPV Chemical Challenge requirements.

4.3 Vapor Pressure

The vapor pressure for DES is listed as 0.191 hPa at 20 °C (DIPPR, 2000). This value is considered adequate to meet the HPV Chemical Challenge requirements.

4.4 Partition Coefficient

The log K_{ow} for DES is predicted by EPIWIN to be 1.14 (U.S. EPA, 2000a). An unpublished reference from Union Carbide provides the same value (Union Carbide; unpublished data). Because of the rapid hydrolysis of DES in water (see below), this value has minimal utility in determining its environmental fate or bioaccumulation in aqueous systems. However, the low value indicates bioaccumulation is not anticipated. These data are considered adequate to meet the HPV Chemical Challenge requirements.

4.5 Water Solubility

DES rapidly hydrolyzes to ethanol and H_2SO_4 (CRC Press, 1975). A water solubility value of 7000 mg/L has been determined (McCormack and Lawes, 1983). The rate at which the hydrolysis occurs has not been adequately addressed. The value of 7000 mg/L is considered an adequate determination of water solubility for the HPV Chemical Challenge requirement and for the conduct of the water stability study (see below).

5.0 Environmental Fate

A data summary for DES is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

5.1 Photodegradation

The model prediction for atmospheric photodegradation provides a second order rate of reaction with hydroxyl radicals of $1.6 \text{ E-}12 \text{ cm}^3/\text{molecule-sec}$ and a $t_{1/2}$ of 6.5 days (U.S. EPA, 2000b). Because of the nature of use of DES, photodegradation is of minimal importance to the overall environmental fate. Degradation from accidental release to the atmosphere, however, is anticipated based on the modeling. These data are considered adequate to meet the HPV Chemical Challenge requirements.

5.2 Stability in Water

DES rapidly hydrolyzes in water with existing data (unpublished) in distilled water indicating the hydrolysis half-life at 8000 mg/L to be approximately 2 hours. Since this study was conducted at or near the maximum anticipated water solubility (guideline studies suggest using half maximum concentrations) and did not identify the hydrolysis products, it is of limited use for predicting behavior of DES in the environment. It is generally understood that the ultimate hydrolysis of DES results in the formation of ethanol and sulfuric acid. However, it is considered possible that ethyl sulfate could be a more stable intermediate. Therefore, a study to determine hydrolysis rate will be conducted following OECD Guideline 111. The concentration to be tested will be 50% of the water solubility, i.e. 3500 mg/L. It is anticipated that the preliminary test at pH 4, 7 and 9 at 50 °C will be adequate to establish the rate of hydrolysis according to the guideline; the products of hydrolysis will be determined. These data will be used to determine the need for aquatic toxicity testing as described in detail below.

5.3 Environmental Transport and Distribution

The Level III fugacity model (U.S. EPA, 2000c) was used to predict the distribution of DES released to the environment. DES is not routinely released to the environment because of the controls in place to avoid human exposure and because it is used exclusively as a chemical intermediate. Therefore, only accidental releases were considered for the fugacity modeling. Two scenarios, 100% release to air and 100% release to water were examined. For the air release the model predicted a distribution of 77% into atmosphere, 15% into water, 9% into soil, and < 0.1% into sediment. For the water release the model predicted a distribution of < 1% into atmosphere, 99% into water, < 0.1% into soil, and < 1% into sediment. These data are considered adequate to meet the HPV Chemical Challenge requirements.

5.4 Biodegradability

A study measuring the Biological Oxygen Demand provided a value of 57% degradation after 20 days (Price *et al.*, 1974). Based on this study effectively showing rapid biodegradation after 20 days along with the knowledge that rapid hydrolysis of DES occurs (see above), additional biodegradation studies are unwarranted. These data are considered adequate to meet the HPV Chemical Challenge requirements.

6.0 Ecotoxicity

A data summary for DES is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

6.1 Toxicity to Fish

Two 96 hour LC₅₀ values for DES in freshwater fish are reported; 95 mg/L for the fathead minnow (*Pimephales promelas*; Waggy and Payne, 1974) and 20 mg/L for rainbow trout (*Salmo gairdneri*; Nisso Maruzen Chemical Co., in-house data). The limited information available makes the reliability of these studies uncertain without further knowledge of the hydrolysis of DES. If hydrolysis to ethanol and sulfuric acid is completed in a short period of time (e.g. < 24 hours), these values are likely the result of sulfuric acid toxicity (LC₅₀ ~ 100 mg/L). It is proposed that the usefulness of these data be reexamined after completion of the hydrolysis testing. If complete hydrolysis occurs in less than 24 hours, these data support the conclusion that sulfuric acid is the proper test chemical and no further testing is proposed (the effects of ethanol and sulfuric acid being well understood); therefore, the available information is considered adequate to meet the HPV Chemical Challenge requirements. However, if slower hydrolysis or significant production of ethyl sulfate is indicated, an additional test with controlled timing is proposed (procedures to be determined). This study will not include analytical measurements, however, because these data are not relevant with continuous hydrolysis of the test chemical.

6.2 Toxicity to Aquatic Invertebrates

The ECOSAR model provides an EC₅₀ value for daphnia of 742 mg/L (U.S. EPA, 2000d). A similar approach to that described for fish will be used to determine the need and procedures for additional testing. If the hydrolysis of DES to ethanol and sulfuric acid is shown to be

complete, or nearly complete, in less than 24 hours, the knowledge of toxicity of sulfuric acid and ethanol is considered adequate to meet the HPV Chemical Challenge requirements.

6.3 Toxicity to Aquatic Plants

The ECOSAR model provides an EC₅₀ value for daphnia of 5.2 mg/L (U.S. EPA, 2000d). Testing may be indicated by the hydrolysis information. If the hydrolysis of DES to ethanol and sulfuric acid is shown to be complete, or nearly complete, in less than 24 hours, the knowledge of toxicity of sulfuric acid and ethanol is considered adequate to meet the HPV Chemical Challenge requirements.

7.0 Human Health-Related Data

A data summary for DES is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

7.1 Acute Toxicity

The acute oral LD₅₀ for DES is 880 mg/kg bw (Smyth *et al.*, 1949). Inhalation of DES results in an LC₅₀ between 250 (1275 mg/L) to 500 ppm (3150 mg/L) with no deaths at 250 ppm and 100% mortality at 500 ppm following four hours of exposure (Smyth *et al.*, 1949). The acute dermal LD₅₀ is 706 mg/kg/bw (Smyth *et al.*, 1951). These data are considered adequate to meet the HPV Chemical Challenge requirements.

7.2 Repeated Dose Toxicity

There are no subchronic studies available for DES. DES is classified by IARC (2A; “Probably carcinogenic to humans”) and NTP (“Anticipated carcinogen”) as a carcinogen. This classification is based on a study in which DES was administered dermally to male mice for the lifespan of the animals. Repeated dermal application of undiluted DES produced malignant skin neoplasms in 21 mice out of a surviving effective group of 27 animals (Peterson, 1979). Based on these data, the consistent mutagenic response of DES (see below) and the classification of DES as a carcinogen, the production, labeling and handling of DES are specifically designed to minimize exposure to carcinogenic chemicals. Further testing at higher doses in subchronic studies and/or identification of additional toxic responses will not alter these procedures and controls. Therefore, the available data are considered adequate to meet the HPV Chemical Challenge requirements.

7.3 Genetic Toxicity

7.3.1 *In vitro*

DES has been shown to be positive in the Salmonella preincubation reverse mutation assay (Ohtsuka and Maekawa, 1992). Although this study evaluated only one tester strain (TA100), the strong positive response precludes the need for additional testing. In this assay, DES resulted in a maximum of a 35-fold greater induction of revertants compared to the control with a clear dose response. No induction was observed at 500 µg/plate with a 6-fold increase at 1000 µg/plate and the 35-fold induction at 2000 µg/plate. DES has also been shown to be positive in mammalian cell assays. In the HGPRT mutation assay with CHO cells, a dose-related increase in induction of mutations with and without metabolic activation was observed

(Slesinski *et al.*, 1980). The maximum response varied from 8 to 35-fold induction of mutations compared to the solvent control. A sister chromatid exchange assay without metabolic activation also showed a dose-related increase in response with a maximum 2.5-fold increase in the number of SCE per chromosome (Slesinski *et al.*, 1980). In an unscheduled DNA synthesis assay, a non-dose related increase in DNA synthesis, as measured by radioactive thymidine, was observed at all concentrations ranging from 0.0001 to 0.1% (v/v) (Slesinski *et al.*, 1980). The available data are considered adequate to meet the HPV Chemical Challenge requirements.

7.3.2 *In vivo*

DES increased the incidence of micronucleated erythrocytes in a mouse micronucleus assay at one time point (48 hours) at the highest single i.p. dose (400 mg/kg) tested (Asita *et al.*, 1992). The results of a second mouse micronucleus study were also positive at 30 hours following an i.p. injection of 160 mg/kg of DES with no effect seen at 80 mg/kg (Hagashikuni and Shizuyo, 1995). A study using intrascrotal injection of DES resulted in dominant lethal effects (Malashenko, 1971). Although this study used a highly unusual dosing regimen, a second dominant lethal study is briefly reported as being positive using the more conventional intraperitoneal injection (Ehling and Neuhauser-Klaus, 1988). The available data confirm the biological activity of DES on the genome and are considered adequate to meet the HPV Chemical Challenge requirements.

7.4 Reproductive and Developmental Toxicity

There are no studies available for DES that evaluate potential reproductive or developmental toxicity. Production, labeling and handling of DES are specifically designed to minimize exposure to carcinogenic chemicals. Further testing at higher doses in studies designed to evaluate reproductive and developmental toxicity, and/or identification of positive effects in such studies, will not alter the procedures and controls currently in place for the use and handling of DES. Therefore, the available data are considered adequate to meet the HPV Chemical Challenge requirements.

8.0 Conclusion

Adequate information is available for melting point, boiling point, vapor pressure and partition coefficient for DES. Photodegradation and environmental distributions are adequately supported by the appropriate model data. Water solubility and hydrolysis will be examined in appropriate OECD guideline testing. Based on the results of these studies, the need for additional aquatic toxicity tests will be determined. If hydrolysis of DES to ethanol and sulfuric acid is complete, or nearly complete, within 24 hours, data for these daughter chemicals are considered adequate to describe the environmental hazards for DES. DES is biodegradable. In bacterial and mammalian cell systems and *in vivo* mutagenicity assays, DES is mutagenic, and it has been shown to be carcinogenic in animal studies. Based on these findings, production, labeling and handling of DES are specifically designed to minimize exposure to carcinogenic chemicals and are considered adequate for other potential toxic hazards. Additional animal testing, appropriate to meet the HPV Challenge Program requirements, will not further the understanding of DES hazard or alter current procedures for labeling and handling. Therefore, the available data are considered adequate.

9.0 References

- Asita, A.O., M. Hayashi, Y. Kodama, A. Matsuoka, T. Suzuki and T. Sofuni. 1992. Micronucleated Reticulocyte Induction by Ethylating Agents in Mice. *Mutat. Res.* 271: 29-37.
- CRC Press. 1975. *Handbook of Chemistry & Physics*, 56th Edition, CRC Press, Cleveland, Ohio.
- DIPPR (The Design Institute for Physical Properties). 2000. *The DIPPR Information and Data Evaluation Manager*, Version 1.5.0, Copyright BYU-TPL2000.
- Ehling, U.H. and A. Neuhauser-Klaus. 1988. *Mutat. Res.* 199:191-198.
- Hagashikuni, N. and S. Shizuyo. 1995. An optimal generalized sampling time of 30 +- 6 h after double dosing in the mouse peripheral blood micronucleus test. *Mutagenesis* 10:313-319.
- Malashenko, A.M. 1971. Sensitivity of mouse testis cells to the induction of dominant lethals by diethyl sulfate. *Genetika* 7:84-91.
- McCormack, W.B., and B.C. Lawes. E. I. du Pont de Nemours and Co., Inc., Wilmington, DE, USA. Sulfuric and sulfurous esters. Editor(s): Grayson, Martin; Eckroth, David. *Kirk-Othmer Encycl. Chem. Technol.*, 3rd Ed. (1983), 22 233-54. Publisher: Wiley, New York, N. Y CODEN: 37ASAA Conference; General Review written in English. CAN 98:181501 AN 1983:181501 CAPLUS
- Nisso Maruzen Chemical Co.; in-house data.
- Ohtsuka, M. and K. Maekawa. 1992. A Straight Correlation Between Mutagenic Activity and B-galactosidase Activity Induced by Monofunctional Alkylating Agents. *Mutat. Res.* 283(1):83-86.
- Peterson, L.G. 1979. Evaluation of the Dermal Carcinogenic Potential of Diethyl Sulfate. Chemical Hygiene Fellowship. Carnegie-Mellon Institute of Research, Carnegie-Mellon University. Project report 42-49.
- Price, K.S., G.T. Waggy and R.A. Conway. 1974. Brine Shrimp Bioassay and Seawater BOD of Petrochemicals. *J. WPCF* 46(1):63.
- Slesinski, R.S., P.J. Guzzie, M.W. Gaunt and W.C. Hengler. 1980. Diethyl Sulfate, In Vitro Mutagenesis Studies: 3-Test Battery. Bushy Run Research Center. Project Report 43-97.
- Smyth, H.F., Jr., C.P. Carpenter and C.S. Weil. 1949. Range-Finding Toxicity Data: List III. *J. Ind. Hyg. Toxicol.* 31:60.

Smyth, H.F., Jr., C.P. Carpenter, C.B. Shaffer and C.S. Weil. 1951. Progress report for the month ended May 31, 1951. Mellon Institute of Industrial Research, University of Pittsburgh. Report 14-50.

Union Carbide; unpublished data. Central Research and Engineering Technology Center.

U. S. EPA (U.S. Environmental Protection Agency). 2000a. EPI Suite™, Version 3.11; KOWWIN Program, Version 1.67; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

U.S. EPA (U.S. Environmental Protection Agency). 2000b. EPI Suite™, Version 3.11; AOPWIN Program, Version 1.91; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

U.S. EPA (U.S. Environmental Protection Agency). 2000c. EPI Suite, Version 3.11; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

U.S. EPA (U.S. Environmental Protection Agency). 2000d. EPI Suite™, Version 3.11; ECOSAR Version 0.99g; PC-Computer software developed by ECOSAR Program, Risk Assessment Division (7403), Washington, D.C.

Waggy, G.T. and J.R. Payne. 1974. Product Analysis; Acute Aquatic Toxicity Testing. UCC R&D Report 19133.

Table 1: HPV Data Summary				
Sulfuric Acid, Diethyl Ester (Diethyl Sulfate)				
CAS RN: 64-67-5		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point		Handbook Data (CRC)	-24.5 °C
2.2	Boiling Point		Handbook Data (CRC)	208 °C
2.4	Vapor Pressure		Handbook Data (DIPPR)	0.191 hPa (at 20 °C)
2.5	Partition Coefficient (log K _{ow})		KOWWIN v. 1.67; UCC Unpub. Data	1.14
2.6	Water Solubility		Not specified Handbook Data (CRC)	7000 mg/L Decomposes to ethanol and H ₂ SO ₄ ;
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		AOPWIN v. 1.91	half-life: 6.5 days (OH Rate Constant)
3.1.2	Stability in Water		Handbook Data (CRC)	Hydrolyzes to ethanol and sulfuric acid
3.3	Transport and Distribution		Mackay Level III 100% release to air	77% into atmosphere, 15% into water, 9% into soil, < 0.1% into sediment
			Mackay Level III 100% release to water	< 1% into atmosphere, 99% into water, < 0.1% into soil, < 1% into sediment
3.5	Biodegradation		BOD20	57% after 20 days
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	<i>Pimephales promelas</i>	EPA/600/4-85/013 Not specified	LC ₅₀ (96 hours) = 95 mg/L LC ₅₀ (96 hours) = 20 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates	Daphnid	ECOSAR v 0.99g	EC ₅₀ (48 hours) = 742 mg/L
4.3	Toxicity to Aquatic Plants e.g. Algae	Green algae	ECOSAR v 0.99g	EC ₅₀ (96 hours) = 5.2 mg/L

Table 1: HPV Data Summary
Sulfuric Acid, Diethyl Ester (Diethyl Sulfate)

CAS RN: 64-67-5					SPECIES	PROTOCOL	RESULTS
TOXICOLOGY							
5.1.1	Acute Oral Toxicity	Rat					LD ₅₀ : 880 mg/kg bw
5.1.2	Acute Inhalation Toxicity	Rat					LC ₅₀ (4 hr): >250 ppm (1275 mg/L); <500 ppm (3150 mg/L)
5.1.3	Acute Dermal Toxicity	Rabbit					LD ₅₀ : 706 mg/kg bw
5.4	Repeated Dose Toxicity						See Text
5.5	Genetic Toxicity <i>In Vitro</i>						
	Bacterial Test (Gene mutation)	Salmonella typhimurium TA 100 only	Ames				Positive
		CHO	HGPRT -Similar to guideline				Positive
		CHO	SCE - Similar to guideline				Positive
		Rat	Hepatocyte UDS - similar to guideline				Positive
5.6	Genetic Toxicity <i>In Vivo</i>	Mouse	Micronucleus - Similar to guideline				Positive
		Mouse	Dominant lethal				Positive
5.8	Toxicity to Reproduction / Impairment of Fertility						See Text
5.9	Developmental Toxicity / Teratogenicity						See Text