

# **Skin Notation (SK) Profile**

## **Dimethyl sulfate (DMS)**

**[CAS No. 77-78-1]**

**Department of Health and Human Services**  
Centers for Disease Control and Prevention  
National Institute for Occupational Safety and Health

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## Foreword

As the largest organ of the body, the skin performs multiple critical functions, such as serving as the primary barrier to the external environment. For this reason, the skin is often exposed to potentially hazardous agents, including chemicals, which may contribute to the onset of a spectrum of adverse health effects ranging from localized damage (e.g., irritant contact dermatitis and corrosion) to induction of immune-mediated responses (e.g., allergic contact dermatitis and pulmonary responses), or systemic toxicity (e.g., neurotoxicity and hepatotoxicity). Understanding the hazards related to skin contact with chemicals is a critical component of modern occupational safety and health programs.

In 2009, the National Institute for Occupational Safety and Health (NIOSH) published *Current Intelligence Bulletin (CIB) 61 – A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009-147]. This document provides the scientific rationale and framework for the assignment of multiple hazard-specific skin notations (SK) that clearly distinguish between the systemic effects, direct (localized) effects, and immune-mediated responses caused by skin contact with chemicals. The key step within assignment of the hazard-specific SK is the determination of the hazard potential of the substance, or its potential for causing adverse health effects as a result of skin exposure. This determination entails a health hazard identification process that involves use of the following:

- Scientific data on the physicochemical properties of a chemical
- Data on human exposures and health effects
- Empirical data from *in vivo* and *in vitro* laboratory testing
- Computational techniques, including predictive algorithms and mathematical models that describe a selected process (e.g., skin permeation) by means of analytical or numerical methods.

This *Skin Notation Profile* provides the SK assignments and supportive data for dimethyl sulfate (DMS). In particular, this document evaluates and summarizes the literature describing the hazard potential of the substance and its assessment according to the scientific rationale and framework outlined in CIB 61. In meeting this objective, this *Skin Notation Profile* intends to inform the audience—mostly occupational health practitioners, researchers, policy- and decision-makers, employers, and workers in potentially hazardous workplaces—so that improved risk-management practices may be developed to better protect workers from the risks of skin contact with the chemicals of interest.

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## Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
ATSDR	Agency for Toxic Substances and Disease Registry
CIB	Current Intelligence Bulletin
cm <sup>2</sup>	squared centimeter(s)
cm/hour	centimeter(s) per hour
cm/s	centimeter(s) per second
DEREK	Deductive Estimation of Risk from Existing Knowledge
DIR	skin notation indicating the potential for direct effects to the skin following contact with a chemical
DMS	dimethyl sulfate
EC	European Commission
ECB	European Chemicals Bureau
GHS	Globally Harmonized System for Classification and Labelling of Chemicals
GPMT	guinea pig maximization test
IARC	International Agency for Research on Cancer
(IRR)	subnotation of SK: DIR indicating the potential for a chemical to be a skin irritant following exposure to the skin
$k_{aq}$	coefficient in the watery epidermal layer
$k_p$	skin permeation coefficient
$k_{pol}$	coefficient in the protein fraction of the stratum corneum
$k_{psc}$	permeation coefficient in the lipid fraction of the stratum corneum
LD <sub>50</sub>	dose resulting in 50% mortality in the exposed population
LD <sub>Lo</sub>	dermal lethal dose
LLNA	local lymph node assay
LOAEL	lowest-observed-adverse-effect level
log $K_{OW}$	base-10 logarithm of a substance's octanol–water partition
$M$	molarity
m <sup>3</sup>	cubic meter(s)
mg	milligram(s)
mg/cm <sup>2</sup> /hour	milligram(s) per square centimeter per hour
mg/kg	milligram(s) per kilogram body weight
mg/m <sup>3</sup>	milligram(s) per cubic meter
mL	milliliter(s)
mL/kg	milliliter(s) per kilogram body weight
MW	molecular weight
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no-observed-adverse-effect level
NTP	National Toxicology Program
OEL	occupational exposure limit
OSHA	Occupational Safety and Health Administration

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ppm	parts per million
REL	recommended exposure limit
RF	retention factor
SEN	skin notation indicating the potential for immune-mediated reactions following exposure of the skin
SI ratio	ratio of skin dose to inhalation dose
SK	skin notation
$S_w$	solubility in water
SYS	skin notation indicating the potential for systemic toxicity following exposure of the skin
USEPA	United States Environmental Protection Agency

DRAFT

## Glossary

**Absorption**—The transport of a chemical from the outer surface of the skin into both the skin and systemic circulation (including penetration, permeation, and resorption).

**Acute exposure**—Contact with a chemical that occurs once or for only a short period of time.

**Cancer**—Any one of a group of diseases that occurs when cells in the body become abnormal and grow or multiply out of control.

**Contaminant**—A chemical that is (1) unintentionally present within a neat substance or mixture at a concentration less than 1.0% or (2) recognized as a potential carcinogen and present within a neat substance or mixture at a concentration less than 0.1%.

**Cutaneous (or percutaneous)**—Referring to the skin (or through the skin).

**Dermal**—Referring to the skin.

**Dermal contact**—Contact with (touching) the skin.

**Direct effects**—Localized, non-immune-mediated adverse health effects on the skin, including corrosion, primary irritation, changes in skin pigmentation, and reduction/disruption of the skin barrier integrity, occurring at or near the point of contact with chemicals.

**Immune-mediated responses**—Responses mediated by the immune system, including allergic responses.

**Sensitization**—A specific immune-mediated response that develops following exposure to a chemical, which, upon re-exposure, can lead to allergic contact dermatitis (ACD) or other immune-mediated diseases such as asthma, depending on the site and route of re-exposure.

**Substance**—A chemical.

**Systemic effects**—Systemic toxicity associated with skin absorption of chemicals after exposure of the skin.

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# 1.0 Introduction

## 1.1 General Substance Information

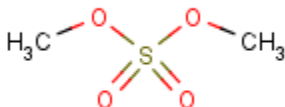
**Chemical:** Dimethyl sulfate

**CAS No:** 77-78-1

**Molecular weight (MW):** 126.1

**Molecular formula:** (CH<sub>3</sub>)<sub>2</sub>SO<sub>4</sub>

**Structural formula:**



**Synonyms:** DMS; Methyl sulfate; Dimethyl ester of sulfuric acid; Dimethylsulfate

**Uses:** Dimethyl sulfate (DMS) is primarily used as a methylating and sulfonating agent during the manufacturing of organic compounds [ACGIH 2001].

## 1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with DMS and (2) the rationale behind the hazard-specific skin notation (SK) assignment for DMS. The SK assignment is based on the scientific rationale and logic outlined in the *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009]. The summarized information and health hazard assessment are limited to an evaluation of the potential health effects of dermal exposure to DMS. A literature search was conducted through February 2013 to identify information on DMS, including but not limited to data relating to its toxicokinetics, acute toxicity, repeated-dose systemic toxicity, carcinogenicity, biological system/function-specific effects (including reproductive and developmental effects and immunotoxicity), irritation, and sensitization. Information was considered from studies of humans, animals, or appropriate modeling systems that are relevant to assessing the effects of dermal exposure to DMS.

## 1.3 Overview of SK Assignment

DMS is potentially capable of causing numerous adverse health effects following skin contact. A critical review of available data has resulted in the following SK assignment for DMS: **SK: SYS-DIR (COR)**. Table 1 provides an overview of the critical effects and data used to develop the SK assignment for DMS.

**Table 1. Summary of the SK Assignment for DMS**

<b>Skin Notation</b>	<b>Critical Effect</b>	<b>Available Data</b>
SK: SYS	Hematological effects; Hepatotoxicity; central nervous system effects	Sufficient human data; limited animal data
SK: DIR (COR)	Skin corrosion	Sufficient human data; sufficient animal data

## 2.0 Systemic Toxicity from Skin Exposure (SK: SYS)

Quantitative information of absorption via the dermal route of exposure to DMS has not been identified. However, the chemical is considered to be rapidly absorbed through intact skin [Rippey and Stallwood 2005]. In an occupational exposure study, Schettgen et al. [2004] observed a significant increase in hemoglobin adducts of DMS in a group of employees that worked in a specific building of a chemical plant where stationary monitoring of DMS showed only values below the limit of detection (reported as  $10 \mu\text{g}/\text{m}^3$ ) data collected with area samples, which are less accurate for estimating worker exposure than personal breathing zone samples. According to these investigators, the high exposures to DMS was attributed to skin contact with residues of unreacted DMS in the product [Schettgen et al. 2004]. Based on this qualitative information, the chemical may be considered to have the potential to be absorbed following dermal exposure. The potential of DMS to pose a skin absorption hazard was also evaluated, with use of a predictive algorithm for estimating and evaluating the health hazards of dermal exposure to substances [NIOSH 2009]. The evaluation method compares an estimated dose accumulated in the body from skin absorption and an estimated dose from respiratory absorption associated with a reference occupational exposure limit. On the basis of this algorithm, a ratio of the skin dose to the inhalation dose (SI ratio) of 12.8 was calculated for DMS. An SI ratio of  $\geq 0.1$  indicates that skin absorption may significantly contribute to the overall body burden of a substance [NIOSH 2009]; therefore, DMS is considered to be absorbed through the skin following dermal exposure. Additional information on the SI ratio and the variables used in its calculation are included in the appendix.

No dermal lethal dose ( $\text{LD}_{\text{Lo}}$ ) for humans or dermal  $\text{LD}_{50}$  values (the dose resulting in 50% mortality in the exposed animals) in experimental animals have been identified.

Although no epidemiological studies or dermal repeated-dose studies using DMS have been identified, several reports in the literature demonstrate systemic and pulmonary toxicity resulting from skin contamination through spills, though, in such cases, there might have been some contribution by inhalation exposure [Littler and McConnell 1955; Wang et al. 1988; Schettgen et al 2004; Yagami et al. 2009]. Although no quantitative information on the exposure dose was provided, these case reports demonstrate that dermal exposure to DMS can result in systemic effects (e.g., albuminuria, hematuria, hypoglycemia) indicating involvement of the liver and nausea, headache and irritability, indicating central nervous system effects.

No repeat-dose or subchronic standard toxicity or specialty studies evaluating biological system/function specific effects (including reproductive and developmental effects and immunotoxicity) or standard

cancer bioassays following dermal exposure to DMS were identified in animals. Hoffman [1980] indicated that DMS is a methylating material that can act as a mutagenic substance for nucleic acids. However, in animal studies, van Duuren et al. [1974] observed no carcinogenic effects when 0.1 mL (corresponding to 133 mg) solution of DMS in 0.1 mL acetone was applied to the skin of 20 mice three times per week for a period of 385 or 475 days. The authors also observed no cancers when the chemical was combined with the tumor promotor phorbol myristate acetate and did not report any findings on the non-neoplastic changes in this study [van Duuren et al. 1974]. Although no studies were identified that demonstrate the potential of DMS to be carcinogenic, the chemical has been evaluated for carcinogenicity via other routes of exposure. Table 2 summarizes carcinogenic designations of multiple governmental and nongovernmental organizations for DMS.

**Table 2. Summary of the carcinogenic designations\* for DMS by numerous governmental and nongovernmental organizations**

<b>Organization</b>	<b>Carcinogenic designation</b>
NIOSH [2005]	Potential occupational carcinogen
NTP [2014]	Reasonably anticipated to be human carcinogen
European Parliament [2008]	GHS Category 1B: May cause cancer
USEPA [2014]	Group B2: Probable human carcinogen
IARC [2012]	Group 2A: Probably carcinogenic to humans
EC [2013] <sup>†</sup>	R45: May cause cancer
ACGIH [2001]	Group A3: Confirmed animal carcinogen with unknown relevance to humans

ACGIH = American Conference of Governmental Industrial Hygienists; EC = European Commission, Joint Research, Institute for Health and Consumer Protection; GHS = Globally Harmonized System for Classification and Labelling of Chemicals; IARC = International Agency for Research on Cancer; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; USEPA = United States Environmental Protection Agency.

\* The listed cancer designations were based on data from nondermal (such as oral or inhalation) exposure since studies using the dermal route of exposure were unavailable.

<sup>†</sup>Date accessed.

Based on the limited information from occupational case reports [**Little and McConnell 1955; Wang et al. 1988; Schettgen et al 2004; Yagami et al. 2009**]<sup>1</sup> and supported by a mathematical model, DMS is systemically available and toxic following dermal exposure. Therefore, on the basis of the data for this assessment, DMS is assigned the SK: SYS notation.

### 3.0 Direct Effects on Skin (SK: DIR)

No human or animal *in vivo* studies on corrosivity of DMS or *in vitro* tests for corrosivity using human skin models or *in vitro* tests of skin integrity using cadaver skin were identified. However, several case reports were identified that indicate varying skin changes from simple redness to skin burns depending on the length of contact. For example, Little and McConnell [1955] reported burns from a direct spill on the skin of a student, who dropped and broke a 2.5 L bottle that was almost full of DMS. The liquid

<sup>1</sup>References in **bold** text indicate studies that serve as the basis of the SK assignments.

soaked through his pants to involve the genitalia and left thigh, Littler and McConnell [1955] also reported a worker whose job duties included working on an analgesic drug to which dimethyl sulfate was added. The worker whose work clothing was likely splashed with dimethyl sulfate, experienced disturbances in vision, breathing difficulties, and swollen and vesicated skin [Littler and McConnell 1955]. Wang et al. [1988] reported that within 1-2 hours of skin exposure to DMS, redness, swelling, pain, bleb formation, and burns were present. Yagami et al. [2009] reported a patient that spilled 100% DMS in his lap; the patient developed severe irritation, redness, swelling, and blisters at the exposure site. In the cases reported by Littler and McConnell [1955], Wang et al. [1988] and Yagami et al. [2009], there was a delay in onset but symptoms were still occurring. DMS has anesthetic effects; thus, the sensation of skin contact may not be noticed until the onset of significant tissue damage.

In animals, Dow [1938] reported necrosis, blistering and deep ulceration when 0.001 cubic centimeters per square centimeter (cc/cm<sup>2</sup>) was applied to the ear and abdomen (species unspecified). A review by Browning [1965] reported that the chemical caused secondary and tertiary burns when applied directly to animal skin, although no further detailed information was provided. No irritation was observed when 0.01 ml undiluted DMS were applied to the skin of guinea pigs, but 0.1 ml was sufficient to produce moderate to severe skin irritation [E.I. du Pont de Nemours and Company 1972]. The structure activity relationship model, Deductive Estimation of Risk from Existing Knowledge (DEREK) for Windows, predicted DMS to be a plausible skin irritant.

Taken together, human [Littler and McConnell 1955; Wang et al. 1988; Yagami et al. 2009] and animal data [Dow 1938; Browning 1965; E.I. du Pont de Nemours and Company 1972] demonstrate that DMS is corrosive at high doses and prolonged dermal exposure, and irritating at low concentrations. Therefore, on the basis of the data for this assessment, DMS is assigned the SK: DIR (COR) notation.

#### 4.0 Immune-mediated Responses (SK: SEN)

There is limited information identified from occupational exposures. Yagami et al. [2009] reported a patient that spilled 100% DMS in his lap; the patient developed severe irritation, redness, swelling, and blisters at the exposure site. The authors suspected that the patient developed allergic contact dermatitis to DMS, and patch tested him using 0.1% pet. DMS and noted a positive skin reaction [Yagami et al. 2009]. In guinea pigs, 0.05 ml (67 mg) of 0.5% and 1% DMS solution was sufficient to cause positive responses upon the challenge dose, although no guinea pigs were sensitized [E.I. du Pont de Nemours and Company 1972]. Ashby et al. [1995] suggested that DMS is a potential skin sensitizer based on the results of their murine local lymph node assay (LLNA). In this assay, topical application of 0.25, 0.5 and 1% DMS in acetone/olive oil (80/20 v/v) resulted in greater than a 3-fold increase in thymidine isotope incorporation in the lymph nodes of exposed mice compared with vehicle controls [Ashby et al. 1995]. Ashby et al. [1995] considered a 3-fold increase to be determinant of sensitizing activity. The ECB [2002] review of the Ashby et al. [1995] study noted that the positive response observed may be due to the corrosive properties of the chemical. A non-standard, Ear-Flank Test was also conducted, and which the authors [Stevens 1967] concluded that the chemical was not a skin sensitizer. In guinea pigs, 0.05 ml (67 mg) of 0.5% DMS solution was not sufficient to cause sensitization when applied to the intact skin of guinea pigs [E.I. du Pont de Nemours and Company 1972].

Although positive responses were observed in the murine LLNA test [Ashby et al. 1995] and in a single human patch test [Yagami et al. 2009], conflicting evidence in animal studies [Stevens 1967; E.I. du Pont de Nemours and Company 1972] suggest that DMS is not capable of causing immune-mediated responses (i.e., sensitization) following skin contact and that the positive responses may be attributable to corrosive properties of the chemical. Therefore, on the basis of the data for this assessment, DMS is not assigned the SK: SEN notation.

## 5.0 Summary

Although limited information was identified on the toxicokinetics and systemic toxicity of DMS, occupational case reports [Littler and McConnell 1955; Wang et al. 1988; Schettgen et al 2004; Yagami et al. 2009] supported by the mathematical model prediction demonstrates that DMS is systemically available and toxic following dermal exposure. DMS is corrosive at high doses and following prolonged dermal exposure and irritating at lower concentrations based on human [Littler and McConnell 1955; Wang et al. 1988; Yagami et al. 2009] and animal [Dow 1938; Browning 1965; E.I. du Pont de Nemours and Company 1972] studies. Although positive responses were observed in the murine LLNA test [Ashby et al. 1995] and in a single human patch test [Yagami et al. 2009], conflicting evidence in animal studies [Stevens 1967; E.I. du Pont de Nemours and Company 1972] suggests that DMS is not capable of causing immune-mediated responses (i.e., sensitization) following skin contact and that the positive responses may be attributable to corrosive properties of the chemical. Therefore, on the basis of these assessments, DMS is assigned a composite skin notation of **SK: SYS-DIR (COR)**.

Table 3 summarizes the skin hazard designations for DMS previously issued by NIOSH and other organizations. The equivalent dermal designations for DMS, according to the Globally Harmonized System (GHS) of classification and labeling of chemicals, the equivalent GHS classification for DMS are Skin Corrosion Category 1B (Causes severe skin burns and eye damage) and Skin Sensitization Category 1 (May cause an allergic skin reaction) [European Parliament 2008].

**Table 3. Summary of previous skin hazard designations for DMS**

<b>Organization</b>	<b>Skin hazard designation</b>
NIOSH [2005]	[skin]: Potential for dermal absorption
OSHA [2015] <sup>*</sup>	[skin]: Potential for dermal absorption
ACGIH [2001]	[skin]: Based on systemic toxicity reported for workers from dermal contact with DMS
EC [2013] <sup>*</sup>	R34: Causes burns R43: May cause sensitization by skin contact

ACGIH = American Conference of Governmental Industrial Hygienists; EC = European Commission, Joint Research, Institute for Health and Consumer Protection; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration.

<sup>\*</sup>Date accessed.

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**Note:** Asterisks (\*) denote sources cited in text; daggers (†) denote additional resources.

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## Appendix: Calculation of the SI Ratio

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for DMS. Although the SI ratio is considered in the determination of a substance's hazard potential following skin contact, it is intended only to serve as supportive data during the assignment of the NIOSH SK. An in-depth discussion on the rationale and calculation of the SI ratio can be found in Appendix B of the *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009].

### Overview

The SI ratio is a predictive algorithm for estimating and evaluating the health hazards of skin exposure to substances. The algorithm is designed to evaluate the potential for a substance to penetrate the skin and induce systemic toxicity [NIOSH 2009]. The goals for incorporating this algorithm into the proposed strategy for assigning SYS notation are as follows:

- (1) Provide an alternative method to evaluate substances for which no clinical reports or animal toxicity studies exist or for which empirical data are insufficient to determine systemic effects.
- (2) Use the algorithm evaluation results to determine whether a substance poses a skin absorption hazard and should be labeled with the SYS notation.

The algorithm evaluation includes three steps:

- (1) determining a skin permeation coefficient ( $k_p$ ) for the substance of interest,
- (2) estimating substance uptake by the skin and respiratory absorption routes, and
- (3) evaluating whether the substance poses a skin exposure hazard.

The algorithm is flexible in the data requirement and can operate entirely on the basis of the physicochemical properties of a substance and the relevant exposure parameters. Thus, the algorithm is independent of the need for biologic data. Alternatively, it can function with both the physicochemical properties and the experimentally determined permeation coefficient when such data are available and appropriate for use.

The first step in the evaluation is to determine the  $k_p$  for the substance to describe the transdermal penetration rate of the substance [NIOSH 2009]. The  $k_p$ , which represents the overall diffusion of the substance through the stratum corneum and into the blood capillaries of the dermis, is estimated from the compound's molecular weight ( $MW$ ) and base-10 logarithm of its octanol–water partition coefficient ( $\log K_{ow}$ ). In this example,  $k_p$  is determined for a substance with use of Equation 1. A self-consistent set of units must be used, such as outlined in Table A1. Other model-based estimates of  $k_p$  may also be used [NIOSH 2009].

### Equation 1: Calculation of Skin Permeation Coefficient ( $k_p$ )

$$k_p = \frac{1}{\frac{1}{k_{psc} + k_{pol}} + \frac{1}{k_{aq}}}$$

where  $k_{psc}$  is the permeation coefficient in the lipid fraction of the stratum corneum,  $k_{pol}$  is the coefficient in the protein fraction of the stratum corneum, and  $k_{aq}$  is the coefficient in the watery epidermal layer. These components are individually estimated by

$$\begin{aligned} \log k_{psc} &= -1.326 + 0.6097 \times \log K_{ow} - 0.1786 \times MW^{0.5} \\ k_{pol} &= 0.0001519 \times MW^{-0.5} \\ k_{aq} &= 2.5 \times MW^{-0.5} \end{aligned}$$

The second step is to calculate the biologic mass uptake of the substance from skin absorption (skin dose) and inhalation (inhalation dose) during the same period of exposure. The skin dose is calculated as a mathematical product of the  $k_p$ , the water solubility ( $S_w$ ) of the substance, the exposed skin surface area, and the duration of exposure. Its units are milligrams (mg). Assume that the skin exposure continues for 8 hours to unprotected skin on the palms of both hands (a surface area of 360 squared centimeters [ $\text{cm}^2$ ]).

### Equation 2: Determination of Skin Dose

$$\begin{aligned} \text{Skin dose} &= k_p \times S_w \times \text{Exposed skin surface area} \times \text{Exposure time} \\ &= k_p(\text{cm/hr}) \times S_w(\text{mg/cm}^3) \times 360 \text{ cm}^2 \times 8 \text{ hr} \end{aligned}$$

The inhalation dose (in mg) is derived on the basis of the occupational exposure limit (OEL) of the substance—if the OEL is developed to prevent the occurrence of systemic effects rather than sensory/irritant effects or direct effects on the respiratory tract. Assume a continuous exposure of 8 hours, an inhalation volume of 10 cubic meters ( $\text{m}^3$ ) inhaled air in 8 hours, and a factor of 75% for retention of the airborne substance in the lungs during respiration (retention factor, or RF).

### Equation 3: Determination of Inhalation Dose

$$\begin{aligned} \text{Inhalation dose} &= \text{OEL} \times \text{Inhalation volume} \times \text{RF} \\ &= \text{OEL}(\text{mg/m}^3) \times 10 \text{ m}^3 \times 0.75 \end{aligned}$$

The final step is to compare the calculated skin and inhalation doses and to present the result as a ratio of skin dose to inhalation dose (the SI ratio). This ratio quantitatively indicates (1) the significance of dermal absorption as a route of occupational exposure to the substance and (2) the contribution of dermal uptake to systemic toxicity. If a substance has an SI ratio greater than or equal to 0.1, it is considered a skin absorption hazard.

## Calculation

Table A1 summarizes the data applied in the previously described equations to determine the SI ratio for DMS. The calculated SI ratio was 12.8. On the basis of these results, DMS is predicted to represent a skin absorption hazard.

**Table A1. Summary of Data used to Calculate the SI Ratio for DMS**

Variables Used in Calculation	Units	Value
<b>Skin permeation coefficient</b>		
Permeation coefficient of stratum corneum lipid path ( $k_{psc}$ )	cm/hr	$5.8309 \times 10^{-4}$
Permeation coefficient of the protein fraction of the stratum corneum ( $k_{poi}$ )	cm/hr	$1.3525 \times 10^{-5}$
Permeation coefficient of the watery epidermal layer ( $k_{aq}$ )	cm/hr	0.2226
Molecular weight ( $MW$ ) <sup>*</sup>	amu	126.13
Base-10 logarithm of its octanol–water partition coefficient ( $\text{Log } K_{ow}$ ) <sup>*</sup>	None	0.16
Calculated skin permeation coefficient ( $k_p$ )	cm/hr	$5.9502 \times 10^{-4}$
<b>Skin dose</b>		
Water solubility ( $S_w$ ) <sup>*</sup>	mg/cm <sup>3</sup>	28
Calculated skin permeation coefficient ( $k_p$ )	cm/hr	$5.9502 \times 10^{-4}$
Estimated skin surface area (palms of hand)	cm <sup>2</sup>	360
Exposure time	hr	8
Calculated skin dose	mg	47.98
<b>Inhalation Dose</b>		
Occupational exposure limit (OEL) <sup>†</sup>	mg/m <sup>3</sup>	0.5
Inhalation volume	m <sup>3</sup>	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	3.75
<b>Skin dose–to–inhalation dose (SI) ratio</b>	None	12.8

<sup>\*</sup>Variables identified from SRC [ND].

<sup>†</sup>The OEL used in calculation of the SI ratio for DMS was the NIOSH recommended exposure limit (REL) [NIOSH 2005].

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