NIOSH Skin Notation Profiles

Methyl Isocyanate

SK

ID^{SK}

[~~SK~~]

SYS

SYS (FATAL)

DIR

DIR (IRR)

DIR (COR)

SEN

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

NIOSH Skin Notation (SK) Profiles

Methyl Isocyanate
[CAS No. 624-83-9]

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 hepatoxicity). 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 methyl isocyanate (MIC). 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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Contents

Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
ATSDR	Agency for Toxic Substances and Disease Registry
CIB	Current Intelligence Bulletin
cm^2	square centimeter(s)
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
EC	European Commission
GHS	Globally Harmonized System for Classification and Labelling of Chemicals
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_{50}	dose resulting in 50% mortality in the exposed population
LD_{Lo}	dermal lethal dose
LOAEL	lowest-observed-adverse-effect level
log K_{OW}	base-10 logarithm of a substance's octanol–water partition
M	molarity
m^3	cubic meter(s)
mg	milligram(s)
mg/cm^3	milligram(s) per cubic centimeter
mg/kg	milligram(s) per kilogram body weight
MIC	methyl isocyanate
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
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
SYS	skin notation indicating the potential for systemic toxicity following exposure of the skin
TDI	toluene diisocyanate
USEPA	United States Environmental Protection Agency

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 Introduction

1.1 General Substance Information

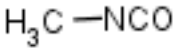
Chemical: Methyl isocyanate (MIC)

CAS No: 624-83-9

Molecular weight (*MW*): 57.1

Molecular formula: CH_3NCO

Structural formula:



Synonyms:

MIC; Isocyanate methane; Isocyanatomethane; Isocyanomethane; Methyl carbonyl amine; Methyl ester, Isocyanic acid

Uses:

MIC is primarily used as a chemical intermediate during the manufacturing of carbamate and other pesticides [ACGIH 2001].

1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with MIC and (2) the rationale behind the hazard-specific skin notation (SK) assignment for MIC. 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 MIC. A literature search was conducted through April 2014 to identify information on MIC, 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 MIC.

1.3 Overview of SK Assignment

MIC 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 MIC: **SK: SYS-DIR (COR)-SEN**. Table 1 provides an overview of the critical effects and data used to develop the SK assignment for MIC.

2 Systemic Toxicity from Skin Exposure (SK: SYS)

There have been no documented dermal absorption studies of MIC in humans or animals.

Table 1. Summary of the SK assignment for MIC

Skin notation	Critical effect	Data available
SK: SYS	Acute toxicity	Sufficient animal data
SK: DIR (COR)	Skin corrosion	Sufficient animal data
SK: SEN	Skin allergy	Sufficient animal data

The potential of MIC 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 3.7 was calculated for MIC. An SI ratio of ≥0.1 indicates that skin absorption may significantly contribute to the overall body burden of a substance [NIOSH 2009]; therefore, MIC 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 estimated dermal lethal dose (LD_{Lo}) for humans was identified. However, dermal LD_{50} (the dose resulting in 50% mortality in the exposed animals) values of 1800 milligrams per kilogram body weight (mg/kg) and 0.22 milliliters (undiluted) per kilogram (mL/kg) [corresponding to 203 mg/kg] have been reported in rabbits [Mellon Institute 1963, 1970; Smyth et al. 1969; Vernot et al. 1977]. In guinea pigs, Eastman Kodak Company [1990] reported a dermal LD_{50} value of 1 to 5 mL/kg [corresponding to 923 mg/kg to 4615 mg/kg]. Because the reported acute dermal LD_{50} values for these species are lower than the critical dermal LD_{50} value of 2000 mg/kg body weight that identifies chemical substances with the potential for acute dermal toxicity [NIOSH 2009], MIC is considered systemically available and acutely toxic by the dermal route.

No effects data were identified regarding dermal repeat-dose (21-day or 28-day), sub-chronic (90-day), or chronic (at least 12-month) toxicity of MIC in humans or animals. No standard toxicity or specialty studies evaluating biological system/function specific effects (including reproductive and developmental effects and immunotoxicity) of MIC following dermal exposures were identified. No epidemiological studies or standard animal carcinogenicity studies were identified that evaluated the potential of the chemical to cause tumors. However, studies following the industrial disaster in Bhopal, India in 1984 examined these outcomes following exposure to the eyes, respiratory tract and skin from the MIC gas cloud, which might have also included exposure to toxic byproducts and contaminants [Dhara 2002]. While researchers found limited evidence of carcinogenesis, there was evidence that exposure to MIC depressed phagocytic activity of lymphocytes, indicating a toxicological effect [Saxena 1988]. Exposure to MIC from the disaster was also found to lead to reproductive outcomes such as spontaneous abortion [Bhandari 1990]. Table 2 summarizes carcinogenic designations of multiple governmental and nongovernmental organizations for MIC.

No toxicokinetic studies following dermal exposure to MIC were identified. However, the capacity of the compound to penetrate the skin can be inferred from the fact that values for the dermal median lethal dose (LD_{50}) have been reported, and is supported by a predictive mathematical model (see Appendix) that indicate the chemical can be absorbed through the skin. In addition, acute dermal toxicity studies showed that the MIC is acutely toxic. No repeat-dose or prolonged dermal toxicity studies were identified in humans or animals. Based primarily on observed acute toxicity following dermal exposure **[Mellon Institute 1963, 1970; Smyth et al. 1969; Vernot et al. 1977; Eastman Kodak Company 1990]** *, there are sufficient data in animals to conclude that MIC is systemically absorbed and acutely toxic. Therefore, on the basis of the data for this assessment, MIC is assigned the SK: SYS notation.

*References in bold text indicate studies that serve as the basis of the SK assignments.

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

Organization	Carcinogenic designation
NIOSH [2005]	No designation
NTP [2011]	No designation
USEPA [2012]	No designation
European Parliament [2008]	No designation
IARC [2007]	No designation
EC [2014]†	No designation
ACGIH [2001]	No designation

ACGIH = American Conference of Governmental Industrial Hygienists; EC = European Commission, Joint Research, Institute for Health and Consumer Protection; 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 rather than dermal exposure.
†Date accessed.

3 Direct Effects on Skin (SK: DIR)

No human data on direct effects (corrosivity or irritancy) of MIC were identified. Several experimental animal studies were identified that investigated the direct effects of MIC on skin. Necrosis of the skin occurred at the site of application when undiluted MIC was applied to intact rabbit skin [Mellon Institute 1963, 1970; Smyth et al. 1969], and moderate erythema and marked capillary injection occurred when a 10% solution of MIC was applied to intact rabbit skin [Mellon Institute 1963]. Guinea pigs receiving undiluted applications of 1.0-10.0 mL/kg MIC exhibited gross edema, necrosis, and hemorrhaging [Eastman Kodak Company 1990]. In another study in guinea pigs, single administrations of 10% or less of MIC produced no irritation to the intact skin, whereas 25% to 100% solutions produced mild, moderate or strong erythema and severity of erythema and edema varied depending on the concentration [E.I. du Pont de Nemours and Company 1968]. E.I. du Pont de Nemours and Company [1968] also reported that a second application of MIC to the intact skin of the guinea pigs resulted in increased skin irritation. Dow Chemical Company [1990] reported slight to extensive hyperemia, edema and slight necrosis when the undiluted material was applied twice to the intact or abraded belly of rabbits, whereas no irritation was observed following 10 applications of a 2% solution to the intact belly or ear or three applications of the same solution to abraded belly of rabbits. Predictions using structure activity relationship models provide some additional information regarding this endpoint. The structure activity relationship model, Deductive Estimation of Risk from Existing Knowledge (*DEREK*) for Windows, predicted MIC to be negative for skin irritation, indicating that the substance does not have structural alerts for skin irritation.

Although no case reports of skin effects resulting from dermal exposure to MIC were identified and the *DEREK* model predicted MIC to be negative for skin irritation, there was evidence of skin irritation and corrosion in animals. Animal studies **[Mellon Institute 1963, 1970; E.I. du Pont de Nemours and Company 1968; Smyth et al. 1969; Dow Chemical Company 1990; Eastman Kodak 1990]** showed that the undiluted material or concentrated solutions are corrosive, while weaker dilutions tend to be non-irritating or slightly irritating to the skin. Therefore, on the

basis of the data for this assessment, MIC is assigned the SK: DIR (COR) notation.

4 Immune-mediated Responses (SK: SEN)

No human reports were identified that suggest that MIC is a skin sensitizer. However, skin sensitization studies in guinea pigs demonstrate that the chemical is a skin sensitizer. The Mellon Institute [1963, 1970] reported that MIC was a confirmed sensitizing agent in 16 of 16 guinea pigs following an intradermal sensitization test that involved injection of 0.05 mL of a 0.01% solution in peanut oil followed by a series of seven 0.1 mL sensitizing injections. E.I. du Pont de Nemours and Company [1968] reported allergic dermatitis in 9 of 10 guinea pigs challenged with 5-25% MIC in a 1:1 solution of acetone and dioxane containing 13% guinea pig fat on intact and abraded skin. Five animals received nine applications of 5% to 25% MIC in guinea pig fat on abraded skin during a three-week period and the remaining five received two intradermal dermal injections of 1% MIC in dimethyl phthalate seven days apart [E.I. du Pont de Nemours and Company 1968]. Although the Mellon Institute [1963, 1970] observed no cross-sensitization in guinea pigs that were previously sensitized with toluene diisocyanate (TDI), Union Carbide Corporation [1987] reported that 7 of 20 guinea pigs produced positive reactions when the animals were previously sensitized intradermally with 8 applications of MIC followed by a challenge with intradermal injections of TDI. In a similar study, cross-sensitization was observed in 15 of 16 guinea pigs that received intradermal injections of TDI followed by an intradermal challenge with MIC [Union Carbide Corporation 1987]. Supplemental support for the occurrence of cross-sensitization was noted for both TDI and MIC following repeated intranasal instillations of TDI only [Svesson et al. 2009]. *DEREK* predicted MIC to be a plausible skin sensitizer.

Although no diagnostic human patch tests were identified that assessed the potential of MIC to be a skin sensitizer in humans, isocyanates are known to cause occupation-related allergic contact dermatitis and respiratory sensitization. Sufficient data were identified from predictive tests in guinea pigs **[Mellon Institute 1963, 1970; E.I. du Pont de Nemours and Company 1968; Union Carbide Corporation 1987]**, supported by results from a modeling prediction, to conclude that MIC induces skin sensitization and can cross-react with other isocyanates. Therefore, on the basis of the data for this assessment, MIC is assigned the SK: SEN notation.

5 Summary

Toxicokinetic studies that evaluated the potential of MIC to be absorbed through the skin following dermal exposure were not identified. However, predictions from a mathematical model indicate that MIC has the potential to be absorbed through the skin. The dermal absorption potential of the chemical is supported by several acute dermal toxicity studies in animals **[Mellon Institute 1963, 1970; Smyth et al. 1969; Vernot et al. 1977; Eastman Kodak Company 1990]** that show that the chemical is acutely toxic. No case reports of skin effects resulting from dermal exposure to MIC were identified. However, several skin irritation studies in rabbits and guinea pigs **[Mellon Institute 1963; E.I. du Pont de Nemours and Company 1968; Smyth et al. 1969; Dow Chemical Company 1990; Eastman Kodak 1990]** demonstrate that MIC produces skin damage and is corrosive in undiluted or very concentrated form, while weaker concentrations produce skin irritation. No diagnostic human patch tests were identified that assessed the potential of MIC to be a skin sensitizer in humans. However, isocyanates generally are known to cause occupation-related allergic contact dermatitis and respiratory sensitization. The potential to cause skin sensitization and to cross-react with related isocyanates is demonstrated by

Table 3. Summary of previous skin hazard designations for MIC

Organization	Skin hazard designation
NIOSH [2005]	[skin]: Potential for dermal absorption
OSHA [2014]*	[skin]: Potential for dermal absorption
ACGIH [2001]	[skin]: Based on the reported mortality in rabbits following topical application and absorption of MIC.
EC [2014]*	R24: Toxic in contact with skin
	R38: Irritating to skin
	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.
*Date accessed.

several predictive tests in guinea pigs **[Mellon Institute 1963; E.I. du Pont de Nemours and Company 1968; Union Carbide Corporation 1987]**, supported by results from a modeling prediction. Based on the available data, this assessment concludes that there are sufficient data in animals to demonstrate that MIC is absorbed through the skin, is acutely toxic, is corrosive to the skin and can cause skin sensitization and cross-reactivity with other isocyanates. Therefore, on the basis of these assessments, MIC is assigned a composite skin notation of **SK: SYS-DIR (COR)-SEN**.

Table 3 summarizes the skin hazard designations for MIC previously issued by NIOSH and other organizations. The equivalent dermal designations for MIC, according to the Global Harmonization System (GHS) of Classification and Labelling of Chemicals, are Acute Toxicity Category 3 (Hazard statement: Toxic in contact with the skin), Skin Irritation Category 2 (Hazard statement: Causes skin irritation), and Skin Sensitization Category 1 (Hazard statement: May cause an allergic skin reaction) [European Parliament 2008]. In addition, MIC is identified as a Category 2 Reproductive Toxicant (Hazard statement: Suspected of damaging the unborn child.) [European Parliament 2008].

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Appendix: Calculation of the SI Ratio for MIC

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for MIC. 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)

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

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

$$\log k_{psc} = -1.326 + 0.6097 \times \log K_{ow} - 0.1786 \times MW^{0.5}$$

$$k_{pol} = 0.0001519 \times MW^{-0.5}$$

$$k_{aq} = 2.5 \times MW^{-0.5}$$

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 square centimeters [cm^2]).

Equation 2: Determination of Skin Dose

Skin dose

$= k_p \times S_w \times$ Exposed skin surface area × Exposure time

$= k_p$(cm/hour) × S_w (mg/cm^3) × 360 cm^2 × 8 hours

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 (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

Inhalation dose = OEL × Inhalation volume × RF

= OEL (mg/m^3) × 10 m^3 × 0.75

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 MIC. The calculated SI ratio was ~3.7. On the basis of these results, MIC is predicted to represent a skin absorption hazard.

Appendix References

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Table A1. Summary of data used to calculate the SI ratio for MIC

Variables used in calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path(k_{psc})	cm/hr	6.4072×10^{-3}
Permeation coefficient of the protein fraction of the stratum corneum (k_{pol})	cm/hr	2.0111×10^{-5}
Permeation coefficient of the watery epidermal layer (k_{aq})	cm/hr	0.331
Molecular weight (MW)*	amu	57.1
Base-10 logarithm of its octanol–water partition coefficient (Log K_{ow})*	None	0.79
Calculated skin permeation coefficient (k_p)	cm/hr	6.3049×10^{-3}
Skin dose		
Water solubility (S_w)*	mg/cm^3	29.2
Calculated skin permeation coefficient (k_p)	cm/hr	6.3049×10^{-3}
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hr	8
Calculated skin dose	mg	530.22
Inhalation dose		
Occupational exposure limit (OEL)†	mg/m^3	0.05
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	144
Skin dose–to–inhalation dose (SI) ratio	None	3.68

*Variables identified from SRC [2009].
†The OEL used in calculation of the SI ratio for MIC was the NIOSH recommended exposure limit (REL) of 1 part per million (5 mg/m^3) [NIOSH 2005].

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