NIOSH Skin Notation Profiles

Epichlorohydrin

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

Skin Notation (SK) Profile

Epichlorohydrin
[CAS No. 106–89–8]

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 a substance's hazard potential, 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 assignment and supportive data for epichlorohydrin (CAS No. 106–89–8). In particular, this document evaluates and summarizes the literature describing the substance's hazard potential 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 chemical of interest.

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Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
CIB	Current Intelligence Bulletin
cm/hr	centimeter(s) per hour
cm/s	centimeter(s) per second
(COR)	subnotation of SK: DIR indicating the potential for a chemical to be corrosive following exposure of the skin
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 of Classification and Labeling of Chemicals
GPMT	guinea pig maximization test
IARC	International Agency for Research on Cancer
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
log K_{OW}	base-10 logarithm of a substance's octanol–water partition
m^3	cubic meter(s)
mg	milligram(s)
$mg/cm^2/hr$	milligram(s) per square centimeter per hour
mg/kg	milligram(s) per kilogram body weight
mg/m^3	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
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
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: Epichlorohydrin

CAS No: 106–89–8

Molecular weight (MW): 93

Molecular formula: C_3H_5ClO

Structural formula:

Synonyms:

1-chloro-2,3-epoxypropane; 2-chloropropylene oxide; γ-chloropropylene oxide

Uses:

Epichlorohydrin is an organochlorine compound and an epoxide used primarily as a chemical intermediate in the production of epoxy resins and glycerol; it is also applied as a raw material for the manufacturing of glycerol and glycidol derivatives used as plasticizers, stabilizers, solvents, dyestuff intermediates, and pharmaceuticals [USEPA 1984].

1.2 Purpose

This *Skin Notation Profile* presents (1) brief summary of technical data associated with skin contact with epichlorohydrin and (2) the rationale behind the hazard-specific skin notation (SK) assignment for epichlorohydrin. 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 epichlorohydrin. A literature search was conducted through July 2010 to identify information on epichlorohydrin, 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 epichlorohydrin.

1.3 Overview of SK Assignment for Epichlorohydrin

Epichlorohydrin 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 epichlorohydrin: **SK:**

Table 1. Summary of the SK assignment for epichlorohydrin

Skin notation	Critical effect(s)	Available data
SK: SYS	Acute toxicity; Respiratory depression	Limited animal data
SK: DIR(COR)	Skin corrosion; skin tumors (cancer)	Limited human data; limited animal data
SK: SEN	Skin allergy	Sufficient human data; limited animal data

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

2 Systemic Toxicity from Skin Exposure (SK: SYS)

There are few data on the absorption potential of epichlorohydrin in humans and animals following dermal exposure. A few studies of animals were identified that showed epichlorohydrin is absorbed when the chemical is in contact with the skin. For example, immersion of the tails of mice in undiluted epichlorohydrin for 15 to 60 minutes resulted in the death of most mice, indicating systemic poisoning that likely resulted from dermal absorption [Kremneva and Tolgskaja 1961; Pallade et al. 1967]. Lawrence et al. [1972] reported that rabbits died within 7 days following occluded application of epichlorohydrin to the shaved skin for 24 hours. Although these studies did not measure the extent of absorption, it can be concluded on the basis of the observed effects that the chemical was absorbed through the skin following dermal contact. The potential of epichlorohydrin 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 chemical substances [NIOSH 2009]. The evaluation method compares an estimated chemical 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 skin dose to inhalation dose (SI ratio) of 22.7 was calculated for epichlorohydrin. An SI ratio of ≥0.1 indicates that a chemical is capable of producing systemic toxicity from skin exposure [NIOSH 2009]. Additional information on the SI ratio and the variables used in its calculation are included in the appendix.

The dermal lethal dose (LD_{Lo}) for humans has not been determined. However, values for dermal LD_{50} in rabbits (the dose resulting in 50% mortality in the exposed population) have been reported to range from 515 to 1038 milligrams per kilogram body weight (mg/kg) [Mellon Institute 1970; Shell Chemical Company 1977; Hine et al. 1981] or from 0.6389 to 1.3 milliliters per kilogram body weight (mL/kg) (corresponding to 750 to 1528 mg/kg) [Weil et al. 1963; Lawrence et al. 1972]. A dermal LD_{50} of greater than 1.0 mL/kg (corresponding to 1175 mg/kg) was reported for male rats after a 7-day exposure; no toxicity symptoms were detectable in the animals under the conditions of the study [Mobay Chemical Corporation 1967]. Dow

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

Organization	Carcinogenic designation
NIOSH [2005]	Potential occupational carcinogen
NTP [2009]	Reasonably anticipated to be a human carcinogen
USEPA [2009]	Group 2B: Probable human carcinogen (based on sufficient evidence of carcinogenicity in animals)
IARC [2009]	Group 2A: Probably carcinogenic to humans
EC [2010]	R45: May cause cancer
ACGIH [2001]	A3: Confirmed animal carcinogen with unknown relevance to humans

Abbreviations: 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.
*Note: The listed cancer designations were based on data from nondermal (such as oral or inhalation) exposure rather than dermal exposure.

Chemical Company [1976] reported a dermal LD_{50} value of 515 mg/kg for undiluted epichlorohydrin and 250 to 500 mg/kg for a 20% solution in propylene glycol. Because the reported acute dermal LD_{50} values for the rabbit and mouse are both lower than the critical dermal LD_{50} value of 2000 mg/kg that identifies chemical substances with the potential for acute dermal toxicity [NIOSH 2009], epichlorohydrin is considered systemically toxic by the acute dermal route.

No data from epidemiological studies of humans were identified. The literature search revealed only one study involving experimental animals and repeat-dose dermal exposures to epichlorohydrin; in that study, gradual depression of respiration leading to death occurred after repeated application of 0.5 mL/kg to the skin of rats [Shell Chemical Company 1977].

In addition, no standard toxicity or specialty studies evaluating biological system/function–specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure were identified. However, limited data were noted on the potential for epichlorohydrin to cause cancer in experimental animals. The chemical yielded negative results after continuous skin painting in mice, in the absence of a tumor promoter [Weil et al. 1963; Van Duuren et al. 1974]. Table 2 provides a summary of carcinogenic designations for epichlorohydrin from multiple governmental and nongovernmental organizations.

Taken together, the data on systemic effects in animals **[Lawrence et al. 1972*]**, acute toxicity in rabbits **[Lawrence et al. 1972; Hine et al. 1981], and** repeat-dose toxicity **[Shell Chemical Company 1977]** are sufficient to demonstrate that epichlorohydrin is systemically available and toxic following dermal exposure. Therefore, on the basis of the data for this assessment, epichlorohydrin is assigned the SK: SYS notation.

*References in **bold** text indicate studies that served as the basis of the SK assignment.

3 Direct Effects on Skin (SK: DIR)

No data on the corrosivity of epichlorohydrin were identified, and there have been no in vitro tests for corrosivity in human skin models or for skin integrity in cadaver skin specimens. Findings on direct skin effects in humans are limited to those of a single study, by Dow Chemical Company [1970a], in which irritation effects were observed in 22 of 200 volunteers dermally administered epichlorohydrin. In animals, the degree of irritation following epichlorohydrin application was dependent on the concentration and duration of exposure. Application of 0.5 milliliter (mL) of undiluted liquid to rabbit skin for 24 hours [Pallade et al. 1967] or of a 5% solution of epichlorohydrin in cottonseed oil for 2 to 24 hours [Lawrence et al. 1972] caused burns or necrosis. Doses of 0.1 to 0.2 mL undiluted liquid applied to rabbit skin for 2 hours resulted in irritation over a small area that was less severe than with application of 0.5 mL [Pallade et al. 1967]. A 0.3% solution in cottonseed oil applied under an occlusive patch for 24 hours was not irritating [Lawrence et al. 1972], and 0.1 mL applied over 24 hours produced barely perceptible irritation [Pallade et al. 1967]. Mobay Chemical Corporation [1967] reported that application of one drop of undiluted epichlorohydrin into rabbit ear caused no skin reaction, whereas one drop applied to the same skin spot four times in 1 hour caused distinctive injury to the skin. Dow Chemical Company [1953] reported that exposing intact skin for a single short period (15 to 20 minutes) to an unspecified volume of undiluted epichlorohydrin causes no skin reaction, but prolonged exposure results in severe burns. Patch tests with undiluted epichlorohydrin in rabbits produced erythema and edema, with a primary irritation index of 4.84, indicating exposure to a moderate irritant [Proctor and Gamble 1976]. Dow Chemical Company [1970a] reported a fatiguing response, in which repeated exposure to epichlorohydrin weakened the ability of the skin to resist the effects of the chemical. The structure-activity relationship model, Deductive Estimation of Risk from Existing Knowledge (DEREK™) for Windows, predicted epichlorohydrin to be a skin irritant.

Van Duuren [1974] conducted an initiation-promotion study to determine the carcinogenic potential of epichlorohydrin following skin painting. Mice received a single application of 2.0 mg epichlorohydrin in 0.1 mL acetone, followed by repeated applications of a tumor promoter, phorbol myristate acetate. The authors reported that epichlorohydrin acted as a tumor initiator, resulting in the formation of skin papillomas and skin carcinoma.

Taken together, findings from the human experience and animal studies demonstrate that undiluted liquid or solutions of >1% epichlorohydrin are corrosive **[Lawrence et al. 1972]**, whereas diluted solutions (<1%) are irritating **[Lawrence et al. 1972; Proctor and Gamble 1976].** In addition, a single skin-painting study indicates that epichlorohydrin is a tumor initiator. Therefore, on the basis of the data for this assessment, epichlorohydrin is assigned the SK: DIR (COR) notation.

4 Immune-mediated Responses (SK: SEN)

There is sufficient information available, from occupational exposure experience and animal studies, to conclude that

epichlorohydrin is a skin sensitizer. Several work-related cases of contact dermatitis or delayed skin sensitization attributable to dermal exposure to epichlorohydrin have been reported. For example, positive skin sensitization responses have been reported following patch tests with epichlorohydrin on patients with suspected contact dermatitis [Prens et al. 1986; van Joost 1988, 1990]. Other studies, such as those by Fregert and Gruvberger [1970] and Beck and King [1983], have demonstrated that epichlorohydrin caused hypersensitivity or contact dermatitis in humans. Inconsistent results have been observed in sensitization studies with animals, primarily guinea pigs. For example, no sensitization was observed following repeated application of epichlorohydrin to the skin of guinea pigs as a 0.01% solution in cottonseed oil (guinea pig maximization test, or GPMT) [Lawrence et al. 1972] or in another study using 0.1 mL of diluted material (concentration not specified) with a technique that involved intracutaneous injections [Weil et al. 1963]. However, in a Buehler test, 1 of 10 guinea pigs was sensitized after induction with 10% epichlorohydrin in propylene glycol, followed by challenge concentrations of 0.1% or 1% in propylene glycol [Proctor and Gamble 1976]. Dow Chemical Company [1970b] reported sensitization in 10 of 10 guinea pigs with use of a 0.4% v/v or 0.5% w/v solution of epichlorohydrin. Thorgeirsson and Fregert [1977] and Rao et al. [1981] observed sensitization with use of doses greater than 1%. A recent study that ranked contact allergen potency of over 200 chemicals listed epichlorohydrin as a Category A skin sensitizer, demonstrating it is a significant contact allergen in humans and animals [Schlede et al. 2003]. DEREK™ predicted epichlorohydrin to be a skin sensitizer.

On the basis of the human experience **[Prens et al. 1986; van Joost 1988, 1990]** and positive allergenicity results in animals **[Dow Chemical Company 1970b; Thorgeirsson and Fregert 1977; Rao et al. 1981]**, there is adequate evidence that repeated or prolonged contact with epichlorohydrin causes skin sensitization in humans. Therefore, on the basis of the data for this assessment, epichlorohydrin is assigned the SK: SEN notation.

5 Summary

Taken together, the systemic effects observed in animals **[Lawrence et al. 1972]**, the acute toxicity in rabbits **[Lawrence et al. 1972; Hine et al. 1981]**, and the repeated-dose data **[Shell Chemical Company 1977]** are sufficient to demonstrate epichlorohydrin is acutely toxic and induces systemic effects following dermal exposure. It appears on the basis of limited human experience and adequate animal data **[Lawrence et al. 1972; Proctor and Gamble 1976]** that undiluted epichlorohydrin is corrosive, but diluted (<1%) solutions are irritating. In addition, a single initiation-promotion study [Van Duuren 1974] demonstrated the ability of epichlorohydrin to act as a skin tumor initiator. The human experience **[Prens et al. 1986; van Joost 1988, 1990]** and positive allergenicity results in animal studies **[Dow Chemical Company 1970b; Thorgeirsson and Fregert 1977; Rao et al. 1981]** adequately show that repeated or prolonged contact with epichlorohydrin causes skin sensitization in humans. Therefore, on the basis of these assessments, epichlorohydrin is assigned a composite skin notation of **SK: SYS-DIR (COR)-SEN**.

Table 3 summarizes the skin hazard designations for epichlorohydrin previously issued by NIOSH and other organizations.

Table 3. Summary of the previously issued skin hazard designations for epichlorohydrin

Organization	Skin hazard designation
NIOSH [2005]	No skin notation assigned
OSHA [2009]	[skin]: Based on the evidence of dermal absorption and systemic toxicity
ACGIH [2001]	[skin]: Based on the evidence of dermal absorption and systemic toxicity
EC [2010]	R24: Harmful in contact with skin

Abbreviations: 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.

The equivalent dermal designations for epichlorohydrin, according to the Globally Harmonized System (GHS) of Classification and Labeling of Chemicals, are Acute Toxicity Category 3 (Hazard statement: Toxic in contact with the skin), Skin Corrosion Category 1B (Hazard statement: Causes severe skin burns and eye damage), and Skin Sensitization Category 1 (Hazard statement: May cause an allergic skin reaction) [European Parliament 2008]. Epichlorohydrin has been identified as a Category 1B Carcinogen (Hazard statement: May cause cancer).

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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 for Epichlorohydrin

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for epichlorohydrin. 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 the 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 centimeters per hour (cm/hr), outlined in Table A1. Other model-based estimates of K_p may also be used [NIOSH 2009].

Equation 1: Calculation of Skin Permeation Coefficient (Kp)

$$K_p + \frac{1}{\frac{1}{K_{psc} + K_{pol}} + \frac{1}{K_{aq}}}$$

where kpsc 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 kaq is the coefficient in the watery epidermal layer. These components are individually estimated by

$$\log K_{psc} = -1.326 + 0.6097 \times \log K_{OW} - 0.1786 \times MW0.5$$

$$K_{pol} = 0.0001519 \times MW - 0.5$$

$$K_{aq} = 2.5 \times MW - 0.5$$

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 (SW) 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 cm^2).

Equation 2: Determination of Skin Dose

$$\text{Skin dose} = K_p \times S_W \times \text{Exposed skin surface area} \times \text{Exposure time}$$

$$= K_p(cm/hr) \times S_W\ (mg/cm^3) \times 360\ cm^2 \times 8\ hours$$

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

$$\text{Inhalation dose} = \text{OEL} \times \text{Inhalation volume} \times RF$$

$$= \text{OEL}\ (mg/m^3) \times 10\ m^3 \times 0.75$$

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 epichlorohydrin. The calculated SI ratio was 22.7. On the basis of these results, epichlorohydrin is predicted to represent a skin absorption hazard.

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Table A.1 Summary of data used to calculate the SI ratio for epichlorohydrin

Variables used in calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path (K_{psc})	cm/hr	0.0017
Permeation coefficient of the protein fraction of the stratum corneum (K_{pol})	cm/hr	1.57912×10^{-5}
Permeation coefficient of the watery epidermal layer (K_{aq})	cm/hr	0.25990
Molecular weight (MW)*	amu	93
Base-10 logarithm of its octanol–water partition coefficient (Log K_{OW})*	None	0.45
Calculated skin permeation coefficient (K_p)	cm/hr	0.00170
Skin dose		
Water solubility (S_W)*	mg/cm^3	65.9
Calculated skin permeation coefficient (K_p)	cm/hr	0.00170
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hour	8
Calculated skin dose	mg	323.45
Inhalation dose		
Occupational exposure limit (OEL)†	mg/m^3	1.9
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	14.25
Skin dose–to–inhalation dose (SI) ratio	None	22.7

*Variables identified from SRC [2009].
†The OEL used in calculation of the SI ratio was the NIOSH-recommended exposure limit (REL) [NIOSH 2005].

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