

# NIOSH Skin Notation Profiles

Acrylic acid

SK

ID<sup>SK</sup>

[SK]

**SYS**

SYS (FATAL)

DIR

DIR (IRR)

**DIR (COR)**

SEN

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# NIOSH Skin Notation (SK) Profile

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Acrylic acid

[CAS No. 79-10-7]

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Naomi L. Hudson and G. Scott Dotson

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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 (such as irritant contact dermatitis and corrosion) to induction of immune-mediated responses (such as allergic contact dermatitis and pulmonary responses), or systemic toxicity (such as 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 (SKs) 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 (such as skin permeation) by means of analytical or numerical methods.

This *Skin Notation Profile* provides the SK assignments and supportive data for acrylic acid. 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

<b>ACGIH</b>	American Conference of Governmental Industrial Hygienists
<b>CIB</b>	Current Intelligence Bulletin
<b>cm<sup>2</sup></b>	square centimeter(s)
<b>cm/hour</b>	centimeter(s) per hour
<b>DAPA</b>	β-diacryloxypropionic acid
<b>DEREK</b>	Deductive Estimation of Risk from Existing Knowledge
<b>DIR</b>	skin notation indicating the potential for direct effects to the skin following contact with a chemical
<b>DMBA</b>	7,12-dimethylbenz[a]anthracene
<b>EC</b>	European Commission
<b>GHS</b>	Globally Harmonized System for Classification and Labelling of Chemicals
<b>GPMT</b>	guinea pig maximization test
<b>FCAT</b>	Freund's Complete Adjuvant test
<b>IARC</b>	International Agency for Research on Cancer
<b>(IRR)</b>	subnotation of SK: DIR indicating the potential for a chemical to be a skin irritant following exposure to the skin
<b><math>k_{aq}</math></b>	coefficient in the watery epidermal layer
<b><math>k_p</math></b>	skin permeation coefficient
<b><math>k_{pol}</math></b>	coefficient in the protein fraction of the stratum corneum
<b><math>k_{psc}</math></b>	permeation coefficient in the lipid fraction of the stratum corneum
<b>LD<sub>50</sub></b>	dose resulting in 50% mortality in the exposed population
<b>LD<sub>Lo</sub></b>	dermal lethal dose
<b>LLNA</b>	local lymph node assay
<b>LOAEL</b>	lowest-observed-adverse-effect level
<b>log <math>K_{ow}</math></b>	base-10 logarithm of a substance's octanol–water partition
<b><math>M</math></b>	molarity
<b>m<sup>3</sup></b>	cubic meter(s)
<b>mg</b>	milligram(s)
<b>mg/kg</b>	milligram(s) per kilogram body weight
<b>mg/m<sup>3</sup></b>	milligram(s) per cubic meter
<b>mL</b>	milliliter(s)
<b>mL/kg</b>	milliliter(s) per kilogram body weight
<b>MW</b>	molecular weight
<b>NIOSH</b>	National Institute for Occupational Safety and Health
<b>NOAEL</b>	no-observed-adverse-effect level
<b>NTP</b>	National Toxicology Program
<b>OEL</b>	occupational exposure limit
<b>OSHA</b>	Occupational Safety and Health Administration
<b>pmol/g</b>	picomoles per gram

<b>REL</b>	recommended exposure limit
<b>RF</b>	retention factor
<b>SEN</b>	skin notation indicating the potential for immune-mediated reactions following exposure of the skin
<b>SI ratio</b>	ratio of skin dose to inhalation dose
<b>SK</b>	skin notation
$S_w$	solubility in water
<b>SYS</b>	skin notation indicating the potential for systemic toxicity following exposure of the skin
v/v	volume per volume
<b>US EPA</b>	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 occur 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:

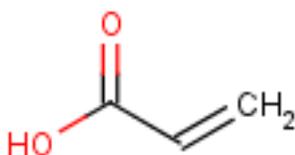
**Chemical:** Acrylic acid

**CAS No:** 79-10-7

**Molecular weight (MW):** 72.1

**Molecular formula:** CH<sub>2</sub>=CHCOOH

**Structural formula:**



**Synonyms:** Acroleic acid, Aqueous acrylic acid (technical grade is 94%), Ethylenecarboxylic acid, Glacial acrylic acid (98% in aqueous solution), 2-Propenoic acid

**Uses:** The primary use for acrylic acid is as a chemical intermediate during the manufacturing of acrylic resins [ACGIH 2001].

## 1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with acrylic acid and (2) the rationale behind the hazard-specific skin notation (SK) assignment for acrylic acid. 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 acrylic acid. A literature search was conducted through May 2016 to identify information on acrylic acid, 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 acrylic acid. The criteria for the search strategy, evaluation, and selection of data are described in Appendix E in the aforementioned *CIB 61* [NIOSH 2009].

## 1.3 Overview of SK Assignment

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

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

Limited toxicokinetic data following dermal exposure to acrylic acid were identified. No *in vivo* data for humans or *in vitro* data from using excised human cadaver skin were identified. Winter and Sipes [1993] applied 100 microliters

**Table 1. Summary of the SK assignment for acrylic acid**

Skin notation	Critical effect	Available data
SK: SYS	Acute toxicity	Sufficient animal data
SK: DIR (COR)	Skin corrosion	Sufficient animal data

( $\mu\text{L}$ ) of a 4% solution of acrylic acid in acetone to the mid-thoracic region of rats under a charcoal trap mounted on the skin. Seventy-three percent of the applied dose volatilized and was captured in the charcoal traps; 6% was still detected on the skin; and approximately 17% was detected in urine, feces,  $\text{CO}_2$ , and tissue from major organs [Winter and Sipes 1993]. Black et al. [1995] reported dermal absorption of approximately 11% of acrylic acid in mice and 24% dermal absorption in rats after 40 mg/kg of a solution of acrylic acid and acetone (1:100) was applied to the shaved dorsal skin of the mice and rats. Basic Acrylic Monomer Manufacturers [1993] reported 18% of a 10-mg/kg dose and 25% of a 40-mg/kg dose of  $^{14}\text{C}$ -labelled acrylic acid was absorbed through the skin of rats, and 11% of a 10-mg/kg dose and 11% of a 40-mg/kg dose were absorbed in mice.

The potential of acrylic acid 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 150 was calculated for acrylic acid. 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, acrylic acid has the potential to be absorbed through the skin and to become available systemically following dermal exposure. Additional information on the SI ratio and the variables used in its calculation are included in the appendix.

Although no estimated dermal lethal dose ( $\text{LD}_{10}$ ) for humans was identified, the reported dermal  $\text{LD}_{50}$  (lethal dose in 50% of exposed animals) values for rabbits were 0.28 milliliter per kilogram body weight (mL/kg) and 0.95 mL/kg (corresponding to 294 mg/kg and 998 mg/kg, respectively) [Smyth et al. 1962; Carpenter et al. 1974]. Because the reported acute dermal  $\text{LD}_{50}$  values for the rabbit are lower than the critical dermal  $\text{LD}_{50}$  value of 2000 mg/kg body weight that identifies chemical substances with the potential for acute dermal toxicity [NIOSH 2009], acrylic acid is considered acutely toxic following dermal exposure.

A limited number of repeat-dose studies following dermal exposure in animals were identified. One such study was a 13-week subchronic dermal toxicity study in which three strains of mice were topically exposed to 0.1 mL acrylic acid in acetone 3 times a week for 13 weeks at concentrations of 0%, 1%, or 4% (approximately 1 or 4 mg/mouse/application). In this study, McLaughlin et al. [1995] found no effect on body weight, the only systemic effect reported. A lifetime dermal exposure of mice to 1% acrylic acid in acetone, volume/volume (v/v; reported as approximately 0.2 mg/mouse/application) three times per week did not elicit any statistically significant effects on survival [DePass et al. 1984]. No standard toxicity or specialty studies evaluating biological system/function-specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure of animals to acrylic acid were identified.

No human reports or standard cancer bioassays were identified that evaluated the systemic carcinogenic potential of acrylic acid following dermal exposure. However, the dermal carcinogenic potential of acrylic acid was assessed in

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

Organization	Carcinogenic designation
NIOSH [2005]	No designation
NTP [2016]	No designation
US EPA [1994]	No designation
European Parliament [2008]	No GHS designation
IARC [2007]	Group 3: Not classifiable as to carcinogenicity to humans
ACGIH [2001]	A4- Not classifiable as a human carcinogen

ACGIH = American Conference of Governmental Industrial Hygienists; 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; US EPA = 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.

mice. In this study, DePass et al. [1984] found no epidermal tumors in any of the 40 mice topically exposed to 1% acrylic acid solution in acetone (v/v) (approximately 0.20 mg/mouse/application) three times per week for a lifetime.

Table 2 summarizes carcinogenic designations for acrylic acid by multiple governmental and nongovernmental organizations.

No studies were identified that fully evaluated the potential systemic effects of acrylic acid following repeated or prolonged dermal exposure. There is sufficient information from dermal absorption and penetration data (available from *in vivo* and *in vitro* studies in animals [Basic Acrylic Monomer Manufacturers 1993; Winter and Sipes 1993; Black et al. 1995] and acute dermal toxicity studies in rabbits [Smyth et al. 1962; Carpenter et al. 1974]), supported by mathematical model predictions, to demonstrate that acrylic acid has the potential to be absorbed, systemically available, and acutely toxic following dermal exposure. Therefore, on the basis of the data for this assessment, acrylic acid is assigned the SK: SYS notation.

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

No human or animal *in vivo* studies or *in vitro* tests for corrosivity using human skin models or *in vitro* tests of skin integrity using cadaver skin were identified. The European Chemicals Bureau (ECB) [2002] reported three cases from an unpublished 1992 study by BASF, in which two of three workers exposed to acrylic acid between 1967 and 1992 reported corrosion to the skin. In animal studies, topical application of an undiluted solution of acrylic acid resulted in necrosis of the skin of rabbits [Smyth et al. 1962; Carpenter et al. 1974]. ECB cited results from two unpublished studies by BASF, conducted in 1998 and 1958, in which necrosis occurred when undiluted acrylic acid was applied to rabbits [ECB 2002]. Applications of 5%, but not 1%, acrylic acid solution in acetone for 2 weeks caused skin irritation (peeling and flaking of the skin) in mice [DePass et al. 1984]. Tegeris et al. [1988] and McLaughlin et al. [1995] found no externally visible signs of skin irritation in mice with application of 1% solution of acrylic acid for

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

13 weeks. However, a 4% solution caused significant skin irritation (desquamation, fissures, and eschar), and proliferative, degenerative inflammatory changes were detected histologically in the epidermis and dermis from weeks 1 and 2 in these animals. The structure activity relationship model, Deductive Estimation of Risk from Existing Knowledge (*DEREK*) [Sanderson and Earnshaw 1991], predicted acrylic acid to be negative for skin irritation.

The available studies indicate that acrylic acid is an irritant at concentrations from 4% [DePass et al. 1984] and corrosive to the skin when undiluted [Smyth et al. 1962; Carpenter et al. 1974]. Therefore, on the basis of the data for this assessment, acrylic acid is assigned the SK: DIR (COR) notation.

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

Very limited data were identified that concerned the potential for acrylic acid to be a skin sensitizer in humans. Immediate hypersensitivity testing in a chemical worker showed a severe local reaction to 2% acrylic acid but no reaction to other acrylate compounds, and re-exposure to acrylic acid in the workplace resulted in generalized urticaria [Fowler 1990]. Daecke et al. [1993] reported positive response in a patch test in a woman with contact urticaria due to acrylic acid in a polyacrylic monomer in tape adhesive. Conde-Salazar et al. [1988] investigated the sensitization potential in six cases presenting with dermatitis due to acrylate-based sealants. Patch tests with 0.1% acrylic acid in petrolatum yielded negative results, indicating no cross-sensitization to acrylic acid; however, positive responses were observed with other acrylate compounds.

In animals, inconsistent results were reported with regard to the sensitization potential of acrylic acid. For example, a few studies utilizing the guinea-pig maximization test (GPMT) and the Landsteiner Draize and Polak tests in guinea pigs [Parker and Turk 1983] indicated that acrylic acid is a skin sensitizer. Waegemaekers and van der Walle [1984] observed a positive

result in the Freund's complete adjuvant test (FCAT) in guinea pigs; however, the positive response was thought to be due to the impurity of  $\alpha,\beta$ -diacryloxypropionic acid (DAPA), since there was no reaction when the animals were tested with distilled acrylic acid and acrylic acid that did not contain the contaminant DAPA. Waegemaekers and van der Walle [1984] concluded that allergic response to acrylic acid was due to the contaminant DAPA. DAPA is not a contaminant in acrylic acid produced by current distillation processes [IPCS 1997]. *DEREK* [Sanderson and Earnshaw 1991] predicted acrylic acid to be negative as a skin sensitizer.

The available data suggest that the strong sensitization from commercial acrylic acid is due to the presence of impurities (such as DAPA) [Waegemaekers and van der Walle 1984] or polymerization inhibitors of acrylic acid (such as methoxyphenol, phenothiazine, and diphenyl-p-phenylenediamine) [IPCS 1997]. In contrast, distilled acrylic acid was not demonstrated to cause skin sensitization, so the SK: SEN is not assigned to acrylic acid.

## 5 Summary

Although no studies were identified that fully evaluated potential systemic effects following repeated or prolonged dermal exposure, sufficient data were identified from dermal absorption and penetration studies in animals [Basic Acrylic Monomer Manufacturers 1993; Winter and Sipes 1993; Black et al. 1995] and acute dermal toxicity studies in rabbits [Smyth et al. 1962; Carpenter et al. 1974] to show that acrylic acid has the potential to be absorbed through the skin and is acutely toxic following dermal exposure. Undiluted acrylic acid [Smyth et al. 1962; Carpenter et al. 1974;] and possibly concentrations greater than 5% are corrosive to rabbit or rat skin, whereas concentrations up to 5% may be irritating to the skin [DePass et al. 1984]. Results from skin sensitization studies suggest that distilled acrylic acid is not likely to be a skin sensitizer, whereas commercial preparations using methods that do not include distillation are likely to contain impurities or

**Table 3. Summary of previous skin hazard designations for acrylic acid**

Organization	Skin hazard designation
NIOSH [2005]	[skin]: Potential for dermal absorption; prevent skin contact
OSHA [2017]*	No designation
ACGIH [2001]	[skin]: Based on the LD <sub>50</sub> values following single, topical application of undiluted acrylic acid

ACGIH = American Conference of Governmental Industrial Hygienists; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration.

\*Date accessed.

polymerization inhibitors that are potential skin sensitizers [Waegemaekers and van der Walle 1984; IPCS 1997]. Therefore, on the basis of these assessments, acrylic acid is assigned a composite skin notation of **SK: SYS-DIR (COR)**.

Table 3 summarizes the skin hazard designations for acrylic acid previously issued by NIOSH and other organizations. The equivalent dermal designations for acrylic acid, according to the Globally Harmonized System (GHS) for Classification and Labelling of Chemicals, are Acute Toxicity Category 4 (Hazard statement: Harmful in contact with the skin) and Skin Corrosion Category 1A (Hazard statement: Causes severe skin burns and eye damage) [European Parliament 2008].

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## Appendix: Calculation of the SI Ratio for Acrylic acid

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for acrylic acid. Although the SI ratio is considered in the determination of a substance's hazard potential following skin contact, it is intended to serve only 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 [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

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

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 square centimeters [ $\text{cm}^2$ ]).

#### Equation 2: Determination of Skin Dose

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

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

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

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 acrylic acid. The calculated SI ratio was 150. On the basis of these results, acrylic acid 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 acrylic acid**

Variables used in calculation	Units	Value
<b>Skin permeation coefficient</b>		
Permeation coefficient of stratum corneum lipid path ( $k_{psc}$ )	cm/hour	$2.3512 \times 10^{-3}$
Permeation coefficient of the protein fraction of the stratum corneum ( $k_{pol}$ )	cm/hour	$1.7894 \times 10^{-5}$
Permeation coefficient of the watery epidermal layer ( $k_{aq}$ )	cm/hour	0.294505
Molecular weight ( $MW$ )*	amu	72.06
Base-10 logarithm of its octanol–water partition coefficient ( $\text{Log } K_{ow}$ )*	None	0.35
Calculated skin permeation coefficient ( $k_p$ )	cm/hour	$2.3502 \times 10^{-3}$
<b>Skin dose</b>		
Water solubility ( $S_w$ )*	mg/cm <sup>3</sup>	1000
Calculated skin permeation coefficient ( $k_p$ )	cm/hour	$2.3502 \times 10^{-3}$
Estimated skin surface area (palms of hand) §	cm <sup>2</sup>	360
Exposure time	hour	8
Calculated skin dose	mg	6768.57
<b>Inhalation Dose</b>		
Occupational exposure limit (OEL)†	mg/m <sup>3</sup>	6
Inhalation volume	m <sup>3</sup>	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	45
<b>Skin dose–to–inhalation dose (SI) ratio</b>	<b>None</b>	<b>150</b>

\*Variables identified from SRC [ND].

†The OEL used in calculation of the SI ratio for acrylic acid was the NIOSH recommended exposure limit (REL) [NIOSH 2005].

§Hayes WA [2008]. Principles and methods of toxicology. 5th ed. New York: Informa Healthcare USA.



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