Skin Notation (SK) Profile

Ethyl acrylate

[CAS No. 140-88-5]

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 ethyl acrylate. 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
CIB	Current Intelligence Bulletin
cm^2	square centimeter(s)
cm/hour	centimeter(s) per hour
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
EC3	Effective concentration inducing a 3-fold increase in proliferation of lymph node cells
FCAT	Freund's complete adjuvant test
GHS	Globally Harmonized System for Labelling and Classification 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
kaq	coefficient in the watery epidermal layer
k_p	skin permeation coefficient
kpol	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
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^3	cubic meter(s)
µmoles	micromoles
µL	microliter(s)
mg	milligram(s)
mg/kg	milligram(s) per kilogram body weight
mg/kg-day	milligrams per kilogram body weight per day
mg/m^3	milligram(s) per cubic meter
mL	milliliter(s)
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
USEPA	United States Environmental Protection Agency
µmoles	micromoles
µL	microliters

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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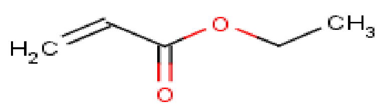
1.0 Introduction

1.1 General Substance Information:

Chemical: Ethyl acrylate
CAS No: 140-88-5
Molecular weight (*MW*): 100.1
Molecular formula: CH_2=$CHCOOC_2H_2$
Structural formula:



Synonyms: Ethyl acrylate (inhibited); Ethyl ester of acrylic acid; Ethyl propenoate

Uses: Ethyl acrylate is used primarily as a chemical intermediate during the production of polymers including resins, plastics, and rubber [HSDB 2010].

1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with ethyl acrylate and (2) the rationale behind the hazard-specific skin notation (SK) assignment for ethyl acrylate. 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 ethyl acrylate. A literature search was conducted through September 2012 to identify information on ethyl acrylate, 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 ethyl acrylate.

1.3 Overview of SK Assignment

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

Table 1. Summary of the SK Assignment for ethyl acrylate

Skin Notation	Critical Effect	Available Data
SK: SYS	Acute toxicity	Sufficient animal data
SK: DIR (COR)	Skin corrosion	Sufficient animal data
SK: SEN	Skin allergy	Sufficient human and animal data

2.0 Systemic Toxicity from Skin Exposure (SK: SYS)

No *in vivo* or *in vitro* toxicokinetic data that estimated the dermal absorption of ethyl acrylate following dermal exposure were identified. Some evidence of absorption through the skin was provided by acute dermal toxicity studies in which dermal application of the substance resulted in the deaths of rats, mice, and rabbits [Pozzani 1949; Treon et al. 1949; Sokal et al. 1980; Rohm and Haas Company 1986]. The potential of ethyl acrylate 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 1.09 was calculated for ethyl acrylate. An SI ratio of ≥0.1 indicates that skin absorption may significantly contribute to the overall body burden of a substance [NIOSH 2009]; therefore, ethyl acrylate 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 doses (LD_{Lo}) of ethyl acrylate for humans have been identified. However, dermal LD_{50} (the dose resulting in 50% mortality in the exposed animals) values of 1200-2000 milligrams per kilogram body weight (mg/kg) in rabbits [Pozzani et al. 1949; Dow Chemical Company 1957; Bio/dynamics Inc. 1990; Mellon Institute 1972; Soka et al. 1980], and 1800 mg/kg to greater than 5000 mg/kg in rats [Rohm and Haas Company 1986; Soka et al. 1980] have been reported. Because the reported acute dermal LD_{50} values for rabbits are 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], ethyl acrylate demonstrates acute toxicity following dermal exposure.

No systemic effects associated with occupational exposures to ethyl acrylate or standard, repeat-dose studies in animals were identified. However, a mouse skin-painting study evaluated the systemic effects of ethyl acrylate. In this study, Nylander-French and French [1998] applied 60, 300 or 600 micromoles (µmoles) of ethyl acrylate in 200 microliters (µL) acetone vehicle to the skin of female transgenic mice, 3 times per week for 20 weeks. Although no statistical analysis of the systemic effects observed was provided, graphical representation indicated that the Lowest-Observed-Adverse-Effect Level (LOAEL) for ethyl acrylate that produced systemic toxicity, as evidenced by depression of body weights, was 300 µmoles/mouse [corresponding to 1000 milligrams per kilogram per day (mg/kg-day)] [Nylander-French and French 1998]. This study also identified a No-Observed-Adverse-Effect Level (NOAEL) of 60 µmoles/mouse [corresponding to 200 mg/kg-day]. Based on this study, ethyl acrylate is systemically available and toxic because the NOAEL is lower than the critical dermal NOAEL value of 1000 mg/kg-day that identifies chemical substances with the potential for repeated-dose dermal toxicity [NIOSH 2009].

No standard toxicity or specialty studies evaluating biological system/function specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure to ethyl acrylate were identified. Few studies were identified that evaluated the carcinogenicity potential of ethyl acrylate following dermal exposure. Union Carbide Corporation [1982] and DePass et al. [1984] evaluated the dermal carcinogenic potential of ethyl acrylate by applying 25 µL of the undiluted substance [corresponding to 23 mg] to the backs of male C3H/HeJ mice three times a week throughout the lifetime of the animals. Table 2 summarizes carcinogenic designations of multiple governmental and nongovernmental organizations for ethyl acrylate.

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

Organization	Carcinogenic designation
NIOSH [2005]	Potential occupational carcinogen
NTP [2011]	No designation
USEPA [2012]	No designation
GHS [European Parliament 2008]	No designation
IARC [2012]	Group 2B: Possibly carcinogenic to humans
EC [2012]**	No designation
ACGIH [2001]	Group A4: Not classifiable as a human carcinogen

ACGIH = American Conference of Governmental Industrial Hygienists; EC = European Commission, Joint Research, Institute for Health and Consumer Protection; GHS = Globally Harmonized System for Labelling and Classification 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 rather than dermal exposure.

**Date accessed.

No studies that evaluated the dermal absorption of ethyl acrylate were identified. However, mathematical modeling, several dermal acute toxicity studies **[Pozzani et al. 1949; Treon et al. 1949; Dow Chemical Company 1957; Sokal et al. 1980; Bio/dynamics Inc. 1990]** *, and a repeat-dose study **[Nylander-French and French 1998]** indicate that the substance is absorbed through the skin and can cause systemic toxicity including bodyweight depression. Therefore, on the basis of the data for this assessment, ethyl acrylate is assigned the SK: SYS notation.

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

3.0 Direct Effects on Skin (SK: DIR)

No human or animal *in vivo* studies for corrosivity of ethyl acrylate or *in vitro* tests for corrosivity using human or animal skin models or *in vitro* tests of skin integrity using cadaver skin were identified. No standard irritation studies were identified for humans upon which the skin corrosion or irritation potential of ethyl acrylate can be evaluated. However, several studies conducted according to standard methods were identified in animals that show ethyl acrylate is corrosive or a skin irritant. Rohm and Haas Company [1991] reported that ethyl acrylate was corrosive to the skin of rabbits following application of 0.5 milliliters (mL) of undiluted ethyl acrylate to the shaved intact skin for 4 hours under occlusive conditions. Application of 25 µL [corresponding to 23 mg] of undiluted ethyl acrylate to the skin of mice three times per week for the life of the mouse caused epidermal necrosis, keratin necrosis, dermal fibrosis, and hyperkeratosis [Union Carbide Corporation 1982; DePass et al. 1984], indicating that prolonged and repeated exposure to the substance can lead to severe skin effects (skin corrosion). Earlier studies conducted by Pozzani et al. [1949] and Dow Chemical Company [1957] also showed that repeated, prolonged contact with the skin causes tissue damage. However, Industrial Bio-Test Laboratories Inc. [1972] found ethyl acrylate applied undiluted under occlusive conditions to abraded or intact skin of rabbits to be non-corrosive after rabbits were exposed to ethyl acrylate for four hours. Other studies reported that undiluted ethyl acrylate applied occluded to rabbit skin was moderately to severely irritating [Treon et al. 1949; Dow Chemical Company 1957; Safepharm Laboratories Limited 1984]. Applications under unoccluded conditions were slightly irritating [Pozzani et al. 1949]. Ethyl acrylate at concentrations up to 30% did not induce significant irritancy as measured by ear swelling in mice [Hayes and Meade 1999]. These studies indicate that the severity of irritation and tissue damage is dependent upon the concentration, duration, and frequency of exposure. The structure activity relationship model, Deductive Estimation of Risk from Existing Knowledge (*DEREK*) for Windows, predicted ethyl acrylate to be negative for skin irritation.

In a short-term carcinogenicity skin-painting study in female Tg.AC mice, Nylander-French and French [1998] found no statistically significant increase in skin papillomas when mice were administered doses of 60-600 µmoles/200 µL of ethyl acrylate in acetone (corresponding to 200 mg to 2000 mg/kg-day) 3 times per week for 20 weeks compared to acetone controls. In another transgenic mice study, Tennant et al. [1995] found topically applied ethyl acrylate (30 mg, 3 times per week for 20 weeks) to be inactive. These studies suggest that ethyl acrylate is not carcinogenic under the conditions of the tests.

Although human data were not located, sufficient data were identified from standard irritation tests. There are sufficient data to indicate that ethyl acrylate is an irritant, and prolonged and repeated dermal exposure studies to the undiluted substance in animal's causes skin corrosion **[Pozzani et al. 1949; Treon et al. 1949; Dow Chemical Company 1957; Union Carbide Corporation 1982; DePass et al. 1984; Safepharm Laboratories Limited, 1984; Rohm and Haas Company 1991]**. On the basis of the assembled data, ethyl acrylate is assigned the SK: DIR (COR) notation.

4.0 Immune-mediated Responses (SK: SEN)

Several studies were identified that evaluated the potential of ethyl acrylate to cause skin sensitization in humans and animals. In humans, Kanerva et al. [1997] compiled statistics on 10 years of patch testing with 30 (meth)acrylates and reported the frequency of allergic reactions caused by ethyl acrylate (0.1%) as 16/192 (8.3%) during 1985-1995, 9/124 (7.3%) from 1985-1990, and 7/68 (10.3%) during 1991-1995. In an earlier study, Kanerva et al. [1988] reported that 3/24 patients were sensitized to ethyl acrylate (0.5% in petrolatum). Drucker and Pratt [2011] conducted a retrospective chart review of patients attending a contact dermatitis clinic in Ontario, Canada and reported 28 (64%) patients had positive reactions when patch tested to ethyl acrylate. Tucker and Beck [1999] patch tested patients with a history of exposure (occupational and non-occupational) to (meth) acrylates with Chemotechniqes series and to their own suspected products when possible. Out of 255 patients tested, 22 (8.6%) were sensitized to ethyl acrylate at a concentration of 0.5%. Bjorkner et al. [1980] reported two of six patients patch tested with ethyl acrylate showed positive allergic reactions. A manicurist who presented with dermatitis tested positive to ethyl acrylate and other acrylates when patch tested using the International Contact Dermatitis Research Group (ICDRG) recommendations [Torres et al. 2005]. Brandao [2001] described a nurse who, after developing skin lesions, edema, and erythema from working with bone cement, showed cross-reactivity to (meth) acrylates, including ethyl acrylate. Pérez-Formoso et al. [2010] noted that 1 of 8 patients patch tested to acrylates had a positive reaction for ethyl acrylate.

In guinea pigs, ethyl acrylate (greater than 99% pure) was reported to be a skin sensitizer in Freund's complete adjuvant test (FCAT) [van der Walle et al. 1982a, 1982b], but not a sensitizer in the guinea pig maximization test. Warbrick et al. [2001] reported a maximum stimulation index of 5.01 in response to ethyl acrylate when a concentration of 50% was applied, with indices of less than 3 reported when lower concentrations (10 and 25%) were applied. Based on these results, these investigators estimated the effective concentration (EC3) value (%) [the concentration of chemical required to induce a stimulation index of three in the murine local lymph node assay (LLNA)] to be 28.7%. In an earlier study, ethyl acrylate at concentrations up to 30% did not increase lymph node cell proliferation over controls in the LLNA [Hayes and Meade 1999]. The same concentrations of ethyl acrylate did not exhibit allergic potential as measured by the mouse ear swelling test [Hayes and Meade 1999]. These investigators also found no cross-reactivity between ethyl acrylate, n-butyl acrylate or trimethylol propane triacrylate. *DEREK* predicted ethyl acrylate to be a plausible skin sensitizer.

Based on numerous reports of sensitization in humans **[Bjorkner et al. 1980; Kanerva et al. 1988, 1997; Tucker and Beck 1999; Drucker and Pratt 2011]**, and the weight of evidence from standard skin sensitization tests in animals including FCAT and LLNA **[van der Walle 1982a, 1982b; Warbrick et al. 2001]**, supported by the prediction from structure-activity relationship model, this assessment concludes that sufficient data exist to conclude that ethyl acrylate is a skin sensitizer in humans and animals. Therefore, on the basis of the data for this assessment, ethyl acrylate is assigned the SK: SEN notation.

5.0 Summary

Although no studies that evaluated the dermal absorption of ethyl acrylate were identified, mathematical modeling, several acute dermal **[Pozzani 1949; Treon et al. 1949; Dow Chemical Company 1957; Sokal et al. 1980; Bio/dynamics Inc. 1990]**, and repeat-dose **[Nylander-French and French 1998]** toxicity studies show that the substance is absorbed through the skin and can cause systemic toxicity including body weight depression. No studies were identified that evaluated the potential of ethyl acrylate to cause skin effects in humans following dermal exposure. However, sufficient data were identified from standard skin irritation tests and prolonged and repeated-dose studies that showed that the undiluted substance is corrosive to the skin of rabbits and mice **[Pozzani et al. 1949; Union Carbide Corporation 1982; DePass et al. 1984; Rohm and Haas Company 1991]**, while the diluted substance tends to be irritating. Numerous reports of skin sensitization in humans **[Bjorkner et al. 1980; Kanerva et al. 1988, 1997; Tucker and Beck 1999; Drucker and Pratt 2011]**, and the weight of evidence from standard skin sensitization tests in animals (FCAT and LLNA) **[van der Walle 1982a, 1982b; Warbrick et al. 2001]**, supported by the prediction from structure-activity relationship model, demonstrate that ethyl acrylate is a skin sensitizer in both humans and animals. Therefore, on the basis of these assessments, ethyl acrylate is assigned a composite skin notation of **SK: SYS-DIR (COR)-SEN**.

Table 3 summarizes the skin hazard designations for ethyl acrylate previously issued by NIOSH and other organizations. The equivalent dermal designations for ethyl acrylate, according to the Global Harmonization System (GHS) of Classification and Labelling of Chemicals, are Acute Toxicity Category 4 (Hazard statement: Harmful in contact with 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].

Table 3. Summary of previous skin hazard designations for ethyl acrylate

Organization	Skin hazard designation
NIOSH [2005]	[skin]
OSHA [2012]*	[skin]: Potential for dermal absorption
ACGIH [2001]	No designation
EC [2012]*	R21: Harmful if 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.
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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 Ethyl acrylate

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for ethyl acrylate. 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 *kp* 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

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

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 $\times$ Exposure time
= k_p(cm/hour) $\times$ 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

Inhalation dose = OEL $\times$ Inhalation volume $\times$ RF
= 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 ethyl acrylate. The calculated SI ratio was 1.09. On the basis of these results, ethyl acrylate is predicted to represent a skin absorption hazard.

Table A1. Summary of Data used to Calculate the SI Ratio for ethyl acrylate

Variables Used in Calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path(k_{psc})	cm/hour	4.043×10^{-3}
Permeation coefficient of the protein fraction of the stratum corneum (k_{pol})	cm/hour	1.152×10^{-5}
Permeation coefficient of the watery epidermal layer (k_{aq})	cm/hour	0.2499
Molecular weight (MW)[a]	amu	100.1
Base-10 logarithm of its octanol–water partition coefficient (Log K_{ow})[a]	None	1.18
Calculated skin permeation coefficient (k_p)	cm/hour	3.992×10^{-3}
Skin dose		
Water solubility (S_w)[a]	mg/cm^3	15
Calculated skin permeation coefficient (k_p)	cm/hour	3.992×10^{-3}
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hour	8
Calculated skin dose	mg	172.45
Inhalation Dose		
Occupational exposure limit (OEL)[b]	mg/m^3	21
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	157.5
Skin dose–to–inhalation dose (SI) ratio	None	1.09

[a]Variables identified from SRC [2009].
[b]The OEL used in calculation of the SI ratio for ethyl acrylate was the NIOSH recommended exposure limit (REL) [NIOSH 2005].

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