NIOSH Skin Notation Profiles

2-Hydroxypropyl acrylate (HPA)

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

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NIOSH Skin Notation (SK) Profile

2-Hydroxypropyl acrylate (HPA)

[CAS No. 999-61-1]

Naomi L. Hudson and G. Scott Dotson

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

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Foreword

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

In 2009, the National Institute for Occupational Safety and Health (NIOSH) published *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009-147]. This document provides the scientific rationale and framework for the assignment of multiple hazard-specific skin notations (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 (e.g., skin permeation) by means of analytical or numerical methods.

This *Skin Notation Profile* provides the SK assignments and supportive data for 2-hydroxypropyl acrylate (HPA). 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
GHS	Globally Harmonized System for Classification and Labelling of Chemicals
GPMT	guinea pig maximization test
HPA	2-hydropropyl acrylate
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
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)
mg	milligram(s)
mg/kg	milligram(s) per kilogram body weight
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 in water
SYS	skin notation indicating the potential for systemic toxicity following exposure of the skin
USEPA	United States Environmental Protection Agency
w/w	weight by weight percentage

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

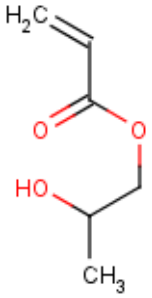
1.1 General Substance Information:

Chemical: 2-Hydroxypropyl acrylate

CAS No: 999-61-1

Molecular weight (*MW*)**:** 130.2

Structural formula:



Molecular formula:
CH_2=CHCOOCH_2CH(CH_3)OH

Synonyms: HPA; beta-Hydroxypropyl acrylate; Propylene glycol monoacrylate; Acrylic acid, 2-hydroxypropyl ester; 1,2-Propanediol,1-acrylate

Uses: HPA is a monomer used in the manufacture of thermosetting resins for surface coatings [OSHA 2010a], adhesives and sealants, textiles, paper coatings, fibers, and plastic copolymers.

1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with HPA and (2) the rationale behind the hazard-specific skin notation (SK) assignment for HPA. 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 HPA. A literature search was conducted through June 2017 to identify information on HPA, 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 HPA. The criteria for the search strategy, evaluation, and selection of data are described in Appendix E in *CIB 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009].

1.3 Overview of SK Assignment

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

2 Systemic Toxicity from Skin Exposure (SK: SYS)

No toxicokinetic studies following dermal exposure to HPA were identified in humans or animals. Frasch et al. [2014] conducted *in vitro* permeation studies from HPA-H2O binary mixtures through human silicone membranes. It was not possible to evaluate the potential of HPA to

Table 1. Summary of the SK assignment for HPA

Skin notation	Critical effect	Available data
SK: SYS (FATAL)	Acute toxicity	Limited animal data
SK: DIR (COR)	Skin corrosion	Limited human and sufficient animal data
SK: SEN	Skin allergy	Sufficient human and animal data

pose a skin absorption hazard with 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 (OEL). The ratio of the skin dose to the inhalation dose (SI ratio) could not be calculated on the basis that the OEL was not based on systemic effects. As such, the potential for skin absorption could not be determined using the SI ratio. More information about the SI ratio can be found in the appendix.

No dermal lethal concentrations (LD_{Lo}) for humans were identified. A dermal LD_{50} (lethal dose in 50% of exposed animals) value of 0.16 milliliters per kilogram of bodyweight (mL/kg) [corresponding to 168 milligrams per kilograms of bodyweight (mg/kg)] was reported for rabbits [Smyth et al. 1969]. Because the reported acute dermal LD_{50} values for the rabbit is lower than the critical dermal LD_{50} value of 200 mg/kg that identifies chemical substances that are potentially fatal at relatively low doses following dermal exposure [NIOSH 2009], HPA is considered potentially fatal following acute dermal exposure.

No epidemiological studies or case reports were identified that evaluated the toxic effects of HPA. No reliable repeat-dose, subchronic, or chronic toxicity studies following dermal exposure were identified in humans or animals. No standard toxicity or specialty studies evaluating biological system/function specific effects (including genotoxicity, reproductive and developmental effects and immunotoxicity) following dermal exposure to HPA were identified. No studies were identified that evaluated the potential of HPA to be carcinogenic in animals following dermal exposure. Table 2 summarizes carcinogenic designations of multiple governmental and nongovernmental organizations for HPA.

No dermal absorption data for HPA were identified, thereby preventing the assessment of hazards of the substance following contact with the skin. However, acute toxicity data **[Smyth et al. 1969]** suggest that HPA is dermally absorbed, systemically available, and has the potential to cause systemic effects including fatality. Therefore, on the basis of these data, HPA is assigned the SK: SYS (FATAL) notation.

3 Direct Effects on Skin (SK: DIR)

No human or animal *in vivo* studies on corrosivity of HPA or *in vitro* tests for corrosivity using human or animal skin models or in vitro tests of skin integrity using cadaver skin were identified. Limited information was available on irritant contact dermatitis potential of HPA in occupationally-exposed workers. A case report exists for 11 workers who developed irritation immediately after contact and 2 patients developed blisters 5-6 hours after exposure to HPA while employed in the manufacturing process of an acrylate chemical [Lovell et al. 1985]. Kanerva et al. [1988] conducted patch tests with 28 commercial (meth) acrylates (derivatives of methacrylic acid that are common monomers in polymer plastics)

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

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

Organization	Carcinogenic designation
NIOSH [2005]	No designation
NTP [2014]	No designation
USEPA [2017]	No designation
European Parliament [2008]	No GHS designation
IARC [2012]	No designation
ACGIH [2014]	No designation

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; USEPA = United States Environmental Protection Agency.
*The listed cancer designations were based on data from nondermal (such as oral or inhalation) exposure, since studies using the dermal route of exposure were unavailable.

on 24 patients and reported that 6 patients who showed irritation but were not sensitized to HPA.

Smyth et al. [1969] noted severe irritation on uncovered rabbit belly after exposure to HPA. In a study by BP Chemicals, Inc. [1981], a 0.25 milliliter (mL) aliquot of HPA was applied to the abraded and non-abraded occluded dorsal skin of rabbits for 24 hours. The authors found the substance to be a severe irritant producing necrosis, subcutaneous hemorrhaging, and pitting edema over a wide area of skin. The structure activity relationship model, Deductive Estimation of Risk from Existing Knowledge (*DEREK*) for Windows, predicted HPA to be a plausible skin irritant.

Occupational case reports **[Lovell et al. 1985; Kanerva et al. 1988]** suggest that HPA is a skin irritant and sufficient animal data **[Smyth et al. 1969; BP Chemicals, Inc. 1981]** that indicate HPA is a severe irritant and corrosive to the skin. Therefore, on the basis of the data for this assessment, HPA is assigned the SK: DIR (COR) notation.

4 Immune-mediated Responses (SK: SEN)

There is sufficient information available to conclude that HPA is a human skin sensitizer based on several human patch tests and a number of case reports. In human patch tests conducted by Kanerva et al. [1988], three out of 24 patients with irritation upon initial exposure to (meth) acrylates including HPA were sensitized to HPA, with sensitization to HPA being confirmed in re-testing in 2 patients. A diagnostic patch test conducted on a maintenance technician at a manufacturing plant of HPA and methacrylate indicated that this worker was sensitized by HPA, and the subject also developed cross-sensitivity to methacrylates to which he was previously exposed [Lovell et al. 1985]. Kanerva [1992b] described a case in which an orthodontist developed recurrent pharyngitis at work without any skin symptoms or reactions. However, the orthodontist developed a positive allergic reaction in a diagnostic patch test with 0.1% (w/w) HPA. Kanerva [1992a] also reported a woman who became sensitized with acrylates including HPA, which was confirmed upon retesting. After the retesting,

however, the woman developed further positive acrylate patch reactions indicating that the second patch test session sensitized her. Jordan [1975] reported that 5 people developed allergic contact dermatitis to component(s) used in a commercial adhesive tape, of which 2 were strongly positive to HPA. Jolanki et al. [1995] reported that a patient who was occupationally exposed and sensitized to BIS-GA (2,2-bis[4-(2-dydroxy-3-acryloxypropoxy) phenyl]-propane), 1,6-hexanediol diacrylate (HDDA), and tripropylene glycol diacrylate (TRPGDA) may have developed cross-sensitiziation to HPA.

Several studies were identified that evaluated the skin sensitization potential of HPA in animals. In a guinea pig maximization test, all guinea pigs (12/12) reacted positively to a dermal challenge with 0.3% HPA after dermal induction with a 5% aqueous 2-hydroxy-1-propyl acrylate solution and a 48-hour occlusive application of 0.4 mL of a 25% 2-hydroxypropyl acrylate solution [Clemmensen 1984]. However, Rao et al. [1981] observed no skin sensitization response in a guinea pig maximization study when nine guinea pigs were induced and challenged with the substance. Other skin sensitization tests investigated the cross-reactivity potential of HPA with other acrylates and methacrylate esters. In guinea pig maximization studies in which animals were induced with hydroxymethyl methacrylate followed by a challenge with HPA, two out of 15 guinea pigs reacted positively in one study [Clemmensen 1984] whereas no cross-reactivity between 2-hydroxypropyl methacrylate and HPA was observed in another study [Bjorkner 1984]. Clemmensen [1984] also reported that induction with hydroxyethyl acrylate followed by a challenge with HPA resulted in skin sensitization in all 12 animals. *DEREK* predicted HPA to be a skin sensitizer.

The human patch tests **[Kanerva et al. 1988, 1992a,b; Lovell et al. 1985]** and guinea pig maximization tests **[Clemmensen 1984]** sufficiently demonstrated the skin sensitization potential of HPA. Therefore, on the basis of the data for this assessment, HPA is assigned the SK: SEN notation.

5 Summary

No studies that evaluated the dermal absorption of HPA were identified in humans or animals. However, acute toxicity data **[Smyth et al. 1969]** suggest that HPA is dermally absorbed, systemically available, and potentially fatal. Occupational case reports **[Lovell et al. 1985; Kanerva et al. 1988]** and animal data **[Smyth et al. 1969; BP Chemicals, Inc. 1981]** demonstrate that HPA is an irritant and corrosive to the skin. Human patch tests **[Lovell et al. 1985; Kanerva et al. 1988, 1992a, b]** and guinea pig maximization tests **[Clemmensen 1984]** sufficiently demonstrate the skin sensitization potential of HPA. Therefore, on the basis of these assessments, HPA is assigned a composite skin notation of **SK: SYS (FATAL)-DIR (COR)-SEN**.

Table 3 summarizes the skin hazard designations for HPA previously issued by NIOSH and

Table 3. Summary of previous skin hazard designations for HPA

Organization	Skin hazard designation
NIOSH [2005]	[skin]: Potential for dermal absorption
OSHA [2017]*	None assigned
ACGIH [2014]	[skin]: Based on dermal LD_{50} values reported for rabbits DSEN notation: Based on animal data indicating that HPA may be a potential, but weak, skin sensitizer

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

other organizations. The equivalent dermal designations for HPA, according to the Globally Harmonized System (GHS) of Classification and Labelling 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].

References

ACGIH (American Conference of Governmental Industrial Hygienists) [2014]. 2-hydroxypropyl acrylate. In: TLVs and BEIs, Based on the documentation of threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

Bjorkner B [1984]. Contact allergy to 2-Hydroxypropyl-Methacrylate (2-HPMA) in an ultraviolet curable ink. Acta Derm. Venerol *64*(3):264–267.

BP Chemicals, Inc. [1981]. Irritation and mutagenicity tests of hydroxyethyl methacrylate. BP Group Occupational Health Centre, Toxicology report 25-09-0044. On file with the U.S. Environmental Protection Agency under TSCA Section 8D. OTS #0556083. Document #88-920010901.

Clemmensen S [1984]. Cross-reaction patterns in guinea pigs sensitized to acrylic monomers. Drug and Chemical Toxicology *7*(6):527–540.

European Parliament, Council of the European Union [2008]. Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJEU, Off J Eur Union *L353*:1–1355, http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:EN:PDF. Accessed: 06-06-17.

Frasch HF, Barbera AM, Dotson GS, Bunge AL [2014]. Dermal permeation of 2-hydroxypropyl acrylate, a model water-miscible compound: Effects of concentration, thermodynamic activity and skin hydration. Int J Pharm *460* (1–2):240–7.

IARC (International Agency for Research on Cancer) [2012]. Agents reviewed by the IARC monographs. In: IARC monographs on the evaluation of carcinogenic risks to humans, http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php. Accessed: 06-06-17.

Jolanki R, Kanerva L, Estlander T [1995]. Occupational allergic contact dermatitis caused by epoxy diacrylate in ultraviolet-light-cured paint, and bisphenol A in dental composite resin. Contact Dermatitis *33*(2):94–99.

Jordan WP Jr [1975]. Cross-sensitization patterns in acrylate allergies. Contact Dermatitis *1*:13–15.

Kanerva L, Estlander T, Jolanki R [1988]. Sensitization to patch test acrylates. Contact Dermatitis *18*:10–15.

Kanerva L, Estlander T, Jolanki R [1992a]. Double active sensitization caused by acrylics. Am J Contact Dermat *3*(1):23–26.

Kanerva L, Estlander T, Jolatiki R, Pekkarinen E [1992b]. Occupational pharyngitis associated with allergic patch test reactions from acrylics. Allergy *47*(5):571–573.

Lovell CR, Rycroft RJ, Williams DM, Hamlin JW [1985]. Contact dermatitis from the irritancy (immediate and delayed) and allergenicity of hydroxypropyl acrylate. Contact Derm *12*:117–118.

NIOSH [2005]. NIOSH pocket guide to chemical hazards. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2005-149, http://www.cdc.gov/niosh/npg/. Accessed: 06-06-17.

NIOSH [2009]. Current intelligence bulletin 61: a strategy for assigning new NIOSH skin notations. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2009-147, http://www.cdc.gov/niosh/docs/2009-147/pdfs/2009-147.pdf. Accessed: 06-06-17.

NTP [2014]. Report on Carcinogens. Thirteenth Edition. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service. National Toxicology Program, https://ntp.niehs.nih.gov/annualreport/2015/glance/roc/index.html. Accessed: 06-06-17.

OSHA (Occupational Safety and Health Administration) [ND]. 2-Hydroxypropyl acrylate. In: OSHA occupational chemical database, https://www.osha.gov/chemicaldata/chemResult.html?recNo=327. Accessed: 06-06-17.

Rao KS, Betso JE, Olson KJ [1981]. A collection of guinea pig sensitization test results—grouped by

chemical class. Drug and Chemical Toxicology *4*(4):331–351.

Smyth HF, Carpenter CP, Weil CS, Pozzani UC, Striegel JA, Nycum JS [1969]. Range-finding toxicity data: List VII. Am Ind Hyg Assoc J *30*(5):470–476.

USEPA (United States Environmental Protection Agency) [2015]. Integrated Risk Information System (IRIS), https://www.epa.gov/iris. Accessed: 06-06-17.

Appendix: Calculation of the SI Ratio for HPA

This appendix presents an overview of the SI ratio. 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]. The ratio of the skin dose to the inhalation dose (SI ratio) could not be calculated for 2-HPA on the basis that the OEL was not based on systemic effects. As such, the potential for skin absorption could not be determined using the SI ratio.

Overview

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

1. Provide an alternative method to evaluate substances for which no clinical reports or animal toxicity studies exist or for which empirical data are insufficient to determine systemic effects.

2. Use the algorithm evaluation results to determine whether a substance poses a skin absorption hazard and should be labeled with the SYS notation.

The algorithm evaluation includes three steps:

1. determining a skin permeation coefficient (k_p) for the substance of interest,

2. estimating substance uptake by the skin and respiratory absorption routes, and

3. evaluating whether the substance poses a skin exposure hazard.

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

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

Equation 1: Calculation of Skin Permeation Coefficient (k_p)

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

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

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

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

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

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 (m^3) inhaled air in 8 hours, and a factor of 75% for retention of the airborne substance in the lungs during respiration (retention factor, or RF).

Equation 3: Determination of Inhalation Dose

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

The final step is to compare the calculated skin and inhalation doses and to present the result as a ratio of skin dose to inhalation dose (the SI ratio). This ratio quantitatively indicates (1) the significance of dermal absorption as a route of occupational exposure to the substance and (2) the contribution of dermal uptake to systemic toxicity. If a substance has an SI ratio greater than or equal to 0.1, it is considered a skin absorption hazard. However, the SI ratio could not be calculated on the basis that the OEL was not based on systemic effects.

Appendix References

NIOSH [2009]. Current intelligence bulletin 61: a strategy for assigning new NIOSH skin notations. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2009-147, http://www.cdc.gov/niosh/docs/2009-147/pdfs/2009-147.pdf. Accessed: 06-06-17.

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