

# **Skin Notation (SK) Profile**

## **Acrylic acid**

**[CAS No. 79-10-7]**

## Disclaimer

Mention of any company or product does not constitute endorsement by the National Institute for Occupational Safety and Health (NIOSH). In addition, citations to Web sites external to NIOSH do not constitute NIOSH endorsement of the sponsoring organizations or their programs or products. Furthermore, NIOSH is not responsible for the content of these Web sites.

## Ordering Information

To receive this document or information about other occupational safety and health topics, contact NIOSH:

Telephone: 1-800-CDC-INFO (1-800-232-4636)

TTY: 1-888-232-6348

E-mail: [cdcinfo@cdc.gov](mailto:cdcinfo@cdc.gov)

Or visit the NIOSH Web site: [www.cdc.gov/niosh](http://www.cdc.gov/niosh)

For a monthly update on news at NIOSH, subscribe to *NIOSH eNews* by visiting [www.cdc.gov/niosh/eNews](http://www.cdc.gov/niosh/eNews).

## Suggested Citation

NIOSH [20XX]. NIOSH skin notation profile: Acrylic acid. By Hudson NL, Dotson GS. 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. XXX

DHHS (NIOSH) Publication No. XXX

## 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 (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 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.

John Howard, M.D.  
Director  
National Institute for Occupational Safety and Health  
Centers for Disease Control and Prevention

# Contents

<a href="#">FOREWORD</a> .....	III
<a href="#">ABBREVIATIONS</a> .....	V
<a href="#">GLOSSARY</a> .....	VII
<a href="#">ACKNOWLEDGMENTS</a> .....	VIII
<a href="#">1.0 INTRODUCTION</a> .....	1
<a href="#">1.1 GENERAL SUBSTANCE INFORMATION:</a> .....	1
<a href="#">1.2 PURPOSE</a> .....	1
<a href="#">1.3 OVERVIEW OF SK ASSIGNMENT</a> .....	1
<a href="#">2.0 SYSTEMIC TOXICITY FROM SKIN EXPOSURE (SK: SYS)</a> .....	2
<a href="#">3.0 DIRECT EFFECTS ON SKIN (SK: DIR)</a> .....	4
<a href="#">4.0 IMMUNE-MEDIATED RESPONSES (SK: SEN)</a> .....	4
<a href="#">5.0 SUMMARY</a> .....	5
<a href="#">REFERENCES</a> .....	7
<a href="#">APPENDIX: CALCULATION OF THE SI RATIO FOR ACRYLIC ACID</a> .....	10
<a href="#">OVERVIEW</a> .....	10
<a href="#">CALCULATION</a> .....	12
<a href="#">APPENDIX REFERENCES</a> .....	13

## Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
CIB	Current Intelligence Bulletin
cm <sup>2</sup>	squared centimeter(s)
cm/hour	centimeter(s) per hour
DAPA	β-diacryloxypropionic acid
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
DMBA	7,12-dimethylbenz[a]anthracene
EC	European Commission
GHS	Globally Harmonized System for Classification and Labelling of Chemicals
GPMT	guinea pig maximization test
FCAT	Freunds Complete Adjuvant 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
$k_{aq}$	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 <sub>50</sub>	dose resulting in 50% mortality in the exposed population
LD <sub>Lo</sub>	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 <sup>3</sup>	cubic meter(s)
mg	milligram(s)
mg/kg	milligram(s) per kilogram body weight
mg/m <sup>3</sup>	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
NOAEL	no-observed-adverse-effect level
NTP	National Toxicology Program
OEL	occupational exposure limit
OSHA	Occupational Safety and Health Administration
pmol/g	picomoles per gram

*This information is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines. It has not been formally disseminated by the National Institute for Occupational Safety and Health. It does not represent and should not be construed to represent any agency determination or policy.*

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
v/v	volume per volume
USEPA	United States Environmental Protection Agency

DRAFT

## 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.

## Acknowledgments

This document was developed by the Education and Information Division (Paul Schulte, Ph.D., Director). G. Scott Dotson, Ph.D., was the project officer for this document, assisted in great part by Naomi Hudson, Dr.P.H., MPH, Todd Niemeier, M.Sc., and Mark Toraason, Ph.D. The basis for this document was a report (*Toxicology Excellence for Risk Assessment [TERA]*) contracted by NIOSH and prepared by Bernard Gadagbui, Ph.D., and Andrew Maier, Ph.D.

For their contribution to the technical content and review of this document, special acknowledgment is given to the following NIOSH personnel:

### **Denver Field Office**

Eric Esswein, M.Sc.

### **Division of Applied Research and Technology**

Clayton B'Hymer, Ph.D.

John Snawder, Ph.D.

### **Division of Respiratory Disease Studies**

Gregory A. Day, Ph.D.

Aleksander Stefaniak, Ph.D.

### **Division of Surveillance, Hazard Evaluations, and Field Studies**

Matt Dahm, M.Sc.

Aaron Sussell, Ph.D.

Loren Tapp, M.D.

### **Education and Information Division**

Devin Baker, M.Ed.

Charles L. Geraci, Ph.D.

Thomas J. Lentz, Ph.D.

Richard Niemeier, Ph.D.

Sudha Pandalai. M.D., Ph.D.

### **Health Effects Laboratory Division**

Stacey Anderson, Ph.D.

H. Fredrick Frasch, Ph.D.

Vic Johnson, Ph.D.

Michael Luster, Ph.D.

Anna Shvedova, Ph.D.

Paul Siegel, Ph.D.

Berran Yucesoy, Ph.D.

**National Personal Protection Technology Laboratory**

Heinz Ahlers, M.Sc.

Angie Shephard

For their contribution to the technical content and review of this document, special acknowledgment is given to the following CDC personnel:

**Office of Surveillance, Epidemiology and Laboratory Services/Epidemiology and Analysis Program Office**

Barbara Landreth, M.A.

In addition, special appreciation is expressed to the following individuals for serving as independent, external reviewers and providing comments that contributed to the development or improvement of this document:

- G. Frank Gerberick, Ph.D., The Procter and Gamble Company, Cincinnati, OH
- Dori Germolec, Ph.D., National Toxicology Program, National Institute for Environmental Health Sciences, Research Triangle, NC
- Ben Hayes, M.D., Ph.D., Division of Dermatology, Vanderbilt School of Medicine, Nashville, TN
- Jennifer Sahmel, M.Sc., CIH, ChemRisk, Boulder, CO
- James Taylor, M.D., Industrial Dermatology, The Cleveland Clinic, Cleveland, OH

# 1.0 Introduction

## 1.1 General Substance Information:

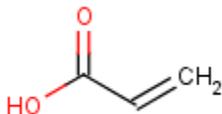
**Chemical:** Acrylic acid

**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 December 2012 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.

## 1.3 Overview of SK Assignment

Acrylic acid 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 acrylic acid: **SK: SYS-**

*This information is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines. It has not been formally disseminated by the National Institute for Occupational Safety and Health. It does not represent and should not be construed to represent any agency determination or policy.*

**DIR (COR).** Table 1 provides an overview of the critical effects and data used to develop the SK assignment for acrylic acid.

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

<b>Skin Notation</b>	<b>Critical Effect</b>	<b>Available Data</b>
SK: SYS	Acute toxicity	Sufficient animal data
SK: DIR (COR)	Skin corrosion	Sufficient animal data

## 2.0 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 using excised human cadaver skin were identified. Winter and Sipes [1993] applied 100 microliters ( $\mu\text{L}$ ) 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% of the dose was still detected on the skin, and approximately 17% of the applied dose 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 and 25% of a 40 mg/kg 14C-labelled acrylic acid dose was absorbed through the skin of rats, and 11% of a 10 mg/kg and 11% of a 40 mg/kg 14C-labelled acrylic acid 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 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. Based on the results of *in vivo* and *in vitro* dermal absorption studies as well as and the predictions of the mathematical algorithms, acrylic acid can be absorbed through the skin and be systemically available following dermal exposure.

While no estimated dermal lethal dose ( $\text{LD}_{\text{Lo}}$ ) 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 were identified in animals. 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 to acrylic acid were identified in animals.

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 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 life time.

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

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

<b>Organization</b>	<b>Carcinogenic designation</b>
NIOSH [2005]	No designation
NTP [2014]	No designation
USEPA [2014]	No designation
European Parliament [2008]	No GHS designation
IARC [2007]	Group 3: Not classifiable as to carcinogenicity to humans
EC [2013] <sup>†</sup>	No designation
ACGIH [2001]	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 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 rather than dermal exposure.

<sup>†</sup>Date accessed.

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 in *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 predications that are sufficient 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.

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

No human or animal *in vivo* studies on corrosivity or *in vitro* tests for corrosivity using human skin models or *in vitro* tests of skin integrity using cadaver skin were identified. ECB [2002] reported 3 cases from an unpublished 1992 study by BASF where 2 of the 3 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 2 unpublished studies by BASF, conducted in 1998 and 1958, that reported necrosis 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 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*), predicted acrylic acid to be negative for skin irritation.

The available studies indicate that undiluted acrylic acid is an irritant at concentrations up to 5% [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.

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

Very limited data were identified that evaluated 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 6 cases presenting with dermatitis to acrylate-based sealants. Patch-tests with 0.1% acrylic acid in petrolatum yielded negative results, indicating no cross-sensitization to acrylic acid; positive responses were, however, 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 guinea-pig maximization test (GPMT) and Landsteiner Draize test and the Polak test 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,  $\alpha,\beta$ -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 using the current distillation processes [IPCS 1997]. *DEREK* 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 (e.g., DAPA) [Waegemaekers and van der Walle 1984] or polymerization inhibitors of acrylic acid (i.e., 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.

## 5.0 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 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) of 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].

**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 [2015]*	No designation
ACGIH [2001]	[skin]: Based on the LD <sub>50</sub> values following single, topical application of undiluted acrylic acid
EC [2013]*	R21: Harmful if in contact with skin R35: Causes severe burns

---

ACGIH = American Conference of Governmental Industrial Hygienists; EC = European Commission, Joint Research, Institute for Health and Consumer Protection; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration.

\*Date accessed.

DRAFT

## References

- ACGIH (American Conference of Governmental Industrial Hygienists) [2001]. Acrylic acidichloropropene. In: Documentation of threshold limit values and biological exposure indices. 7th ed., Vol. 1. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.
- Basic Acrylic Monomer Manufacturers (BAMM) [1993]. Letter from BAMM to USEPA regarding TSCA Section 4 consent order (OPTS-42146-A) on acrylic acid with attachments. Washington, DC: Basic Acrylic Monomer Manufacturers (BAMM). On file with the U.S. Environmental Protection Agency under TSCA Section 8D. OTS #0573001.
- Black KA, Beskitt JL, Finch L, Tallant MJ, Udinsky JR, Frantz SW [1995]. Disposition and metabolism of acrylic acid in C3H mice and Fischer 344 rats after oral or cutaneous administration. *J Toxicol Environ Health* 45(3): 291-311.
- Carpenter CP, Weil CS, Smyth HF Jr [1974]. Range-finding toxicity data: List VIII. *Toxicol Appl Pharmacol* 28: 313-319.
- Conde-Salazar L, Guimaraens D, Romero LV [1988]. Occupational allergic contact dermatitis from anaerobic acrylic sealants. *Contact Dermatitis* 18:129-132.
- Daecke C, Schaller S, Schaller J, Goos M [1993]. Contact urticaria from acrylic acid in Fixomull tape. *Contact Dermatitis* 29(4): 216-217.
- DePass LR, Fowler EH, Meckley DR, Weil CS [1984]. Dermal Oncogenicity Bioassays of Acrylic Acid, Ethyl Acrylate, and Butyl Acrylate. *J Toxicol Environ Health* 14:115-120.
- EC (European Commission) [ND]. Acrylic acid. In: EINECS (European Inventory of Existing Commercial Chemical Substances), <http://ecb.jrc.ec.europa.eu/esis/index.php?GENRE=CASNO&ENTREE=79-10-7>. Accessed: 01-23-13.
- 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, labeling 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://eurex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:EN:PDF>. Accessed: 01-22-15.
- Fowler JR Jr [1990]. Immediate contact hypersensitivity to acrylic acid. *Dermatol Clin* 8(1): 193-195.

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: 01-22-15.

IPCS (International Programme on Chemical Safety) [1997]. Environmental health criteria 191: acrylic acid. In: INCHEM, <http://www.inchem.org/documents/ehc/ehc/ehc191.htm>. Accessed: 01-22-15.

McLaughlin JE, Parno J, Garner FM, Clary JJ, Thomas WC, Murphy SR [1995]. Comparison of the maximum tolerated dose (MTD) dermal response in three strains of mice following repeated exposure to acrylic acid. *Food Chem Toxicol* 33(6): 507-513.

NIOSH [2005]. Acrylic acid. In: 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: 01-22-15.

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: 01-22-15.

NTP [2014]. Report on Carcinogens. Thirteenth Edition; U.S. Department of Health and Human Services, Public Health Service. National Toxicology Program, <http://ntp.niehs.nih.gov/pubhealth/roc/roc13/index.html>. Accessed: 01-22-15.

OSHA [ND]. Acrylic acid. In: OSHA Occupational Chemical Database, <http://www.osha.gov/chemicaldata/chemResult.html?recNo=688>. Accessed: 01-22-15.

Parker D, Turk JL [1983] Contact sensitivity to acrylate compounds in guinea pigs. *Contact Dermatitis* 9(1):55-60.

Smyth HF, Jr., Carpenter CP, Weil CS, Pozzani UC, Striegel JA [1962]. Range-finding toxicity data: List VI. *Am Ind Hyg Assoc J* 23:95-107.

Tegeris AS, Balmer MF, Garner FM, Thomas WC, Murphy SR, McLaughlin E, and Seymour JL [1988]. A 13-week skin irritation study with acrylic acid in 3 strains of mice. *Toxicologist* 8:127.

USEPA [2014]. Integrated Risk Information System: acrylic acid. In: Integrated Risk Information System, <http://www.epa.gov/ncea/iris/subst/0002.htm>. Accessed: 01-22-15.

Waegemaekers TH, van der Walle HB [1984]. Alpha, beta-diacryloxypropionic acid, a sensitizing impurity in commercial acrylic acid. *Dermatol Beruf Umwelt* 32:55-58.

Winter SM, Sipes IG [1993]. The disposition of acrylic acid in the male Sprague-Dawley rat following oral or topical administration. *Food Chem Toxicol*, 31: 615-621.

DRAFT

## 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 only to serve as supportive data during the assignment of the NIOSH SK. An in-depth discussion on the rationale and calculation of the SI ratio can be found in Appendix B of the *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009].

### Overview

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

- (1) Provide an alternative method to evaluate substances for which no clinical reports or animal toxicity studies exist or for which empirical data are insufficient to determine systemic effects.
- (2) Use the algorithm evaluation results to determine whether a substance poses a skin absorption hazard and should be labeled with the SYS notation.

The algorithm evaluation includes three steps:

- (1) determining a skin permeation coefficient ( $k_p$ ) for the substance of interest,
- (2) estimating substance uptake by the skin and respiratory absorption routes, and
- (3) evaluating whether the substance poses a skin exposure hazard.

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

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

### Equation 1: Calculation of Skin Permeation Coefficient ( $k_p$ )

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

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

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

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

### Equation 2: Determination of Skin Dose

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

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 ( $\text{m}^3$ ) 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

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

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.

## 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.

**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 ( $k_{poi}$ )	cm/hour	$1.7894 \times 10^{-5}$
Permeation coefficient of the watery epidermal layer ( $k_{aq}$ )	cm/hour	0.294505
Molecular weight ( $MW$ ) <sup>*</sup>	amu	72.06
Base-10 logarithm of its octanol–water partition coefficient ( $\text{Log } K_{ow}$ ) <sup>*</sup>	None	0.35
Calculated skin permeation coefficient ( $k_p$ )	cm/hour	$2.3502 \times 10^{-3}$
<b>Skin dose</b>		
Water solubility ( $S_w$ ) <sup>*</sup>	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) <sup>†</sup>	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>	None	150

<sup>\*</sup>Variables identified from SRC [ND].

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

## **Appendix References**

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: 01-22-15.

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: 01-22-15.

SRC [2011]. Interactive PhysProp database demo, <http://esc.syrres.com/fatepointer/webprop.asp?CAS=79107>. Accessed: 01-22-15.

DRAFT