NIOSH Skin Notation Profile
Allyl alcohol

[CAS No. 107-18-6]

External Review Draft

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Foreword

As the largest organ of the body, the skin performs multiple critical functions, such as serving as the primary barrier to the external environment. For this reason, the skin is often exposed to potentially hazardous agents, including chemicals, which may contribute to the onset of a spectrum of adverse health effects ranging from localized damage (such as irritant contact dermatitis and corrosion) to induction of immune-mediated responses (such as allergic contact dermatitis and pulmonary responses), or systemic toxicity (such as neurotoxicity and 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]. 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 with an 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 allyl alcohol. 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
ATSDR	Agency for Toxic Substances and Disease Registry
bw	bodyweight
CIB	Current Intelligence Bulletin
cm^3	cubic centimeter(s)
COR	subnotation of SK: COR indicating the potential for a chemical to be a skin corrosive following exposure to the skin
DIR	skin notation indicating the potential for direct effects to the skin following contact with a chemical
ECHA	European Chemicals Agency
IARC	International Agency for Research on Cancer
ID^{SK}	skin notation indicating that a chemical has been evaluated, but insufficient data exist to accurately assess the hazards of skin exposure
IRR	subnotation of SK: DIR indicating the potential for a chemical to be a skin irritant following exposure to the skin
kg	kilogram
LD_{50}	dose resulting in 50% mortality in the exposed population
LD_{Lo}	dermal lethal dose
m^3	cubic meter(s)
mg	milligram(s)
mL	milliliter(s)
mL/kg-bw	milliliter 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
REL	recommended exposure limit

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
~~**SK**~~	skin notation indicating that the reviewed data did not identify a health risk associated with skin exposure
SYS	skin notation indicating the potential for systemic toxicity following exposure of the skin
U.S. EPA	United States Environmental Protection Agency

Glossary

Absorption—The transport of a chemical from the outer surface of the skin into both the skin and systemic circulation (including penetration, permeation, and resorption).

Acute exposure—Contact with a chemical that occurs once or for only a short period of time.

Cancer—Any one of a group of diseases that occurs when cells in the body become abnormal and grow or multiply out of control.

Contaminant—A chemical that is (1) unintentionally present within a neat substance or mixture at a concentration less than 1.0% or (2) recognized as a potential carcinogen and present within a neat substance or mixture at a concentration less than 0.1%.

Cutaneous (or percutaneous)—Referring to the skin (or through the skin).

Dermal—Referring to the skin.

Dermal contact—Contact with (touching) the skin.

Direct effects—Localized, non-immune-mediated adverse health effects on the skin, including corrosion, primary irritation, changes in skin pigmentation, and reduction/disruption of the skin barrier integrity, occurring at or near the point of contact with chemicals.

Immune-mediated responses—Responses mediated by the immune system, including allergic responses.

Sensitization—A specific immune-mediated response that develops following exposure to a chemical, which, upon re-exposure, can lead to allergic contact dermatitis (ACD) or other immune-mediated diseases such as asthma, depending on the site and route of re-exposure.

Substance—A chemical.

Systemic effects—Systemic toxicity associated with skin absorption of chemicals after exposure of the skin.

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1 Introduction

1.1 General Substance Information

Chemical: Allyl alcohol

CAS No: 107-18-6

Molecular weight (*MW*): 58.1

Molecular Formula: C_3H_6O

Structural Formula: $CH_2 = CHCH_2OH$

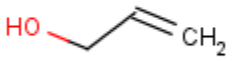

Image source: [NLM, no date]

General substance information was obtained from NIOSH [2007].

Synonyms: allylic alcohol, AA, propenol, 1-propen-3-ol, 2-propenol, vinylcarbinol

Uses: Allyl alcohol is used to produce resins, plasticizers, and pharmaceuticals; it is also used in chemical manufacturing [ACGIH 2020]. The International Fragrance Association (IFRA) specified that allyl esters in fragrances should be less than 0.1% free allyl alcohol [IFRA 2009]

1.2 Purpose

The skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with allyl alcohol and (2) the rationale behind the hazard-specific skin notation (SK) assignment for allyl alcohol. 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 allyl alcohol. A literature search was conducted through July 2023 to identify information on allyl alcohol toxicokinetic properties, 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 in humans, animals, or appropriate modeling systems that are relevant to assessing the effects of dermal exposure to allyl alcohol.

1.3 Overview of SK Assignment for Allyl Alcohol

Allyl alcohol 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 allyl alcohol: **SK: SYS(FATAL)-DIR(IRR)**. Table 1 provides an overview of the critical effects and data used to develop the SK assignment for allyl alcohol.

Table 1. Summary of the SK assignment for allyl alcohol

Skin notations	Critical effect	Available data
SK: SYS(FATAL)	Acute toxicity	Limited animal data
SK: DIR(IRR)	Skin irritation	Limited animal data

2 Systemic Toxicity from Skin Exposure (SK: SYS)

No quantitative studies evaluating toxicokinetic properties following dermal exposure to allyl alcohol were identified in humans or animals. The permeability coefficient was reported for 36 organic solvents from diffusion cell experiments using pig skin [Schenk et al. 2018]. The authors reported the permeability coefficient for allyl alcohol as 2.65×10^{-3}, where 10^{-4} would indicate "moderate" absorption and 10^{-2} would indicate "very high" absorption [Schenk et al. 2018]. There have been considerable improvements and advancements in dermal absorption studies and modeling since the publication of CIB 61 [NIOSH 2017]. In response to expert external peer reviewers' comments regarding the limitation of the skin to inhalation dose (SI) ratio information, NIOSH is no longer providing the SI ratio described in CIB 61 in the individual chemical skin notation profile documents.

No estimated human dermal lethal doses (LD_{LO}) of allyl alcohol were identified. Dermal LD_{50} (the dose resulting in 50% mortality in the exposed animals) values were 38–45 milligrams per kilogram (mg/kg) to 85 mg/kg in rabbits [DuPont 1945; Dunlap et al. 1958; Shell Oil 1945; Smyth and Carpenter 1948] and 683 mg/kg for guinea pigs [Shell Oil 1945]. Smyth and Carpenter [1948] and E.I. Du Pont de Nemours (DuPont) [1945, 1951] reported deaths in rabbits following dermal application of 0.045–0.053 milliliter per kilogram-body weight (mL/kg-bw) (corresponding to 38.4–45 mg/kg) in acute toxicity studies. Shell Oil [1945] reported deaths in rabbits at 0.1 cubic centimeters per

kilogram (corresponding to 85.4 mg/kg) but reported no deaths in guinea pigs until the amount was greater than 0.8 mL/kg-bw (corresponding to 683.2 mg/kg). Dunlap et al. [1958] reported an LD_{50} value in rabbits of 89 mg/kg for percutaneous administration of allyl alcohol. Because the LD_{50} values for the rabbits is less than 200 mg/kg, allyl alcohol is considered fatal following acute dermal exposure [NIOSH 2009].

No epidemiological or occupational case reports were identified following dermal exposure to allyl alcohol. No specialty studies were identified that evaluated biological system/function specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure to allyl alcohol.

No data were identified to evaluate the carcinogenic potential following dermal exposure to allyl alcohol. Table 2 summarizes the carcinogenic designations for allyl alcohol by numerous governmental and nongovernmental organizations.

Table 2. Summary of the carcinogenic designations for allyl alcohol by numerous governmental and nongovernmental organizations

Organization	Carcinogenic designation
ACGIH [2022]	A4 (not classifiable as a human carcinogen) chemical
ECHA [2023]	No designation
IARC [2023]*	No designation
NIOSH [2007]	No designation
NTP [2021]	No designation
U.S. EPA [1987]	No designation

ACGIH = American Conference of Governmental Industrial Hygienists; ECHA = European Chemicals Agency; IARC = International Agency for Research on Cancer; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; U.S. EPA = United States Environmental Protection Agency.

*Year accessed.

No studies were identified that provided quantitative estimates of allyl alcohol absorption through the skin. However, acute toxicity studies in rabbits **[Dunlap et al. 1958; Shell Oil 1942; Smyth and Carpenter 1948]**[1] indicated that the substance can be absorbed

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

through the skin in sufficient amounts to cause systemic toxicity, including death. Therefore, this assessment assigns a **SK: SYS(FATAL)** notation for allyl alcohol.

3 Direct Effects on Skin (SK: DIR)

No studies that evaluated the corrosivity of allyl alcohol or *in vitro* tests for corrosivity using human or animal skin models or *in vitro* tests of skin integrity using cadaver skin were identified. In a case study, U.S. Chemical Safety and Hazard Investigation Board (CSB) [2006] reported one case of minor chemical burns following a release of vapors of allyl alcohol and allyl chloride into the air from a manufacturing facility. Over 154 people were affected by the toxic vapor and had to be treated for respiratory distress and eye and skin irritation; however, exposure to allyl chloride could be responsible for some cases of skin irritation [U.S. CSB 2006].

The skin irritation potential of ally alcohol was evaluated by Dunlap et al. [1958]. The researchers applied allyl alcohol in increments of 0.5 mL to the intact backs of sacrificed rabbits to test for skin irritation. One of three rabbits showed slight erythema 24 hours after application to the intact skin, with symptoms dissipating after 48 hours [Dunlap et al. 1958]. DuPont [1951] reported no irritation to allyl alcohol when applied undiluted to the nonoccluded clipped skin of the rabbit abdomen. However, DuPont [1945] reported severe local irritation to rabbit skin when undiluted allyl alcohol was applied during acute toxicity; they also noted pinpoint hemorrhages. Reports of skin irritation were noted in several acute toxicity studies following the application of allyl alcohol. Shell Oil [1945] reported reddening and discoloration and superficial necrosis following application of allyl alcohol during dermal toxicity studies.

Based upon the information identified, the limited animal studies **[Dunlap et al. 1958; DuPont 1945]** indicated that exposure to allyl alcohol may result in skin irritation. Therefore, this assessment assigns a skin notation of **SK: DIR(IRR)** for allyl alcohol.

4 Immune-mediated Responses (SK: SEN)

No reports of skin sensitization in humans or predictive tests (for example, guinea pig maximization tests, Buehler tests, murine local lymph node assays, or mouse ear swelling tests) or other tests that evaluated the potential of allyl alcohol to cause skin sensitization in animals were identified. Because of the lack of data, the skin sensitization potential of allyl alcohol cannot be evaluated. Therefore, allyl alcohol is not assigned a SK: SEN notation.

5 Summary

No human or animal studies were identified that provided quantitative estimates of allyl alcohol absorption through the skin. Schenk et al. [2018] conducted diffusion cell experiments using pig skin and reported allyl alcohol to be a moderate sensitizer. Acute toxicity studies in rabbits and guinea pigs **[Dunlap et al. 1958; Shell Oil 1945; Smyth and Carpenter 1948]** indicated that the allyl alcohol is acutely toxic and may be fatal following dermal exposure. Based upon the limited data identified in animals **[Dunlap et al. 1958; Shell Oil 1945]**, allyl alcohol is a skin irritant. The available data are insufficient to adequately evaluate the sensitization potential of allyl alcohol. Based on these data, allyl alcohol is assigned a composite **SK: SYS(FATAL)-DIR(IRR)** skin notation.

Table 3 summarizes the skin hazard designations for allyl alcohol issued by NIOSH and other organizations.

Table 3. Summary of previous skin hazard designations for allyl alcohol from NIOSH and other organizations

Organization	Skin hazard designation
ACGIH [2022]	[skin]: Systemic toxicity following dermal contact
ECHA [2023]	Acute Tox 3: Toxic in contact with skin Skin Irrit. 2: Causes skin irritation
NIOSH [2007]	[skin]: Potential for dermal absorption
OSHA [2020]	[skin]: Potential for dermal absorption

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

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