

NIOSH Skin Notation Profile

beta-Chloroprene

SKK

ID^{SK}

[SK]

SYS

SYS (FATAL)

DIR

DIR (IRR)

DIR (COR)

SEN



Centers for Disease Control
and Prevention
National Institute for Occupational
Safety and Health

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NIOSH Skin Notation Profile

beta-Chloroprene

[CAS No. 126-99-8]

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Foreword

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

In 2009, the National Institute for Occupational Safety and Health (NIOSH) published *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009]. 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 (such as skin permeation) by means of analytical or numerical methods.

This *Skin Notation Profile* provides the SK assignments and supportive data for beta-chloroprene. In particular, this document evaluates and summarizes the literature describing the hazard potential of the substance and its assessment according to the scientific rationale and framework outlined in *CIB 61*. In meeting this objective, this *Skin Notation Profile* intends to inform the audience—mostly occupational health practitioners, researchers, policy- and decision-makers, employers, and workers in potentially hazardous workplaces—so that improved risk-management practices may be developed to better protect workers from the risks of skin contact with the chemicals of interest.

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Abbreviations

ACGIH®	American Conference of Governmental Industrial Hygienists
ATSDR	Agency for Toxic Substances and Disease Registry
CIB	Current Intelligence Bulletin
COR	subnotation of SK: DIR indicating the potential for a chemical to be corrosive to the skin following exposure
DIR	skin notation indicating the potential for direct effects to the skin following contact with a chemical
FATAL	subnotation of SK: SYS indicating the potential for the chemical to be fatal during dermal absorption
GHS	Globally Harmonized System for Labelling and Classification of Chemicals
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
LD₅₀	dose resulting in 50% mortality in the exposed population
LD_{Lo}	dermal lethal dose
LOAEL	lowest-observed-adverse-effect level
M	molarity
mg	milligram(s)
mg/L	milligrams per liter
mg/kg	milligram(s) per kilogram
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
ppm	parts per million
SEN	skin notation indicating the potential for immune-mediated reactions following exposure of the skin
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 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

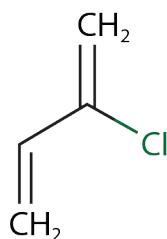
Chemical: beta-Chloroprene

CAS No: 126-99-8

Molecular weight (MW): 88.5

Molecular formula: C₄H₅Cl

Structural formula:



General substance information was obtained from NIOSH [2007].

Synonyms: 2-Chloro-1,3-butadiene; Chloro-butadiene; Chloroprene

Uses: beta-Chloroprene is a high-volume production chemical used primarily as an intermediate in the production of artificial rubber and neoprene; an estimated 626,000 pounds (~284,000 kilograms) were produced in the United States in 1981 [HSDB 2009].

1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with beta-chloroprene and (2) the rationale behind the hazard-specific skin notation (SK) assignment for beta-chloroprene. 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 beta-chloroprene. A literature search was conducted through March 2021 to identify information on beta-chloroprene dermal absorption, 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 beta-chloroprene. The criteria for the search

strategy, evaluation, and selection of data are described in Appendix E in the aforementioned *CIB 61* [NIOSH 2009].

1.3 Overview of SK Assignment for beta-Chloroprene

beta-Chloroprene is potentially capable of causing adverse effects following skin contact. A critical review of the available data has resulted in the following SK assignment for beta-chloroprene: **SK: SYS-DIR(IRR)**. Table 1 provides an overview of the critical effects and data used to develop the SK assignment for beta-chloroprene.

2 Systemic Toxicity From Skin Exposure (SK: SYS)

No *in vivo* or *in vitro* toxicokinetic data were identified for humans or animals that estimated the degree of absorption of beta-chloroprene following dermal exposure. No estimate of the human dermal lethal dose (LD_{Lo}) or animal

Table 1. Summary of the SK assignment for beta-chloroprene

Skin notation	Critical effect	Available data
SK: SYS	Liver, renal, and reproductive effects	Limited animal data
SK: DIR(IRR)	Skin irritancy	Sufficient animal data

dermal LD₅₀ (the dose resulting in 50% mortality in the exposed animals) was identified for beta-chloroprene.

No epidemiological studies or occupational exposure studies were identified that investigated the potential for beta-chloroprene to cause systemic effects following dermal exposure. A case report of fatal intoxication was described by Rickert et al. [2012]. A 29-year-old chemistry company worker was found unconscious and had an acute cardiac arrest in an empty vessel that was used for beta-chloroprene. The worker was wearing a respiratory mask (without an independent air supply), a helmet, trousers and shoes but his upper body was unclothed. Because the worker was wearing a respiratory mask, the investigators assumed that a substantial amount of beta-chloroprene was also absorbed through the skin [Rickert et al. 2012]. The authors concluded that the death was likely caused by both inhalation and dermal absorption in conjunction with lack of oxygen.

No subchronic or chronic toxicity studies in animals were identified that investigated the potential for beta-chloroprene to cause systemic effects following dermal exposure. A repeat-dose toxicity study [von Oettingen et al. 1936] was identified where 0.5 milliliters (mL) (480 milligrams [mg]) of beta-chloroprene was rubbed into the unshaved skin of the back of rats for 1 week. After the animals were left untreated for 2 weeks, 1.5 mL (1440 mg) of beta-chloroprene was applied to the skin for up to the 55th day of the experiment. The rats developed a state of depression that continued for about 2 hours (h) after each daily application of beta-chloroprene. von Oettingen et al. [1936] reported weight loss, scattered hydropic degeneration and lysis of the liver cell nuclei, mild nephrosis (renal damage), hyperemic spleen,

and slightly degenerated testis with calcium deposits. No Lowest Observed Adverse Effect Level (LOAEL) or No Observable Adverse Effects Level (NOAEL) could be identified.

No standard toxicity or specialty studies were identified that evaluated biological system/function specific effects (including reproductive and developmental effects and immunotoxicity) for beta-chloroprene following dermal exposure. However, using a limited number of rats, von Oettingen et al. [1936] reported that beta-chloroprene interfered with reproduction (frequency of successful mating) and may even cause sterility in male rats when the skin of the male rats was painted daily with non-fatal doses of beta-chloroprene for 34 days or 44 days. Similar results were also observed in rats and mice exposed by inhalation to non-fatal doses of beta-chloroprene (0.434–22.419 mg/L or 121–6227 parts per million [ppm] for rats and 0.042–0.548 mg/L or 12–152 ppm for mice) [von Oettingen et al. 1936]. While these data are difficult to evaluate quantitatively because the exact dose of beta-chloroprene that caused the reproductive effects in the skin-painting study was not reported and the number of animals in each skin painting or inhalation exposure was small the results indicate that reproductive effects of beta-chloroprene are not route-specific.

No epidemiological studies or animal bioassays were identified that evaluated the potential for beta-chloroprene to be carcinogenic following dermal exposure. However, other organizations or agencies have evaluated the carcinogenicity of beta-chloroprene via other routes of exposure. Table 2 summarizes the carcinogenic designations for beta-chloroprene from governmental and nongovernmental agencies.

Table 2. Summary of the carcinogenic designations for beta-chloroprene by numerous governmental and nongovernmental organizations

Organization	Carcinogenic designation
NIOSH [2007]	Potential occupational carcinogen
NTP [2016]	Reasonably anticipated to be a human carcinogen
U.S. EPA [2021]	Likely to be carcinogenic to humans
ECHA [2022]	Carcinogenic
IARC [2012]	2B: Possibly carcinogenic to humans
ACGIH* [2018]	[Skin]: based on effects from dermal absorption of beta-chloroprene applied to the skin of rats

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.

No *in vivo* or *in vitro* toxicokinetic data were identified for humans or animals that estimated the degree of absorption of beta-chloroprene through the skin following dermal exposure. No epidemiological studies or occupational exposure studies, and no acute, subchronic, chronic or specialty studies in animals were identified that assessed the potential for beta-chloroprene to cause systemic toxicity following dermal exposure. A case report of a fatality [Rickert et al. 2012] was identified where death was likely caused by both inhalation and dermal absorption of beta-chloroprene in conjunction with lack of oxygen. A repeated-dose toxicity study [von Oettingen et al. 1936]* in rats and mice indicated that beta-chloroprene may cause liver, renal, and reproductive effects. Reproductive effects were also reported at unspecified topical and inhalation doses, indicating that these effects are not route specific. Based on these data, beta-chloroprene is assigned a SK: SYS skin notation.

3 Direct Effects on Skin (SK: DIR)

No human or animal *in vivo* studies on corrosivity of beta-chloroprene 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 occupational exposure studies or case reports were identified that

evaluated the potential for beta-chloroprene to cause direct effects to the skin of humans. Von Oettingen et al. [1936] reported that single or repeated applications of undiluted beta-chloroprene (0.5–1.5 mL) to the abdominal skin of albino rats caused skin irritation. The hair surrounding the site of application turned dark and brittle and fell out, but no damage was done to the hair follicles. E.I. Dupont DeNemours and Company, Inc. (DuPont) [1970] reported mild to moderate erythema following application of 200 mg/kg beta-chloroprene to the clipped skin of rabbits under semi-occluded conditions for 24 h. Based on the results, DuPont considered beta-chloroprene to be a moderate primary skin irritant. Clary et al. [1978] reported mild to moderate skin erythema and edema formation following a topical application of 200 mg/kg beta-chloroprene. Levina [1940] reported that 20 mg of 10% or 20% solutions of beta-chloroprene dimer, but not the monomer, applied to the undisturbed skin of mice every day or every other day for a maximum of 15 or 25 applications produced skin flaking, dermatitis, hair loss, and skin ulceration.

Although no data were identified that assessed the potential for beta-chloroprene to be corrosive

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

to skin, skin irritation tests in animals [Clary et al. 1978; Dupont 1970; Levina 1940; von Oettingen et al. 1936] provide sufficient evidence that beta-chloroprene has the potential to cause skin irritation. Therefore, beta-chloroprene is assigned a SK: DIR(IRR) notation.

4 Immune-mediated Responses (SK: SEN)

No diagnostic (human) patch tests or predictive tests in animals (for example, guinea pig maximization tests, Buehler tests, murine local lymph node assays, or mouse ear swelling tests) or any other studies were identified that evaluated the potential for beta-chloroprene to cause skin sensitization were identified. In the absence of relevant data, beta-chloroprene is not assigned a SK: SEN notation.

5 Summary

No toxicokinetic data or epidemiological studies were identified for humans or animals that estimated the degree of absorption

of beta-chloroprene through the skin following dermal exposure. A case report of a fatality [Rickert et al. 2012] was identified where death was likely caused by both inhalation and dermal absorption of beta-chloroprene in conjunction with lack of oxygen. A repeated-dose toxicity study [von Oettingen et al. 1936] in rats and mice indicated that beta-chloroprene may cause liver, renal, and reproductive effects. Reproductive effects were also reported for topical and inhalation doses, indicating that these effects are not route specific. No data were identified that assessed the potential for beta-chloroprene to be corrosive to human skin, but skin irritation tests in animals [Clary et al. 1978; Dupont 1970; Levina 1940; von Oettingen et al. 1936] provide sufficient evidence that beta-chloroprene has the potential to cause skin irritation. No diagnostic (human) patch tests or predictive tests in animals were identified that evaluated the potential of beta-chloroprene to cause skin sensitization. Based on these data, beta-chloroprene is assigned a composite SK: SYS-DIR(IRR) skin notation.

Table 3 summarizes the previously issued skin hazard designations for beta-chloroprene by NIOSH and other organizations.

Table 3. Summary of the previously issued skin hazard designations for beta-chloroprene from NIOSH and other organizations

Organization	Skin hazard designation
NIOSH [2007]	No designation
OSHA [2018]*	[Skin]: Potential for dermal absorption
ACGIH* [2018]	[Skin]: Limited data of effects from dermal absorption of beta-chloroprene applied to the skin of rats

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

*Year accessed.

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Note: Asterisks (*) denote sources cited in text; daggers (†) denote additional resources.

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