Skin Notation (SK) Profile

Chlorinated Camphene

[CAS No. 8001-35-2]

Department of Health and Human Services
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

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Foreword

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

In 2009, the National Institute for Occupational Safety and Health (NIOSH) published *Current Intelligence Bulletin (CIB) 61 – A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009-147]. This document provides the scientific rationale and framework for the assignment of multiple hazard-specific skin notations (SK) that clearly distinguish between the systemic effects, direct (localized) effects, and immune-mediated responses caused by skin contact with chemicals. The key step within assignment of the hazard-specific SK is the determination of the hazard potential of the substance, or its potential for causing adverse health effects as a result of skin exposure. This determination entails a health hazard identification process that involves use of the following:

- Scientific data on the physicochemical properties of a chemical
- Data on human exposures and health effects
- Empirical data from *in vivo* and *in vitro* laboratory testing
- Computational techniques, including predictive algorithms and mathematical models that describe a selected process (e.g., skin permeation) by means of analytical or numerical methods.

This *Skin Notation Profile* provides the SK assignments and supportive data for chlorinated camphene. 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
CIB	Current Intelligence Bulletin
cm^2	squared centimeter(s)
cm/hr	centimeter(s) per hour
cm/s	centimeter(s) per second
CNS	central nervous system
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
hr	hour(s)
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)
$mg/cm^2/hr$	milligram(s) per square centimeter per hour
mg/kg	milligram(s) per kilogram body weight
mg/m^3	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

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
µg	microgram(s)
µg/cm^2	microgram(s) per square centimeter
µg/cm^2/hr	microgram(s) per square centimeter per hour
µL	microliter(s)
µmol	micromole(s)

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 aborption of chemicals after exposure of the skin.

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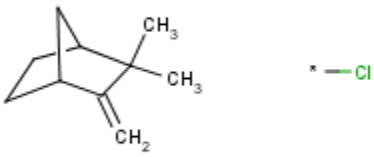
1.0 Introduction

1.1 General Substance Information

Chemical: Chlorinated camphene
CAS No: 8001-35-2
Molecular weight (*MW*): 413.8
Molecular formula: $C_{10}H_{10}Cl_8$
Structural formula:



Synonyms: Chlorocamphene; Octachlorocamphene; Polychlorocamphene; Toxaphene

Uses: Chlorinated camphene was used primarily as an insecticide. The Agency for Toxic Substance and Disease Registry (ATSDR) reported that an estimated that 3.7 million pounds [less than 2 million kilograms (kg)] were produced in the United States in 1982 [ATSDR 1996]. The United States Environmental Protection Agency (USEPA) banned chlorinated camphene in 1990 [55 Fed. Reg. 31164 (1990); ATSDR 2014].

1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with chlorinated camphene and (2) the rationale behind the hazard-specific skin notation (SK) assignment for chlorinated camphene. 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 chlorinated camphene. A literature search was conducted through February 2013 to identify information on chlorinated camphene, 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 chlorinated camphene.

1.3 Overview of SK Assignment

Chlorinated camphene 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 chlorinated camphene: **SK: SYS-DIR (IRR)**. Table 1 provides an overview of the critical effects and data used to develop the SK assignment for chlorinated camphene.

Table 1. Summary of the SK Assignment for chlorinated camphene

Skin Notation	Critical Effect	Available Data
SK: SYS	Central nervous system (CNS), liver, kidney, spleen, thyroid	Limited human and animal data
SK: DIR (IRR)	Skin irritation	Limited animal data

2.0 Systemic Toxicity from Skin Exposure (SK: SYS)

No quantitative toxicokinetic data following dermal exposure to chlorinated camphene were identified for humans or animals. The potential of chlorinated camphene 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 0.01was calculated for chlorinated camphene. An SI ratio of ≥0.1 indicates that a chemical is capable of producing systemic toxicity from skin exposure [NIOSH 2009]; therefore, chlorinated camphene is not considered to be absorbed through the skin following dermal exposure. Additional information on the SI ratio and the variables used in its calculation are included in the appendix.

No estimate of the dermal lethal dose (LD_{LO}) of chlorinated camphene for humans was identified. Dermal LD_{50} (lethal dose in 50% of exposed animals) values of 780 milligrams per kilogram body weight (mg/kg) to 1,075 mg/kg were reported for rats [Gaines 1969]. For rabbits, a dermal LD_{50} range of 1,025 mg/kg to 1,075 mg/kg was reported using a non-standard acute dermal toxicity test that involved immersing the animals in water suspension of wettable chlorinated camphene powder for 2 minutes [Johnston and Eden 1953]. Dermal LD_{50} values ranging from 3,725 mg/kg when applied to skin burned with ultraviolet light to 4,556 mg/kg for intact skin areas have been reported for rabbits after dermal exposure to chlorinated camphene (90% weight/volume in xylene) for 24 hours (hr) [Industrial BioTest Labs 1973]. Because the reported acute dermal LD_{50} values for chlorinated camphene in rats and rabbits are lower than the critical dermal LD_{50} value of 2,000 mg/kg body weight that identifies chemical substances with the potential for systemic toxicity following dermal exposure [NIOSH 2009], chlorinated camphene has the potential to be absorbed through the skin and be systemically available. This is in contrast to the model prediction that indicated a low potential of chlorinated camphene for absorption through the skin.

No epidemiological studies were identified that evaluated the potential of chlorinated camphene to cause systemic toxicity following dermal exposure. A case report by Pollock [1958] described severe systemic effects including generalized muscular aches and pain (particularly of the extremities) and stiffness, semi-consciousness, vomiting, and epigastric pain following a 2 hr contact with a lindane–chlorinated camphene solution. The worker handled the material while mixing the solution into the wool of sheep as a pesticide treatment; the contaminated skin was not washed and symptoms developed 10 hr after exposure. The doses of lindane or chlorinated camphene were not quantified, and it is unclear which chemical produced the systemic effects. Both chlorinated camphene and lindane produce similar symptoms, with the usual sequence of events after ingestion being central nervous system (CNS) stimulation, high temperature, convulsions, gastric irritation, vomiting, diarrhea, respiratory failure, and death [Pollock 1958]. The systemic CNS effects observed, secondary to cutaneous absorption, are similar to those reported following oral ingestion or inhalation exposure in humans [McGee et al. 1952] and animals [DiPietro and Haliburton 1979; Lawrence and Casida 1984], suggesting that chlorinated camphene has the potential to cause CNS effects following prolonged dermal exposure.

No repeated-dose, sub-chronic, or chronic toxicity studies were identified that evaluated dermal exposure to chlorinated camphene in humans or animals. However, several oral exposure studies to chlorinated camphene identified the liver, kidney, spleen, and the immune system as target organs and systems [Agency for Toxic Substances and Disease Registry (ATSDR) 1996]. In a 13-week feeding study rats were given 0, 4.0, 20, 100, or 500 ppm chlorinated camphene [corresponding to 0, 4.0, 20, 100, and 500 mg/kg] [Chu et al. 1986]. Chu et al. [1986] reported that rats receiving 20 mg/kg daily of chlorinated camphene only ingested approximately 1.8 milligrams per kilograms per day (mg/kg-day), and that those rats receiving doses of 20 mg/kg-day and greater had histological changes in liver, kidney and thyroid. Chu et al. [1986] also fed dogs 0.2 to 5.0 mg/kg-day of chlorinated camphene for 13 weeks, and reported increased relative liver weight and histological changes in the liver and thyroid. In a later study, Chu et al. [1988] reported that chlorinated camphene caused increased liver and kidney weights, elevated serum cholesterol, and histological changes in the liver, thyroid and kidney of adult rats in a generation 2 reproductive toxicity study following dietary exposure. These studies indicate that chlorinated camphene, in addition to inducing CNS effects, has the potential to be systemically available and may cause hepatic, liver, spleen and thyroid effects.

No specialty studies were identified that evaluated biological system/function specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure to chlorinated camphene. However, a reproductive toxicity study in which rats were administered chlorinated camphene in the diet observed no impairment in reproductive performance including the gestation index, survival indices, and litter size at doses up to 500 ppm, of which approximately 37 to 49 mg/kg-day was ingested [Chu et al. 1988].

No studies were identified that evaluated the carcinogenic potential of chlorinated camphene following dermal exposures. However, organizations and agencies have evaluated the carcinogenic potential of chlorinated camphene following other routes of exposure. Table 2 summarizes carcinogenic designations of multiple governmental and nongovernmental organizations for chlorinated camphene.

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

Organization	Carcinogenic designation
NIOSH [2005]	Potential occupational carcinogen
NTP [2014]	Reasonably anticipated to be a human carcinogen
USEPA [2014]	B2: Probable human carcinogen
IARC [2012]	2B: Possibly carcinogenic to humans
European Parliament [2008]	GHS Carcinogenicity Category 2: Suspected of causing cancer
EC [2013]†	R40: Limited evidence of a carcinogenic effect
ACGIH [2001]	A3: Confirmed animal carcinogen with unknown relevance to humans

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 since studies using the dermal route of exposure were unavailable.
†Date accessed

No studies were identified that provided quantitative estimates of chlorinated camphene absorption through the skin. Although the percent absorption following dermal exposure has not been estimated and no epidemiological studies or repeated-dose, subchronic or chronic toxicity studies in animals were identified that evaluated the potential of chlorinated camphene to cause systemic effects following dermal exposure, standard acute dermal toxicity study in rats **[Gaines 1969]**[1] and a non-standard acute toxicity test in rabbits **[Johnston and Eden 1953]** suggest that chlorinated camphene is absorbed through the skin following dermal exposure and can be systemically toxic. The potential to cause CNS effects are supported by a human case study which was also exposed to the pesticide lindane [Pollock 1958] and by oral and inhalation toxicity studies [DiPietro and Haliburton 1979; Lawrence and Casida 1984], indicating the CNS effects are not route-specific. In addition, subchronic oral toxicity studies **[Chu et al. [1986, 1988]** have identified the liver, kidney, spleen, and thyroid as target organs for chlorinated camphene at doses up to 2 mg/kg-day. NIOSH [2005] has previously identified chlorinated camphene as a potential occupational carcinogen, but data are not available to assess the carcinogenic potential of dermal exposures. Therefore, on the basis of the data for this assessment, chlorinated camphene is assigned the SK: SYS notation.

3.0 Direct Effects on Skin (SK: DIR)

No human or animal *in vivo* studies that evaluated the corrosivity of chlorinated camphene or *in vitro* tests for corrosivity using human or animal skin models or *in vitro* tests of skin integrity using cadaver skin were identified. A human case report of an individual exposed to a lindane-chlorinated camphene mixture for 2 hr reported itchy skin that was not accompanied by a rash [Pollock 1958], although it is unknown if the irritation was caused by chlorinated camphene or lindane. Standard irritation and

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

corrosivity tests were conducted on albino rabbits using 500 mg of technical grade chlorinated camphene, 0.5 milliliter (mL) of a 90% solution or a formulation of chlorinated camphene – the diluents for the solution and the formulation were not reported– was applied to an area of clipped and abraded skin that was occluded for 4 h [International Research and Development Corporation (IRDC) 1973]. The technical grade chlorinated camphene caused slight to moderate erythema and edema at 24 and 72 hr later on both intact and abraded skin. Similar effects were observed for the 90% solution and the formulated preparation at 4, 24 and 72 hr on both intact and abraded skin. IRDC [1973] defined a primary irritant as a substance which was not corrosive, but which resulted in a score of 5 or more. Because an irritation score of 2.1 was reported for the technical grade, 3.2 for the 90% solution, and 2.6 for the formulated preparation, IRDC [1973] concluded that the dosing regimens used did not result in skin irritation and that the irritation noted was due to the test articles to the skin. However, this assessment concludes that observations at the specified time points (24 and 72 h) show the potential of chlorinated camphene to cause skin irritation. Industrial BioTest [1973] reported moderate to severe edema and erythema, followed by severe desquamation in rabbits after dermal application of very high doses (3,038 mg/kg and greater) of chlorinated camphene (90% in xylene) under occlusion for 24 hr. It is possible that xylene may have contributed to the skin effects observed in the Industrial Bio Test [1973] study, given that xylene causes mild irritation in guinea pigs and rats with a Draize score of 1.2 [Anderson et al. 1986; Chatterjee et al. 2005]. However, the dermal irritation score reported by Industrial Bio Test [1973] exceeds what we would expect to see from xylene alone, suggesting that chlorinated camphene has irritant properties. This is further supported by IRDC [1973], which reports slight to moderate erythema and edema following dermal exposure to technical grade chlorinated camphene.

The standard skin irritation tests identified **[IRDC 1973]** and results from prolonged exposure **[Industrial BioTest Labs 1973]** indicate that chlorinated camphene has the potential to cause mild to moderate skin irritation, and prolonged dermal contact with very high doses may be irritating to the skin. Therefore, on the basis of the data for this assessment, chlorinated camphene is assigned the SK: DIR (IRR) notation.

4.0 Immune-mediated Responses (SK: SEN)

No reports of sensitization in humans, or predictive tests (for example, guinea pig maximization tests, Buehler tests, murine local lymph node assays, mouse ear swelling tests) or other tests were identified that evaluated the potential of chlorinated camphene to cause skin sensitization in animals Lack of data precludes adequate evaluation of chlorinated camphene to cause skin sensitization. Therefore, on the basis of the data for this assessment, chlorinated camphene is not assigned the SK: SEN notation.

5.0 Summary

Although no studies were identified that provided quantitative estimates of absorption of chlorinated camphene through the skin, a standard acute toxicity study in rats **[Gaines 1969]]** and a non-standard acute toxicity test in rabbits **[Johnston and Eden 1953]** indicate that chlorinated camphene has the potential to be absorbed and be systemically toxic. Because neurotoxic effects have also been reported

by a human case study who was also exposed to the pesticide lindane [Pollock 1958] and by following inhalation and ingestion exposure in humans [McGee et al. 1952] and animals [DiPietro and Haliburton 1979; Lawrence and Casida 1984] to chlorinated camphene, the limited dermal exposure data in animals **[Chu et al. 1986; 1988]** support the conclusion that chlorinated camphene causes CNS effects following exposure via skin contact. In addition, subchronic oral toxicity studies with chlorinated camphene have identified the liver, kidney, spleen, and thyroid as target organs at doses of chlorinated camphene up to 2 mg/kg-day **[Chu et al. 1986, 1988]**. The standard irritation tests with a technical grade chlorinated camphene, a 90% solution of chlorinated camphene, and a commercially-available product **[IRDC 1973]** and results from prolonged dermal contact with high doses **[Industrial BioTest Labs 1973]** are sufficient to indicate that the chlorinated camphene has the potential to cause skin irritation. No diagnostic tests in humans or predictive tests in animals were identified to adequately evaluate the potential of chlorinated camphene to cause skin sensitization. Therefore, on the basis of these assessments, chlorinated camphene is assigned a composite skin notation of **SK: SYS-DIR (IRR)**.

Table 3 summarizes the skin hazard designations for chlorinated camphene previously issued by NIOSH and other organizations. The equivalent dermal designations for chlorinated camphene, according to the Global Harmonization System (GHS) of Classification and Labelling of Chemicals, are Acute Toxicity Category 4 (Hazard statement: Harmful in contact with the skin), and Skin Irritation Category 2 (Hazard statement: Causes skin irritation) [European Parliament 2008].

Table 3. Summary of previous skin hazard designations for chlorinated camphene

Organization	Skin hazard designation
NIOSH [2005]	[skin]: Potential for dermal absorption; prevent skin contact
OSHA [2015]*	[skin]: Potential for dermal absorption
ACGIH [2001]	[skin]: Based on the absorption of chlorinated camphene through intact and abraded skin of treated rabbits leading to systemic effects and lethality
EC [2013]*	R21: Harmful if in contact with skin R38: Irritating to skin

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

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

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Appendix: Calculation of the SI Ratio for Chlorinated camphene

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for chlorinated camphene. 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 centimeters per hour (cm/hr), 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 squared centimeters [cm^2]).

Equation 2: Determination of Skin Dose

Skin dose = $k_p \times S_w \times$ Exposed skin surface area × Exposure time
= k_p(cm/hr) × S_w (mg/cm^3) × 360 cm^2 × 8 hr

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 hr, an inhalation volume of 10 cubic meters (m^3) inhaled air in 8 s, and a factor of 75% for retention of the airborne substance in the lungs during respiration (retention factor, or RF).

Equation 3: Determination of Inhalation Dose

Inhalation dose = OEL × Inhalation volume × RF
= OEL (mg/m^3) × 10 m^3 × 0.75

The final step is to compare the calculated skin and inhalation doses and to present the result as a ratio of skin dose to inhalation dose (the SI ratio). This ratio quantitatively indicates (1) the significance of dermal absorption as a route of occupational exposure to the substance and (2) the contribution of dermal uptake to systemic toxicity. If a substance has an SI ratio greater than or equal to 0.1, it is considered a skin absorption hazard.

Calculation

Table A1 summarizes the data applied in the previously described equations to determine the SI ratio for chlorinated camphene. The calculated SI ratio was 0.01. On the basis of these results, chlorinated camphene is predicted not to represent a skin absorption hazard.

Table A1. Summary of Data used to Calculate the SI Ratio for chlorinated camphene

Variables Used in Calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path(k_{psc})	cm/hr	0.0309
Permeation coefficient of the protein fraction of the stratum corneum (k_{pol})	cm/hr	7.1745×10^{-6}
Permeation coefficient of the watery epidermal layer (k_{aq})	cm/hr	0.11808
Molecular weight (MW)*	amu	448.26
Base-10 logarithm of its octanol–water partition coefficient (Log K_{ow})*	None	5.9
Calculated skin permeation coefficient (k_p)	cm/hr	0.02449
Skin dose		
Water solubility (S_w)*	mg/cm^3	5.5×10^{-4}
Calculated skin permeation coefficient (k_p)	cm/hr	0.02449
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hr	8
Calculated skin dose	mg	0.0388
Inhalation Dose		
Occupational exposure limit (OEL)†	mg/m^3	0.5
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	3.75
Skin dose–to–inhalation dose (SI) ratio	None	0.01

*Variables identified from SRC [ND].
†The OEL used in calculation of the SI ratio for chlorinated camphene was the NIOSH recommended exposure limit (REL) [NIOSH 2005].

Appendix References

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