NIOSH Skin Notation Profiles

Dieldrin

SK

ID^{SK}

[~~SK~~]

SYS

SYS (FATAL)

DIR

DIR (IRR)

DIR (COR)

SEN

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

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NIOSH Skin Notation (SK) Profile

Dieldrin
[CAS No. 60-57-1]

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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 dieldrin. 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	square centimeter(s)
cm/hr	centimeter(s) per hour
cm/s	centimeter(s) per second
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
g	gram(s)
g/L	gram(s)/liter
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
IPCS	International Program for Chemical Safety
(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
ppm	parts per million
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
US EPA	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 absorption of chemicals after exposure of the skin.

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1 Introduction

1.1 General Substance Information

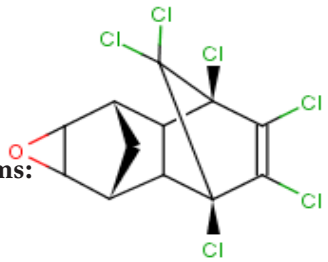
Chemical: Dieldrin

CAS No: 60-57-1

Molecular weight (*MW*): 349.1

Molecular formula: $C_{12}H_8Cl_6O$

Structural formula:



Synonyms:
HEOD; 1,2,3,4,10,10-Hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4-endo,exo-5,8-dimethanonaphthalene

Uses:
Dieldrin is an organochlorine pesticide. An estimated 670,000 pounds (~300,000 kilograms) of dieldrin were used in 2002 [ATSDR 2002].

1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with dieldrin and (2) the rationale behind the hazard-specific skin notation (SK) assignment for dieldrin. 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 dieldrin. A literature search was conducted through August 2014 to identify information on dieldrin, 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 dieldrin.

1.3 Overview of SK Assignment

Dieldrin 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 dieldrin: **SK: SYS (FATAL)**. Table 1 provides

Table 1. Summary of the SK assignment for dieldrin

Skin notation	Critical effect	Available data
SK: SYS (FATAL)	Central nervous system (CNS) effects	Limited human and sufficient animal data

an overview of the critical effects and data used to develop the SK assignment for dieldrin.

2 Systemic Toxicity from Skin Exposure (SK: SYS)

Several toxicokinetic studies in human volunteers and animals were identified that evaluated absorption of dieldrin following dermal exposure. However, none of these studies quantified the rate of absorption, and in most cases the measurements reported were not adequate to estimate the total percent absorption. Feldman and Maibach [1974] reported that, after a single dermal application of 4 micrograms per square centimeter (μg/cm^2) dieldrin in 0.1 milliliters (mL) acetone to the forearm of human volunteers, 7.7% of the dieldrin applied was excreted in the urine over a 5-day period. This value could be an underestimate of total absorption, since urine levels would not account for any dieldrin that was metabolized, stored in the body, or eliminated via other pathways. However, in close agreement with the findings of Feldman and Maibach [1974], Fisher et al. [1985] reported that cumulative estimated absorption over 120 hours as a percentage of the applied dieldrin dose was 7.07% based on data on urinary excretion of radio-labeled dieldrin from intravenous and dermal treatments in humans. The investigators reported that the dermal absorption occurred over the first 4 hours [Fisher et al. 1985]. Several whole-animal studies show that dieldrin effectively penetrates the skin surface [Bundren et al. 1952; O'Brien and Dannelley 1965; Soma Sundaram et al. 1978; Shah et al. 1981]. In mice, topical application of 1 milligram of dieldrin per kilogram body weight (mg/kg) to a one square centimeter (cm^2) area of shaved skin resulted in 94% of dieldrin penetrating over 48 hours. Very little dieldrin was found in the blood or organs 8 hours after exposure, however, relatively high amounts were observed in the carcasses [Shah et al. 1981]. O'Brien and Dannelley [1965] described dieldrin as having a relatively high penetration following application of one microgram (μg) of dieldrin dissolved in 1 microliter (μL) of benzene to shaved bellies of rats for up to 24 hours; however, no quantitative estimate for the degree of penetration was provided. Bundren et al. [1952] and Soma Sundaram et al. [1977] indicated that dieldrin is absorbed by the skin following dermal exposure. Soma Sundaram et al. [1977] applied 0.0001 to 0.1% dieldrin in ethyl acetate covering 4 cm^2, twice a week for 6 months to the shaved skin of dogs and monkeys. The authors reported an increase in dieldrin content in the body. When rabbits were dipped into a dilute emulsion of xylene, Triton x-155, dieldrin and water, Bundren et al. [1952] reported that the animals retained dieldrin in their livers and kidneys; however, the authors did not provide adequate information to estimate the total portion of the dose that was absorbed systemically. The potential of dieldrin to pose a skin absorption hazard was also evaluated using 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 0.007 was calculated for dieldrin. An SI ratio of ≥0.1 indicates that skin absorption may significantly contribute to the overall body burden of a substance [NIOSH 2009]; therefore, dieldrin 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 estimates of the dermal lethal dose (LD_{Lo}) of dieldrin for humans were identified. Gaines [1960] reported the dermal LD_{50} (the dose resulting in 50% mortality in the exposed animals) to range from 60 to 90 mg/kg in rats. Johnston and Eden [1953] reported an LD_{50} of 400–450 mg/kg when rabbits were immersed in water suspensions of dieldrin wettable powder. These acute dermal toxicity

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

Organization	Carcinogenic designation
NIOSH [2005]	Potential occupational carcinogen
NTP [2014]	Not evaluated
USEPA [2014]	B2: probable human carcinogen
European Parliament [2008]	GHS Carcinogenicity Category 2: suspected human carcinogen
IARC [2012]	Group 3: not classifiable as to its carcinogenicity to humans
EC [2014]†	R40: limited evidence of a carcinogenic effect
ACGIH [2010]	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 rather than dermal exposure.
†Date accessed.

studies have reported clinical signs of toxicity including loss of appetite, nervousness, convulsions, and muscular spasms in both rats and rabbits [Johnston and Eden 1953; Gaines 1960], indicating that dieldrin causes neurological effects following dermal exposure. Because the reported acute dermal LD_{50} values for rats is lower than the critical dermal LD_{50} value of 200 mg/kg bodyweight that identifies chemical substances considered fatal when in contact with the skin [NIOSH 2009], dieldrin is considered acutely toxic and potentially fatal following dermal exposure.

A limited number of repeat-dose studies were identified in humans following dermal exposure to dieldrin. In one study, Fletcher et al. [1959] observed no clinical signs of poisoning in sixteen pesticide sprayers who used dieldrin for 6 hours a day, 5.5 days a week for 180 days and were exposed to a minimum of 1.8 mg/kg-day. A No-Observable-Adverse-Effect-Level (NOAEL) of 1.8 mg/kg-day can be estimated for humans. Soma Sundaram et al. [1977] conducted a repeat-dose dermal study in monkeys and dogs in which an area of skin, about 2 × 2 cm in size, of each animal species was sprayed with 3 mL of dieldrin solutions containing concentrations ranging from 0.001 to 0.1% dieldrin in ethyl acrylate [corresponding to 0.03 to 3.0 mg dieldrin applied], twice a week for 6 months. This study indicated that dermal exposure of monkeys and dogs to a solution containing 0.1% dieldrin [corresponding to 0.3 mg/kg-day in monkeys, based on an average body weight calculated to be 2.9 kg and a dose of 0.9 mg dieldrin per week, and corresponding to 0.2 mg/kg-day in dogs, based on an average body weight calculated to be 3.5 kg and a dose of 0.9 mg dieldrin per week] resulted in decreased body weight, reduced food consumption, and increased water consumption. Bundren et al. [1952] conducted a study using both mature and immature rabbits. Mature rabbits that received topical application of 30 mg dieldrin/kg once a week for 10 weeks showed no symptoms of toxicity. However, doses of 70 mg/kg (or 10 mg/kg-day) in mature rabbits caused deaths. Immature rabbits exposed to 50 mg/kg once per week (or 7.1 mg/kg-day) also died. Bundren et al. [1952] reported symptoms including salivation, grinding of teeth, and spasms in both groups of exposed animals. Because the NOAELs identified in the Bundren et al. [1952] and Soma Sundaram et al. [1977] studies are

significantly lower than the critical dermal NOAEL value of 1000 mg/kg for repeat-dose toxicity that identifies chemical substances with the potential for subchronic dermal toxicity [NIOSH 2009], dieldrin is considered systemically available and able to cause general signs of toxicity such as decreased body weight and central nervous system (CNS) effects.

No standard toxicity or specialty studies that evaluated biological system/function specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure to dieldrin were identified. No studies were identified that evaluated the carcinogenicity potential of dieldrin following dermal exposure. Table 2 summarizes carcinogenic designations of multiple governmental and nongovernmental organizations for dieldrin.

Dermal absorption data in humans [Feldman and Maibach 1974; Fisher et al. 1985] and in animals [Bundren et al. 1952; O'Brien and Dannelley 1965; soma Sundaram et al. 1978; Shah et al. 1981] indicate that dieldrin is absorbed through the skin and is systemically available. Acute **[Johnston and Eden 1953; Gaines 1960]*** and repeat dose **[Bundren et al. 1952; Soma Sundaram et al. 1977]** dermal toxicity studies in animals demonstrate that dieldrin is systemically toxic and potentially fatal. Dieldrin may also cause systemic effects such as body weight loss and CNS toxicity following dermal exposure. Based on these data, dieldrin is assigned the SYS(FATAL) skin notation.

3 Direct Effects on Skin (SK:DIR)

No human or animal *in vivo* studies for corrosivity of dieldrin or *in vitro* tests for corrosivity using human or animal skin models or in vitro tests for skin integrity using cadaver skin were identified. Suskind [1959] observed no skin irritation related to dieldrin when 217 volunteers wore patches of cotton or wool flannel impregnated with 0.1% or 0.5% dieldrin for four days. Ross [1964] reported an outbreak of contact dermatitis in police recruits wearing socks that had been mothproofed with a dieldrin solution; however, Ross [1964] reported that the outbreak may have been exacerbated, if not caused, by the presence of a dye used in the socks rather than by dieldrin. In animals, dieldrin produced minimal, if any, irritation to the skin. Histological examinations performed on the skin of monkeys and dogs after 20 to 30 applications of 0.0001% to 0.1% of dieldrin was applied to the skin revealed pale and loose collagen fibers of the dermis, and brittle and dry skin [Soma Sundaram et al. 1977]. The evidence from animal studies suggests that dieldrin is not a skin irritant. The structure-activity relationship model, Deductive Estimation of Risk from Existing Knowledge (*DEREK*) for Windows, predicted dieldrin to be positive for skin irritation, indicating that the chemical has structural alerts for skin irritation.

Although limited information was identified upon which to base the potential of dieldrin to cause skin irritation in humans and animals, the available evidence suggest that dieldrin is not irritating to the skin at low doses or low concentrations. No adequate studies were identified on the direct skin effects of concentrated solutions of dieldrin. Therefore, on the basis of the data for this assessment, dieldrin is not assigned the SK: DIR (IRR) notation.

4 Immune-mediated Responses (SK: SEN)

A limited number of studies were identified that evaluated the potential of dieldrin to cause skin sensitization in humans. Two hundred and seven human volunteers who were re-exposed to fabric containing up to 0.5% dieldrin two weeks after a four-day exposure showed no signs of skin sensitization [Suskind 1959]. Muirehead et al. [1959] reported a case who developed immunohemolytic

*Reference in bold text indicate studies that serve as the basis of the skin notation

anemia after multiple exposures to dieldrin while spraying cotton fields; antibodies for dieldrin-coated or heptachlor-coated red blood cells were found in his serum. While the presence of antibodies for dieldrin suggests the potential for sensitization, this study is limited because exposure to multiple pesticides, including heptachlor and toxaphene, were documented.

No predictive tests (i.e., guinea pig maximization tests, Buehler tests, murine local lymph node assays, mouse ear swelling tests) or other tests that evaluated the potential of dieldrin to cause skin sensitization in animals were identified. The structure activity relationship model, DEREK for Windows, predicted dieldrin to be positive for skin sensitization, indicating that the chemical has structural alerts for skin sensitization.

The limited information available for humans suggests that dieldrin is not likely to be a skin sensitizer and no standard assays in animals were identified; however, a predictive model suggests that dieldrin has structural alerts for skin sensitization. The data are insufficient to adequately evaluate the skin sensitization potential of dieldrin. Therefore, on the basis of the data for this assessment, dieldrin is not assigned the SK: SEN notation.

5 Summary

The dermal absorption data in humans [Feldman and Maibach 1974; Fisher et al. 1985] and animals [Bundren et al. 1952; O'Brien and Dannelley 1965; Soma Sundaram et al. 1978; Shah et al. 1981] indicate that dieldrin is absorbed through the skin and is systemically available. Acute **[Johnston and Eden 1953; Gaines 1960]** and repeat-dose **[Bundren et al. 1952; Soma Sundaram et al. 1977]** dermal toxicity studies in animals demonstrate that dieldrin is systemically toxic and is potentially fatal. Dieldrin may also cause systemic effects such as body weight loss and CNS toxicity following dermal exposure. The limited data identified for skin irritation suggest that dieldrin at low doses or concentrations is not a skin irritant (although concentrated solutions have not been tested) and the data are not sufficient to adequately evaluate the sensitization potential of dieldrin. Therefore, on the basis of these assessments, dieldrin is assigned a composite skin notation of **SK: SYS (FATAL)**.

Table 3 summarizes the skin hazard designations for dieldrin previously issued by NIOSH and other organizations. The equivalent dermal designation for dieldrin, according to the Global Harmonization System (GHS) of Classification and Labelling of Chemicals, is Acute Toxicity Category 1 (Hazard statement: Fatal in contact with the skin) [European Parliament 2008].

References

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

Table 3. Summary of previous skin hazard designations for dieldrin

Organization	Skin hazard designation
NIOSH [2005]	[skin]: potential for dermal absorption
OSHA [2015]*	[skin]: potential for dermal absorption
ACGIH [2010]	[skin]: dieldrin is toxic by all routes of exposure but the greatest hazard is skin absorption
EC [2014]*	R27: very toxic in contact with 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.
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Appendix: Calculation of the SI Ratio

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for dieldrin. 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.
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)

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

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

$$\log K_{psc} = -1.326 + 0.6097 \times \log K_{ow} - 0.1786 \times MW^{0.5}$$

$$K_{pol} = 0.0001519 \times MW^{-0.5}$$

$$K_{aq} = 2.5 \times MW^{-0.5}$$

The second step is to calculate the biologic mass uptake of the substance from skin absorption (skin dose) and inhalation (inhalation

dose) during the same period of exposure. The skin dose is calculated as a mathematical product of the k_p, the water solubility (S_w) of the substance, the exposed skin surface area, and the duration of exposure. Its units are milligrams (mg). Assume that the skin exposure continues for 8 hours to unprotected skin on the palms of both hands (a surface area of 360 square centimeters [cm^2]).

Equation 2: Determination of Skin Dose

$$\text{Skin dose} = k_p \times S_w \times \text{Exposed skin surface area} \times \text{Exposure time}$$

$$= k_p(\text{cm/hour}) \times S_w\,(\text{mg/cm}^3) \times 360\ \text{cm}^2 \times 8\ \text{hours}$$

The inhalation dose (in mg) is derived on the basis of the occupational exposure limit (OEL) of the substance—if the OEL is developed to prevent the occurrence of systemic effects rather than sensory/irritant effects or direct effects on the respiratory tract. Assume a continuous exposure of 8 hours, an inhalation volume of 10 cubic meters (m^3) inhaled air in 8 hours, and a factor of 75% for retention of the airborne substance in the lungs during respiration (retention factor, or RF).

Equation 3: Determination of Inhalation Dose

$$\text{Inhalation dose} = \text{OEL} \times \text{Inhalation volume} \times \text{RF}$$

$$= \text{OEL}\ (\text{mg/m}^3) \times 10\ \text{m}^3 \times 0.75$$

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 dieldrin. The calculated SI ratio was 0.007. On the basis of these results, dieldrin is not predicted to represent a skin absorption hazard.

Appendix References

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Table A1. Summary of data used to calculate the SI ratio for dieldrin

Variables used in calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path(k_{psc})	cm/hr	0.0302
Permeation coefficient of the protein fraction of the stratum corneum (k_{pol})	cm/hr	7.783×10^{-6}
Permeation coefficient of the watery epidermal layer (k_{aq})	cm/hr	0.1281
Molecular weight (MW)*	amu	380.91
Base-10 logarithm of its octanol–water partition coefficient (Log K_{ow})*	None	5.4
Calculated skin permeation coefficient (k_p)	cm/hr	0.0245
Skin dose		
Water solubility (S_w)*	mg/cm^3	1.95×10^{-4}
Calculated skin permeation coefficient (k_p)	cm/hr	0.0245
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hr	8
Calculated skin dose	mg	0.0137
Inhalation Dose		
Occupational exposure limit (OEL)†	mg/m^3	0.25
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	1.8755
Skin dose–to–inhalation dose (SI) ratio	None	0.0073

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

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