Skin Notation (SK) Profile

Dichlorvos

[CAS No. 62-73-7]

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 dichlorvos. 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
ChE	cholinesterase
cm^2	squared centimeter(s)
cm/hour	centimeter(s) per hour
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
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
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^3	milligram(s) per cubic centimeter
mg/kg	milligram(s) per kilogram body weight
mg/min	milligram(s) per minute
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

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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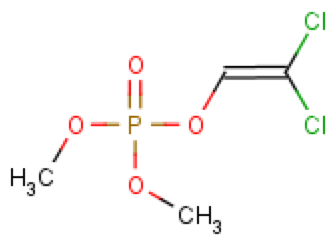
1.0 Introduction

1.1 General Substance Information:

Chemical: Dichlorvos
CAS No: 62-73-7
Molecular weight (*MW*): 221.0
Molecular formula: $(CH_3O)_2P(O)OCH{=}CCl_2$
Structural formula:



Synonyms: 2,2-Dichlorovinyl dimethyl phosphate; Phosphoric acid, 2,2-dichloroethenyl dimethyl ester; 2,2 -Dichloroethenyl phosphoric acid dimethyl ester; 2,2 - Dichlorovinyl dimethyl phosphoric acid ester; DDVP

Uses: Dichlorvos is used primarily as a broad spectrum organophosphate pesticide [ATSDR 1997].

1.2 Purpose

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

1.3 Overview of SK Assignment

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

Table 1. Summary of the SK Assignment for Dichlorvos

Skin Notation	Critical Effect	Available Data
SK: SYS	Histopathological changes in male reproductive system, lungs, liver, lymphatic glands, thymus, and heart; neurotoxicity; inhibition of cholinesterase activity	Sufficient animal data
SK: DIR (IRR)	Skin irritation	Sufficient human and animal data
SK: SEN	Skin allergy, photoallergy	Sufficient human and animal data

2.0 Systemic Toxicity from Skin Exposure (SK: SYS)

Quantitative estimates of dermal absorption in humans were not identified, but the potential for significant dermal absorption is indicated by cases of systemic effects including neurotoxicity resulting from cholinesterase (ChE) activity inhibition after a single episode of dermal exposure [Bisby and Simpson 1975; Mathias 1983] and cholinesterase inhibition-associated symptoms following dermal exposures in animals [Durham et al. 1957; Gajewski and Katkiewicz 1981; Tos-Luty et al.1994]. An animal study was identified that reported skin penetration of dichlorvos. Tos-Luty et al. [1994] applied 0.3%, 0.62%, and 1.5% of dichlorvos in ethanol to the tails of rats for 4 hours. The highest penetration of dichlorvos in the rat tail skin (2.91% absorbed) was at the lowest concentration (0.3%), and 2.02% and 2.23% absorbed reported for concentrations of 0.62% and 1.5% dicholorvos, respectively [Tos-Luty et al. 1994]. The potential of dichlorvos 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 2.55 was calculated for dichlorvos. An SI ratio of ≥0.1 indicates that skin absorption may significantly contribute to the overall body burden of a substance [NIOSH 2009]; therefore, dichlorvos is considered to be absorbed through the skin following dermal exposure. Additional information on the SI ratio and the variables used in its calculation are included in the appendix.

No quantitative estimates of the lethal dermal dose (LD_{Lo}) in humans have been identified. In animals, dermal LD_{50} values (the dose resulting in 50% mortality in the exposed animals) were influenced by the purity of dichlorvos tested, the vehicle used, and condition of the skin. LD_{50} values for rats were reported to range from 75 milligrams per kilogram body weight (mg/kg) to 107 mg/kg [Gaines 1969; Durham et al. 1957]. Gajewski and Katkiewicz [1981] reported an LD_{50} in a negative logarithm of 3.49 mols/kg in rats. Because the reported acute dermal LD_{50} values for experimental animals are all lower than the critical dermal LD_{50} value of 2,000 mg/kg body weight that identifies chemical substances with the potential for acute dermal toxicity [NIOSH 2009], dichlorvos is considered systemically toxic by the dermal route.

Dermal application of dichlorvos to several animal species, including the monkey and rat, over a few days, resulted in significant inhibition of brain, erythrocyte, or serum ChE activity [Durham et al. 1957; Moriearty et al. 1993]. Symptoms of neurotoxicity have been reported within 20 minutes in monkeys after single or repeated dermal exposure to doses of dichlorvos in xylene at doses as low as 50 mg/kg or in rats topically exposed to 75 mg/kg [Durham et al. 1957]. These studies indicate that dichlorvos is a potent cholinesterase (ChE) inhibitor, significantly reducing blood plasma, red blood cell and brain ChE following dermal exposure.

No repeat-dose dermal toxicity studies have been identified that quantified the dose to which humans were exposed. Although no chronic toxicity studies were identified in animals, the potential of dichlorvos to cause systemic toxicity has been evaluated in two repeat-dose and two subchronic dermal toxicity studies. Dermal application of dichlorvos over shorter durations, e.g. daily doses of 50 mg/kg, 75 mg/kg, and 100mg/kg resulted in death in monkeys after 8, 10, and 4 doses, respectively, while cholinergic signs (incoordination, muscle fasciculation, excessive salivation, labored breathing, miosis, and eventually inability or indisposition to move), and significant inhibition of cholinesterase activities in the plasma and red blood cells were qualitatively similar at all dosage levels [Durham et al. 1957]. Luty et al. [1998] also reported dose-dependent histopathological changes in multiple organs (lungs, lymphatic glands and thymus, liver, kidneys and heart muscle) and stimulation of the bactericidal and phagocytic activity of neutrophils in rats exposed for 4 hours/day to 7.5 and 37.5 mg/kg-day dichlorvos for 4 weeks. In a subchronic study, dermal painting of rats with dichlorvos at a dose of 30 mg/kg per day (mg/kg-day) for 90 days did not elicit any symptoms of intoxication or mortality [Ali and Abdalla 1992]. However, histopathological examination revealed changes in testicular and liver tissues, with the cellular damage being prominent in animals treated for 30 days or more [Ali and Abdalla 1992]. Degenerative seminiferous tubules and fewer Leydig cells were observed in the testis, while congestion, atrophy, and cells at different stages of necrobiotic changes were observed in the liver [Ali and Abdalla 1992]. In an earlier 90-day subchronic dermal painting study, rats exposed to 21.4 mg/kg-day for 5 days/week exhibited few clinical symptoms or histopathology changes in the skin or testes [Dikshith et al. 1976]. Histopathologic changes in the testes occurred in one control animal, however, the power to detect a difference between the cases and controls was low, thus the possibility of an effect of the compound at 21.4 mg/kg-day cannot be fully ruled out. The dose of 21.4 mg/kg-day can be regarded as the Lowest Observed-Adverse-Effect Level (LOAEL) for the testicular and hepatic effects. These studies demonstrate that dermal exposure to dichlorvos is systemically toxic, causing histopathological changes in internal organs, ChE inhibition, and central nervous system effects at doses significantly lower than the critical dermal LOAEL value of 1,000 mg/kg for repeat-dose toxicity that identifies chemical substances with the potential for subchronic dermal toxicity [NIOSH 2009].

No standard toxicity or specialty studies evaluating biological system/function-specific effects (including developmental effects) following dermal exposure to dichlorvos were identified in humans or animals. However, reproductive system effects were identified when histopathology examination following a 90-day subchronic dermal exposure to 30 mg/kg/day observed testicular effects [Ali and Abdalla 1992]. The study by Luty et al. [1998] also demonstrates the potential of dichlorvos to affect immune system components (including lymphatic glands and thymus) following dermal exposure.

No studies that evaluated the potential of dermally-applied dichlorvos to cause cancer in humans or animals were identified. Table 2 summarizes carcinogenic designations of multiple governmental and nongovernmental organizations for dichlorvos.

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

Organization	Carcinogenic designation
NIOSH [2005]	No designation
NTP [2014]	No designation
USEPA [2014]	B2: probable human carcinogen
European Parliament [2008]	No GHS designation
IARC [2012]	Group 2B: possibly carcinogenic to humans
EC [2013]†	No designation
ACGIH [2014]	A4: not classifiable as a human carcinogen

ACGIH = American Conference of Governmental Industrial Hygienists; EC = European Commission, Joint Research, Institute for Health and Consumer Protection; GHS = Globally Harmonized System for Classification and Labelling of Chemicals; IARC = International Agency for Research on Cancer; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; USEPA = United States Environmental Protection Agency.
* The listed cancer designations were based on data from nondermal (such as oral or inhalation) exposure since studies using the dermal route of exposure were unavailable.
†Date accessed.

Taken together, the toxicokinetic data in animals **[Tos-Luty et al. 1994]**[1], results from the predictive mathematical algorithm, acute toxicity studies in animals **[Gaines 1969; Durham et al. 1957]**, and subchronic dermal toxicity in animals **[Durham et al. 1957; Dikshith et al. 1976; Ali and Abdalla 1992; Luty et al. 1998]** are sufficient to demonstrate the potential of dichlorvos to be absorbed through the skin and be systemically toxic, causing histopathological changes in testis, lungs, liver, lymphatic glands, thymus, and heart; neurotoxicity; and inhibition of cholinesterase activity following dermal exposure. Therefore, this assessment assigns a skin notation of SK: SYS for dichlorvos.

3.0 Direct Effects on Skin (SK: DIR)

No human or animal *in vivo* studies on corrosivity of dichlorvos or *in vitro* tests for corrosivity using human or animal skin models or *in vitro* tests of skin integrity using cadaver skin were identified. However, cases of irritant contact dermatitis have been reported in humans who came into direct contact

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

with 1% to 10% solutions of, or mixtures containing, dichlorvos [Bisby and Simpson 1975; Cronce and Alden 1968; Mathias 1983]. Flea collar dermatitis – a primary irritant contact dermatitis – has been described in cats and dogs wearing dichlorvos-impregnated PVC flea collars [Breen and Conroy 1971; Fox et al. 1969a, 1969b]. In guinea pigs, Ueda et al. [1994] reported a threshold irritation concentration of 1% dichlorvos, while 0.5% was reported to produce discrete erythema [Fujita 1985]. The structure-activity relationship model, Deductive Estimation of Risk from Existing Knowledge (*DEREK*), predicted dichlorvos to be negative for skin irritation.

Case reports of irritant contact dermatitis in humans **[Bisby and Simpson 1975; Cronce and Alden 1968; Mathias 1983]** and animals **[Breen and Conroy 1971; Fox et al. 1969a, 1969b]** provide sufficient evidence that dilute solutions are irritating to the skin. Therefore, on the basis of the data for this assessment, dichlorvos is assigned the SK: DIR (IRR) notation.

4.0 Immune-mediated Responses (SK: SEN)

There is evidence from occupational exposures that dichlorvos has the potential to cause skin sensitization. For example, human diagnostic patch tests of occupational flower growers or tea growers with a history of pesticide dermatitis have shown allergic contact dermatitis response to dichlorvos [Fujita 1985; Ueda et al. 1994]. Horiuchi and Ando [1978] reported light-induced hypersensitization to dichlorvos in photosensitizing patch tests of workers presenting with dermatitis caused by agricultural pesticides. Dichlorvos has been implicated as a causative agent in contact dermatitis in a case-control study conducted by Matsushita et al. [1985], and may also cause skin sensitization in animals. A positive response was reported in a guinea pig maximization test (GPMT) [Ueda et al. 1994]. Fujita [1985] rated the allergenicity of dichlorvos as moderate using the guinea pig maximization test. *DEREK* also predicted dichlorvos to be a plausible skin sensitizer.

Human diagnostic patch tests conducted on agricultural workers presenting with contact dermatitis show that dichlorvos has the potential to be a skin sensitizer **[Fujita 1985; Matsushita et al. 1985; Ueda et al. 1994]** and a photosensitizer **[Horiuchi and Ando 1978]**. Predictive tests in animals (for example, guinea pig maximization tests) **[Fujita 1985; Ueda et al. 1994]** demonstrate that dichlorvos causes skin sensitization. Therefore, on the basis of the data for this assessment, dichlorvos is assigned the SK: SEN notation.

5.0 Summary

No quantitative estimates of dermal absorption in humans were identified. However, toxicokinetic data **[Tos-Luty et al. 1994]**, acute toxicity studies **[Gaines 1969; Durham et al. 1957]**, and repeat-dose and subchronic dermal toxicity in animals **[Durham et al. 1957; Dikshith et al. 1976; Ali and Abdalla 1992; Luty et al. 1998],** and results from the predictive mathematical algorithm sufficiently demonstrate the potential of dichlorvos to be absorbed through the skin and be systemically toxic, causing diverse effects including histopathological changes in testis, lungs, liver, lymphatic glands, thymus, and heart; neurotoxicity; and inhibition of cholinesterase activity following dermal exposure. Although cases of skin corrosivity were not identified, case reports of irritant contact dermatitis in humans **[Bisby and**

Simpson 1975; Cronce and Alden 1968; Mathias 1983] and animals [**Breen and Conroy 1971; Fox et al. 1969a, 1969b]** provide sufficient evidence that dilute solutions of dichlorvos are irritating to the skin. Human diagnostic patch tests conducted on agricultural workers presenting with contact dermatitis show that dichlorvos has the potential to be a skin sensitizer **[Fujita 1985; Matsushita et al. 1985; Ueda et al. 1994]** and a photosensitizer **[Horiuchi and Ando 1978]**. Predictive tests in animals (for example, guinea pig maximization tests) **[Fujita 1985; Ueda et al. 1994]** demonstrate that dichlorvos causes skin sensitization. Therefore, on the basis of these assessments, dichlorvos is assigned a composite skin notation of **SK: SYS-DIR (IRR)-SEN**.

Table 3 summarizes the skin hazard designations for dichlorvos previously issued by NIOSH and other organizations. The equivalent dermal designations for dichlorvos, according to the Global Harmonization System (GHS) of Classification and Labelling of Chemicals, are Acute Toxicity Category 3 (Hazard statement: Toxic in contact with the skin) and Skin Sensitization Category 1 (Hazard statement: May cause an allergic skin reaction) [European Parliament 2008].

Table 3. Summary of previous skin hazard designations for dichlorvos

Organization	Skin hazard designation
NIOSH [2005]	[skin]: Potential for dermal absorption; prevent skin contact
OSHA [2015]*	[skin]: Potential for dermal absorption
ACGIH [2014]	[skin]: symptoms of organophosphate poisoning have been seen in humans and animals following dermal contact. DSEN: based upon positive patch-test responses in humans and positive responses in the guinea pig maximization test.
EC [2013]*	R24: Toxic in contact with skin R43: May cause sensitization by skin contact

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 Dichlorvos

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for dichlorvos. Although the SI ratio is considered in the determination of a substance's hazard potential following skin contact, it is intended only to serve as supportive data during the assignment of the NIOSH SK. An in-depth discussion on the rationale and calculation of the SI ratio can be found in Appendix B of the *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009].

Overview

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

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

The algorithm evaluation includes three steps:
(1) determining a skin permeation coefficient (k_p) for the substance of interest,
(2) estimating substance uptake by the skin and respiratory absorption routes, and
(3) evaluating whether the substance poses a skin exposure hazard.

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

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

Equation 1: Calculation of Skin Permeation Coefficient (k_p)

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

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/hour) × S_w (mg/cm^3) × 360 cm^2 × 8 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

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 dichlorvos. The calculated SI ratio was 2.55. On the basis of these results, dichlorvos is predicted to represent a skin absorption hazard.

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

Variables Used in Calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path(k_{psc})	cm/hour	8.2281×10^{-4}
Permeation coefficient of the protein fraction of the stratum corneum (k_{pol})	cm/hour	1.0218×10^{-5}
Permeation coefficient of the watery epidermal layer (k_{aq})	cm/hour	0.1682
Molecular weight (MW)*	amu	220.98
Base-10 logarithm of its octanol–water partition coefficient (Log K_{ow})*	None	1.47
Calculated skin permeation coefficient (k_p)	cm/hour	8.2892×10^{-4}
Skin dose		
Water solubility (S_w)*	mg/cm^3	8
Calculated skin permeation coefficient (k_p)	cm/hour	8.2892×10^{-4}
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hour	8
Calculated skin dose	mg	19.1
Inhalation Dose		
Occupational exposure limit (OEL)†	mg/m^3	1
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	7.5
Skin dose–to–inhalation dose (SI) ratio	None	2.55

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

Appendix References

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