NIOSH Skin Notation Profiles

Phenylhydrazine

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

NIOSH Skin Notation (SK) Profiles

Phenylhydrazine
[CAS No. 100-63-0]

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 phenylhydrazine. 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 nterest.

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Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
ADL	approximate dermal lethal
CIB	Current Intelligence Bulletin
cm^2	square 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/kg	milligram(s) per kilogram body weight
mg/m^3	milligram(s) per cubic meter
mL	milliliter(s)
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
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 Introduction

1.1 General Substance Information:

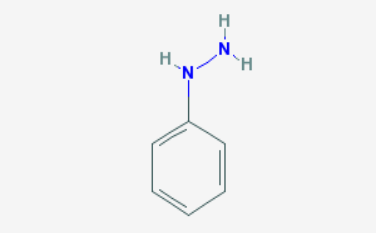
Chemical: Phenylhydrazine

CAS No: 100-63-0

Molecular weight (*MW*): 108.1

Molecular formula: $C_6H_5NHNH_2$

Structural formula:



Synonyms:

Hydrazinobenzene; monophenylhydrazine; hydrazinobenzen

Uses:

Phenylhydrazine is used as an intermediate, reducing agent, and reagent in the production of dyes, sugars, organic compounds, in addition to pharmaceuticals [HSDB 2011].

1.2 Purpose

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

1.3 Overview of SK Assignment

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

Table 1. Summary of the SK assignment for phenylhydrazine

Skin notation	Critical effect	Data available
SK: SYS	Hemolytic effects; Nephrotoxicity; Hepatotoxicity	Limited human and animal data
SK: DIR (IRR)	Skin irritant	Sufficient human data
SK: SEN	Skin allergy	

2 Systemic Toxicity from Skin Exposure (SK: SYS)

No quantitative estimates of the dermal absorption of phenylhydrazine have been identified. The potential of phenylhydrazine 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 304.6 was calculated for phenylhydrazine. An SI ratio of ≥0.1 indicates that skin absorption may significantly contribute to the overall body burden of a substance [NIOSH 2009]; therefore, phenylhydrazine 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 estimated dermal lethal dose (LD_{Lo}) was identified for humans. No dermal LD_{50} values (the dose resulting in 50% mortality in the exposed animals) have been identified. In a study by Derelanko et al. [1987], rabbits topically exposed to a dose of 500 milligrams per kilogram body weight (mg/kg) phenylhydrazine hydrochloride [corresponding to 374 mg/kg phenylhydrazine] under a plastic cover or gauze for 24 hours experienced 20 to 30% mortality, respectively, but no mortality at 10 mg/kg. No fatalities were observed in rats administered the same dose. Derelanko et al. [1987] reported hematological effects (destruction of red blood cells, reduction in erythrocyte count, increased reticulocyte count, methemoglobin formation (rats only), and enlargement of the spleen as systemic effects following acute dermal exposure. DuPont Company [1963] reported an approximate dermal lethal (ALD) dose of 90 mg/kg for the chemical following single dermal dose study in rabbits, with the animals exhibiting initial weight loss, hematuria and pallor for 2 days when administered a single nonlethal dose, and cyanosis, rapid respiration, hematuria, and weight loss following a single lethal dose. Although no animal LD_{50} values were identified, concentrations significantly below 2000 mg/kg body weight are lethal in rabbits, with mortality incidence reaching 30% at a dose of 374 mg/kg [Derlanko et al. 1987]. This result would be consistent with an LD_{50} value below 2000 mg/kg and is sufficient to conclude that phenylhydrazine is acutely toxic following dermal exposure [NIOSH 2009].

Hemolytic anemia was observed in several cases of occupational exposure by both dermal and inhalation routes, although no quantitative measures of exposure were provided. Rukl [1953] reported three cases of hemolytic anemia following dermal exposures to small repeated (unspecified) doses to phenylhydrazine over a period ranging from 2 weeks to 9 months. No subchronic (21-day or 28-day) or chronic (at least 12 months) studies were identified in animals. However, a repeat-dose study was identified in which Dow Chemical Company [1940], administered phenylhydrazine (as the hydrochloride) to the skin of an unspecified number of rabbit at doses of 1, 10, or 100 mg/kg for a total of 20 times over a 29-day period. No deaths were observed in the 1 mg/kg dose group, while an animal exposed to 10 mg/kg died after receiving four applications of the material, and another exposed to 100 mg/kg died after receiving two applications in three days [Dow Chemical Company 1940]. Histological examination showed slight damage to the liver of the rabbit dosed at 1 mg/kg per day and marked damage to the spleen and liver and a less marked damage in the lung and kidney of the animal exposed to 10 mg/kg [Dow Chemical Company 1940]. No histological examination was performed in the animal dosed daily at 100 mg/kg, but blood examination revealed marked anemia and leukocytosis. Although the quality of this study is limited, the results suggest that the liver, kidney and the spleen are potential targets for phenylhydrazine following dermal

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

Organization	Carcinogenic designation
NIOSH [2005]	Potential occupational carcinogen
NTP [2011]	No designation
US EPA [2014]	No designation
European Parliament [2008]	Carcinogenicity Category 1B: May cause cancer
IARC [2012]	No designation
EC [2014]†	R45: May cause cancer
ACGIH [2001]	Group 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; 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.

exposure and that the chemical has the potential to elicit systemic effects at doses as low as 1 mg/kg per day.

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

Toxicokinetic studies that estimated dermal absorption of phenylhydrazine were not identified. Although no acute dermal toxicity studies that estimated the dermal LD_{50} values in animals were identified, ADL doses of 90 mg/kg and greater were reported **[DuPont Company 1963; Derelanko et al. 1987]***. The limited data identified indicate that phenylhydrazine can cause hemolytic effects in both animals **[Derelanko et al. 1987]** and humans **[Rukl 1953]** following dermal exposure. A repeat-dose dermal toxicity study suggests that phenylhydrazine may cause systemic toxicity, including effects on liver, kidney and spleen, following skin contact [**Dow Chemical Company 1940**]. Therefore, on the basis of the data for this assessment, phenylhydrazine is assigned the SK: SYS notation.

3 Direct Effects on Skin (SK: DIR)

No human or animal *in vivo* studies for corrosivity of phenylhydrazine 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, a number of skin irritation tests were identified in animals. For example, Roudabush et al. [1965] conducted primary irritation tests in which 50 mg of undiluted phenylhydrazine was applied to the abraded or intact skin of rabbits and guinea pigs. Results indicated that the chemical was irritating to the skin of these animals. Dow Chemical Company [1940] reported that both phenylhydrazine and its hydrochloride salt caused moderate skin irritation when applied topically to rabbit skin. Derelanko et

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

al. [1987] reported that a single dermal application of phenylhydrazine hydrochloride, under occlusive or semi-occlusive conditions, to the skin of rabbits and rats as a solid moistened with distilled water for 24 hours caused skin irritation and some necrosis at the exposure sites. The investigators noted that the necrosis was severe when the chemical was applied under occlusive and under semi-occlusive conditions [Derlanko et al. 1987]. In a study by von Oettingen and Deichmann-Gruebler [1936], skin irritation was reported in rats following repeated topical application of 1% phenylhydrazine ointment in Vaseline. The structure activity relationship model, Deductive Estimation of Risk from Existing Knowledge (*DEREK*), predicted phenylhydrazine to be negative for skin irritation.

Overall, animal data provide sufficient evidence of dermal exposures to phenylhydrazine causing localized effects at the site of contact. Although Derlanko et al. [1987] noted necrosis under occlusive and semi-occlusive conditions, no other data pertaining to the corrosivity of phenylhydrazine were identified. A weight of evidence analysis indicates that sufficient data exist from animal studies **[von Oettingen and Deichmann-Gruebler 1936; Dow Chemical Company 1940; Roudabush et al. 1965; Derelanko et al. 1987]** to conclude that phenylhydrazine is a moderate skin irritant, however, there is insufficient data are available to classify the substance as a corrosive agent. Therefore, on the basis of the data for this assessment, phenylhydrazine is assigned the SK: DIR (IRR) notation.

4 Immune-mediated Responses (SK: SEN)

The allergenic potential of phenylhydrazine has been demonstrated in humans and animals. Downing [1937] reported dermatitis in a case report resulting from dermal exposure to phenylhydrazine compounds. Patch-testing with the dry powder moistened with water produced positive skin reactions in the patient, indicating skin sensitivity to phenylhydrazine [Downing 1937]. Wright and Joyner [1930] reported a case of skin hypersensitivity following occupational exposures to phenylhydrazine, phenylhydrazine salts, or a mixture of phenylhydrazine hydrochloride and sodium acetate; however following a series of patch tests with potential compounds, this patient was found to be hypersensitive to phenylhydrazine hydrochloride, but not pure phenylhydrazine. Frost and Hjorth [1959] reported cross-reactivity between phenylhydrazine and hydrazine salts when a patient was patch-tested with aqueous solutions of phenylhydrazine (0.2%). The chemical is also a skin sensitizer in animals. Solutions of phenylhydrazine as low as 1% were found to be sensitizing to guinea pigs [Eastman Kodak Company 1957; Stevens 1967]. Predictions using structure activity relationship models provide some information regarding this endpoint. *DEREK* predicted phenylhydrazine to be a plausible skin sensitizer.

Limited number of case reports **[Downing 1937; Frost and Hjorth 1959]** and predictive tests in guinea pigs **[Eastman Kodak Company 1957; Stevens 1967]** demonstrate that phenylhydrazine has the potential to be a skin sensitizer. Therefore, on the basis of the data for this assessment, phenylhydrazine is assigned the SK: SEN notation.

5 Summary

Although no toxicokinetic studies that estimated dermal absorption of phenylhydrazine were identified, predictions of a mathematical algorithm suggest that the chemical has the potential to be absorbed through the skin following dermal exposure. No acute dermal toxicity studies that estimated the dermal LD_{50} in animals were identified, but approximate dermal lethal doses of 90 mg/kg and greater were reported **[DuPont Company 1963; Derelanko et al. 1987]**. Phenylhydrazine has the potential to cause hemolytic effects in both animals **[Derelanko et al. 1987]** and humans **[Rukl 1953]** following acute or repeated dermal exposure. Other potential

Table 3. Summary of previous skin hazard designations for phenylhydrazine

Organization	Skin hazard designation
NIOSH [2005]	[skin]: Potential for dermal absorption
OSHA [2014]*	[skin]: Based on the potential contribution to overall exposure by the cutaneous route
ACGIH [2001]	[skin]: Based on observed significant reduction in body weight of rodents following topical application of phenylhydrazine
EC [2014]*	R24 - Toxic in contact with skin
	R38 - Irritating to 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.

systemic effects following repeated dermal exposure include effects on liver, kidney and spleen [**Dow Chemical Company 1940**]. Based on the information identified from skin irritation studies conducted in animals **[von Oettingen and Deichmann-Gruebler 1936; Dow Chemical Company 1940; Roudabush et al. 1965; Derelanko et al. 1987]**, there is sufficient evidence to conclude that phenylhydrazine is a skin irritant. There is limited information from case reports [**Downing 1937; Frost and Hjorth 1959]** and predictive tests in guinea pigs **[Eastman Kodak Company 1957; Stevens 1967]** that indicate that the chemical is a skin sensitizer. Therefore, on the basis of these assessments, phenylhydrazine is assigned a composite skin notation of **SK: SYS-DIR (IRR)-SEN**.

Table 3 summarizes the skin hazard designations for phenylhydrazine previously issued by NIOSH and other organizations. The equivalent dermal designations for phenylhydrazine, according to the Global Harmonization System (GHS) of Classification and Labeling of Chemicals, are Acute Toxicity Category 3 (Hazard statement: Toxic in contact with skin), Skin Irritation Category 2 (Hazard statement: Causes skin irritation) and Skin Sensitization Category 1 (Hazard statement: May cause an allergic skin reaction) [European Parliament 2008]. In addition, phenylhydrazine has been classified as a Mutagenicity Category 2 (Hazard Statement: Suspected of causing genetic defects) [European Parliament 2008].

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Appendix: Calculation of the SI Ratio for Phenylhydrazine

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

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

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

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

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

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 phenylhydrazine. The calculated SI ratio was 304.6. On the basis of these results, phenylhydrazine is 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 phenylhydrazine

Variables used in calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path(k_{psc})	cm/hr	3.792×10^{-3}
Permeation coefficient of the protein fraction of the stratum corneum (k_{pol})	cm/hr	1.1461×10^{-5}
Permeation coefficient of the watery epidermal layer (k_{aq})	cm/hr	0.2404
Molecular weight (MW)*	amu	108.14
Base-10 logarithm of its octanol–water partition coefficient (Log K_{ow})*	None	1.25
Calculated skin permeation coefficient (k_p)	cm/hr	3.7472×10^{-3}
Skin dose		
Water solubility (S_w)*	mg/cm^3	127
Calculated skin permeation coefficient (k_p)	cm/hr	3.7472×10^{-3}
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hr	8
Calculated skin dose	mg	1370.57
Inhalation dose		
Occupational exposure limit (OEL)†	mg/m^3	0.6
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	4.5
Skin dose–to–inhalation dose (SI) ratio	None	304.6

*Variables identified from SRC [2009].

†The OEL used in calculation of the SI ratio for phenylhydrazine was the NIOSH recommended exposure limit (REL) [NIOSH 2005].

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