NIOSH Skin Notation Profiles

Dinitrobenzene (DNB)
m-Dinitrobenzene (m-DNB)
o-Dinitrobenzene (o-DNB)
p-Dinitrobenzene (p-DNB)

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) Profile

Dinitrobenzene (DNB)
[CAS No. 25154–54–5]

m-Dinitrobenzene (m-DNB)
[CAS No. 99–65–0]

o-Dinitrobenzene (o-DNB)
[CAS No. 528–29–0]

p-Dinitrobenzene (p-DNB)
[CAS No. 100–25–4]

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 a substance's hazard potential, 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 assignment and supportive data for dinitrobenzene (DNB) and its isomers. In particular, this document evaluates and summarizes the literature describing the substance's hazard potential 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 chemical of interest.

John Howard, M.D.
Director, National Institute for Occupational
Safety and Health
Centers for Disease Control and Prevention

Contents

Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
CIB	Current Intelligence Bulletin
cm^2	square centimeter(s)
cm/hr	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
DNB	dinitrobenzene
EC	European Commission
GHS	Globally Harmonized System of Classification and Labeling of Chemicals
IARC	International Agency for Research on Cancer
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
log K_{OW}	base-10 logarithm of a substance's octanol–water partition
m^3	cubic meter(s)
m-DNB	m-dinitrobenzene
MET	minimum elicitation threshold
metHb	methemoglobin
mg	milligram(s)
MW	molecular weight
NIOSH	National Institute for Occupational Safety and Health
NTP	National Toxicology Program
o-DNB	*o*-dinitrobenzene
OE	occupational exposure limit
OSHA	Occupational Safety and Health Administration
p-DNB	*p*-dinitrobenzene
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
w/w	weight by weight

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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Jennifer Sahmel, M.Sc., CIH, ChemRisk, Boulder, Colorado

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1 Introduction

1.1 General Substance Information

Chemical: Dinitrobenzene (DNB); m-dinitrobenzene (m-DNB); o-dinitrobenzene (o-DNB); p-dinitrobenzene (p-DNB)

CAS No: 25154–54–5; 99–65–0; 528–29–0; 100–25–4

Molecular weight (*MW*): 168.11

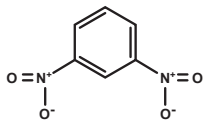
Molecular formula: $C_6H_4N_2O_4$

Structural formula:

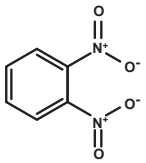
Synonyms: DNB; meta-Dinitrobenzene; 1,3-Dinitrobenzene; ortho-Dinitrobenzene; 1,2-Dinitrobenzene; para-Dinitrobenzene; 1,4-Dinitrobenzene

Uses:

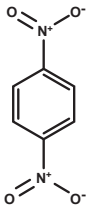
Dinitrobenzene (DNB) is primarily manufactured as a mixture of all isomers and is used in the manufacturing of dyes, explosives, and organic syntheses [ACGIH 2001].



m-DNB
[CAS No. 99–65–0]



o-DNB
[CAS No. 528–29–0]



p-DNB
[CAS No. 100–25–4]

1.2 Purpose

This Skin Notation Profile presents (1) a brief summary of technical data associated with skin contact with DNB* and (2) the rationale behind the hazard-specific skin notation (SK) assignment for DNB. 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 DNB. A literature search was conducted through July 2010 to identify information on DNB, 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),

*The exposure guidelines and SK assignment stated in this document apply to all isomeric forms of DNB, including *m*-, *o*-, and *p*-DNB. Unless otherwise specified, the abbreviation DNB is used to represent all three substances.

Table 1. Summary of the SK assignments for DNB

Skin notation	Critical effect	Available data
SK: SYS	Methemoglobinemia	Limited human data

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 DNB.

1.3 Overview of SK Assignment for DNB

DNB is potentially capable of causing adverse systemic effects following skin contact. A critical review of available data has resulted in the following SK assignment for DNB: **SK: SYS**. Table 1 provides an overview of the critical effects and data used to develop the SK assignment for DNB.

2 Systemic Toxicity from Skin Exposure (SK: SYS)

No in vivo or in vitro toxicokinetic studies that evaluated the potential of DNB to be absorbed through human or animal skin were identified. Ishihara et al. [1976] reported a case of *m*-DNB intoxication involving a woman exposed to an aqueous mixture containing 0.5% (weight by weight; w/w) *m*-DNB while handling parts immersed in the aqueous mixture. After ruling out the possibility of exposure via the inhalation of vaporized *m*-DNB, Ishihara et al. [1976] concluded that the main route of exposure was dermal absorption, despite the use of personal protective equipment in the form of latex gloves. Additional evidence of the ability of DNB to be dermally absorbed was identified in an investigation of the onset of five cases of methemoglobinemia in workers employed as steam-press operators in a rubber plant [NIOSH 1987]. The workers applied an adhesive to bond metal studs into rubber bumper strips, without wearing gloves. Bulk analysis revealed that the adhesive was contaminated with *p*-DNB (1% w/w). The report indicated that the main route of entry for *p*-DNB was skin absorption. The workers experienced yellowing of the hands, cyanosis of the lips and nail beds, headache, dizziness, nausea, chest pain, confusion, and difficulty in concentration [NIOSH 1987].

The potential of DNB to pose a skin absorption hazard was evaluated with use of a predictive algorithm for estimating and evaluating the health hazards of dermal exposure to chemical substances [NIOSH 2009]. The evaluation method compares an estimated chemical 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 0.12 was calculated for DNB. An SI ratio of ≥0.1 indicates that a chemical is capable of producing systemic toxicity from skin exposure [NIOSH 2009]. Additional information on the SI ratio and the variables used in its calculation are included in the appendix.

No dermal lethal concentration (LD_{Lo}) for humans has been identified for DNB. In addition, no dermal LD_{50} value (the dose resulting in 50% mortality in the exposed

population) for animals has been reported. No additional acute toxicity was identified for DNB. The lack of sufficient data precludes adequate evaluation of the potential of DNB to elicit acute toxicity following dermal exposure.

No epidemiological studies or occupational case reports were identified in the literature search. In addition, no repeat-dose, subchronic, or chronic toxicity studies involving animals following dermal exposure to DNB were identified. No reports were found on standard toxicity or specialty studies evaluating biological system/function–specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure to DNB.

The three isomeric forms of DNB and/or their metabolites are considered potent cyanogenic agents in all routes of entry [Linch 1974]. Evidence of a link between dermal exposures to DNB and the formation of methemoglobin (metHb) and the onset of metHb-induced cyanosis (e.g., methemoglobinemia) is limited. Ishihara et al. [1976] described a case of *m*-DNB intoxication in a female worker exposed to an aqueous solution containing 0.5 % w/w *m*-DNB. The woman was employed as a production line worker within a factory manufacturing electronic parts. As part of her job duties, the worker handled parts immersed in the aqueous mixture containing *m*-DNB, while wearing "protective" latex gloves. Within three days of the introduction of the aqueous mixture containing *m*-DNB to the production line, the female worker presented with cyanotic lips and finger nails, in addition to pale skin [Ishihara et al. 1976]. The worker was hospitalized because of a relapse and reemergence of her symptoms following a one-day rest period at home. The clinical diagnosis was hemolytic jaundice associated with exposure to an industrial chemical. The authors concluded that the absence of *m*-DNB in the ambient air and the results of a simulation study conducted as part of this investigation indicated that the worker was dermally exposed to *m*-DNB, potentially resulting in the onset of methemoglobinemia [Ishihara 1976].

Although no epidemiological, repeat-dose, or subchronic or chronic toxicity studies have evaluated the potential of DNB isomers to cause systemic effects in animals following dermal exposure, NIOSH [1987] investigated five cases of methemoglobinemia in workers employed at a rubber plant. The workers were identified as steam-press operators who presented with multiple symptoms, including cyanosis of the lips and nail beds, yellowing of the hands, dizziness, confusion, difficulty concentrating, and chest pains following exposure to a solvent-based adhesive used to bond metal studs to rubber bumper strips [NIOSH 1987]. One worker suffered a seizure. The steam-press operators had handled the adhesive without the use of gloves prior to the onset of the described symptoms. Medical screening of the affected workers revealed blood metHb levels ranging from 3.8% to 41.2% (normal level, <1%) [NIOSH 1987]. Prior to the NIOSH study, a plant supervisor operated the steam-press using the adhesive-coated studs for about 2 hours, as part of a simulation study conducted by the Ohio Industrial Commission. The plant supervisor's blood metHb level after the simulation was 12.5%. The NIOSH investigation revealed that bulk samples of the adhesive were contaminated with *p*-DNB (1% w/w) [NIOSH 1987]. On the basis of the results of the investigation, the manufacturers immediately replaced the *p*-DNB-contaminated adhesive. No

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

Organization	Carcinogenic designation
NIOSH [2005]	None
NTP [2009]	None
USEPA [2009]	Group D: Not classifiable as to human carcinogenicity
IARC [2009]	None
EC [2010]	None
ACGIH [2001]	None

Abbreviation: 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.

*Note: The listed cancer designations were based on data from nondermal (such as oral or inhalation) exposure rather than dermal exposure.

reoccurrence of methemoglobinemia was observed at the rubber plant in a follow-up survey. NIOSH concluded that dermal exposures to *p*-DNB-contaminated adhesive resulted in the formation of metHb and the cyanotic symptoms in the affected workers [NIOSH 1987].

The literature search revealed no standard toxicity or specialty studies evaluating biological system/function–specific effects (including reproductive effects and immunotoxicity) in humans following dermal exposure to DNB isomers. No studies have evaluated the carcinogenic potential of DNB following dermal exposure. Table 2 provides a summary of carcinogenic designations from multiple governmental and nongovernmental organizations for DNB.

Despite the absence of data for *o*-DNB, all isomers are assumed to have similar toxic potency, on the basis of their similar physiochemical properties. For example, the log K_{OW} for the *m*-, *o*-, and *p*-DNB are 1.49, 1.69, and 1.46, respectively [HSDB 2010]. There are few data from acute or repeat-dose toxicity studies upon which the potential for systemic effects following dermal exposure to DNB can be evaluated. Available human data are associated with *m*- and *p*-DNB. These chemicals are readily absorbed through the skin and may substantially contribute to systemic toxicity through the formation of metHb **[Ishihara 1976; NIOSH 1987†]**. Mathematical evaluation of the potential of the substance to pose a skin hazard (according to the NIOSH [2009] methodology based on the *m*-isomer) indicated that DNB has the potential to be absorbed through the skin, be systemically available, and cause methemoglobinemia. Therefore, on the basis of the data for this assessment, DNB is assigned the SK: SYS notation.

3 Direct Effect(s) on the Skin (SK: DIR)

No data on the skin corrosivity of DNB were identified from in vivo tests in humans or animals or from in vitro tests with human or animal skin models or cadaver skin (for skin integrity). Additionally, no

†References in **bold** text indicate studies that served as the basis of the SK assignment.

studies evaluating the skin-irritating potential of the substance in humans or animals were identified. Exposure to a *p*-DNB-contaminated adhesive was reported to cause yellow discoloration of the hands of five workers employed at a rubber plant [NIOSH 1987]. No additional information was provided. The structure-activity relationship model, Deductive Estimation of Risk from Existing Knowledge (DEREK™) for Windows, predicted the substance to be negative for skin irritation. The findings of this assessment show that the data are insufficient to assign the SK: DIR notation to DNB.

4 Immune-mediated Responses (SK: SEN)

No occupational exposure studies that investigated the skin-sensitization potential of DNB were identified. No human patch tests or predictive tests (guinea pig maximization tests, Buehler tests, murine local lymph node assays) or any other studies that evaluated the potential of the substance to cause skin sensitization were identified. DNB is predicted by DEREK™ to be negative for sensitization. This assessment shows that the data are insufficient to assign the SK: SEN notation to DNB.

5 Summary

Limited data were identified for assessing the potential of all isomers of DNB to be absorbed through the skin or to cause systemic toxicity following dermal exposure. On the basis of the similar physical and chemical properties of the isomeric forms of DNB, it is assumed that all three compounds exhibit similar toxic potency. The limited available human data indicate that DNB is readily absorbed through the skin and may result in methemoglobinemia **[Ishihara 1976; NIOSH 1987].** Additional evidence supporting the potential for DNB to pose a skin-absorption hazard is provided by a mathematical evaluation based on data for the *m*-isomer. No studies were identified that investigated the potential of the substance to cause skin irritation or to be corrosive to the skin of humans or animals. A structure-activity-relationship model predicted the substance to be negative for skin irritation and skin sensitization. No studies were identified that evaluated the skin-sensitization potential of the substance. Therefore, on the basis of these assessments, DNB is assigned a composite skin notation of **SK: SYS**.

Table 3 summarizes the skin hazard designations for DNB previously issued by NIOSH and other organizations. The equivalent dermal designation for DNB, according to the Globally Harmonized System (GHS) of Classification and Labeling of Chemicals, is Acute Toxicity Category 1 (Hazard statement: Fatal in contact with the skin).

References

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

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*EC (European Commission) [2009]. Dinitrobenzene. In: EINICS (European Inventory of Existing Commercial Chemical Substances) [http://ecb.jrc.ec.europa.eu/esis/]. Accessed 07–07–10.

*European Parliament, Council of the European Union [2008]. Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification,

Table 3. Summary of the previously issued skin hazard designations for DNB

Organization	Skin hazard designation
NIOSH [2005]	[skin]: Potential for dermal absorption
OSHA [2000]	[skin]: Based on potential contribution to the overall exposure by the cutaneous route, including the mucous membranes and the eyes, either by airborne particles or, more particularly, by direct contact with the substance
ACGIH [2001]	[skin]: Based on data demonstrating toxicity following absorption through intact skin of humans and animals
EC [EC 2010]	R27: Very toxic in contact with skin

Abbreviations: 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 for DNB

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for the dinitrobenzene isomers. 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 the 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.
3. 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 cm^2).

Equation 2: Determination of Skin Dose

$$\text{Skin dose} = K_p \times S_W \times \text{Exposed skin surface area} \times \text{Exposure time}$$

$$= K_p(\text{cm/hr}) \times S_W\ (\text{mg/cm}^3) \times 360\ \text{cm}^2 \times 8\ \text{hr}$$

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 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 DNB. The calculated SI ratio was 0.12. On the basis of these results, DNB 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 DNB

Variables used in calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path(K_{psc})	cm/hr	0.00245
Permeation coefficient of the protein fraction of the stratum corneum (K_{pol})	cm/hr	1.17155×10^{-5}
Permeation coefficient of the watery epidermal layer (K_{aq})	cm/hr	0.19282
Molecular weight (MW)*	amu	168.11
Base-10 logarithm of its octanol–water partition coefficient (Log K_{OW})*	None	1.69
Calculated skin permeation coefficient (K_p)	cm/hr	0.00243
Skin dose		
Water solubility (S_w)*	mg/cm^3	0.13
Calculated skin permeation coefficient (K_p)	cm/hr	0.00243
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hr	8
Calculated skin dose	mg	0.93
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	0.12

*Variables identified from SRC [2009].
†The OEL used in calculation of the SI ratio was the NIOSH-recommended exposure limit (REL) [NIOSH 2005].

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