NIOSH Skin Notation Profiles

Dinitrotoluene; 2,4-Dinitrotoluene (2,4-DNT)
2,6-Dinitrotoluene (2,6-DNT)

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

Dinitrotoluene
[CAS No. 25321–14–6]

2,4-Dinitrotoluene (2,4-DNT)
[CAS No. 121–14–2]

2,6-Dinitrotoluene (2,6-DNT)
[CAS No. 606–20–2]

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

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Foreword

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

In 2009, the National Institute for Occupational Safety and Health (NIOSH) published *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009-147]. This document provides the scientific rationale and framework for the assignment of multiple hazard-specific skin notations (SK) that clearly distinguish between the systemic effects, direct (localized) effects, and immune-mediated responses caused by skin contact with chemicals. The key step within assignment of the hazard-specific SK is the determination of 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 dinitrotoluene (DNT) 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.

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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
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
DNT	dinitrotoluene
2,4-DNT	2,4-dinitrotoluene
2,6-DNT	2,6-dinitrotoluene
EC	European Commission
GHS	Globally Harmonized System for Classification and Labeling of Chemicals
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
log K_{OW}	base-10 logarithm of a substance's octanol–water partition coefficient
m^3	cubic meter(s)
mg	milligram(s)
mg/kg	milligram(s) per kilogram body weight
mg/m^3	milligram(s) per cubic meter
MW	molecular weight
NIOSH	National Institute for Occupational Safety and Health
NTP	National Toxicology Program
OEL	occupational exposure limit
OSHA	Occupational Safety and Health Administration
REL	recommended exposure limit
RF	retention factor
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
µg/cm^2	microgram(s) per square centimeter

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

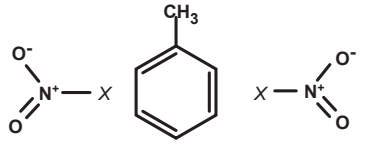
Chemical: Dinitrotoluene (DNT); 2,4-Dinitrotoluene (2,4-DNT); 2,6-Dinitrotoluene (2,6-DNT)

CAS No: 25321–14–6; 121–14–2; 606–20–2

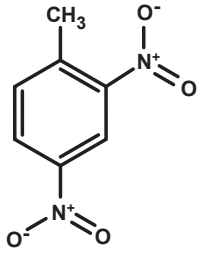
Molecular weight (MW): 182.14

Molecular formula: $C_7H_6N_2O_4$

Structural formula:



DNT
(CAS No. 25321–14–6)



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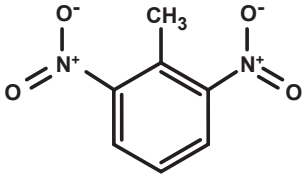

2,6-DNT
(CAS No. 606–20–2)

Synonyms:

DNT; Dinitrotoluol; Dinitrophenylmethane; Methyldinitrobenzene; Various isomers of DNT [2,4-DNT; 2,6-DNT]; Technical (commercial) grade DNT; TNDT

Use:

Technical (commercial) grade dinitrotoluene (DNT) is composed of approximately 76% 2,4-dinitrotoluene (2,4-DNT), 19% 2,6-dinitrotoluene (2,6-DNT), and 5% of the other four dinitrotoluene isomers; DNT is used primarily as a chemical intermediate in the production of organic compounds, such as toluene diisocyanate [ATSDR 1998]. Secondary applications include its use as a gelatinizing-plasticizing agent in both commercial and military explosive compositions and as a chemical intermediate in the production of rubber chemicals [ECB 2008].

1.2 Purpose

This *Skin Notation Profile* presents (1) brief summary of technical data associated with skin contact with DNT* and (2) the rationale behind the hazard-specific skin notation (SK) assignment for DNT. 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 DNT. A literature search was conducted through July 2010 to identify information on DNT, including but not limited to data relating to its toxicokinetics, acute toxicity,

*The exposure guidelines and SK assignment stated in this document apply to DNT, 2,4-DNT, and 2,6-DNT. Unless otherwise specified, the abbreviation DNT is used to represent all three substances.

Table 1. Summary of the SK assignment for DNT

Skin notation	Critical effect	Data available
SK: SYS	Gastrointestinal;, hematological (i.e., methemoglobinemia leading to cyanosis); neurological; hepatological	Limited human data; limited animal data
SK: DIR (IRR)	Skin irritation	Limited animal data

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 DNT.

1.3 Overview of SK Assignment for DNT

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

2 Systemic Toxicity from Skin Exposure (SK: SYS)

Woollen et al. [1985] provided evidence of significant dermal absorption of DNT within loaders and operators employed at a DNT manufacturing plant. The authors reported levels of urinary metabolites of 2,4- and 2,6-DNT in DNT-exposed workers at levels that exceeded those that would have resulted from inhaled concentrations, indicating dermal absorption of the substances. The results of their study provide evidence that within occupational settings, skin contact with DNT may be the most important exposure pathway, resulting in absorption of significant quantities of the substance. Eastman Kodak [1974] reported fatigue, nausea, vomiting, loss of weight, and methemoglobinemia leading to cyanosis following dermal contact, indicating the substance is absorbed by the skin. An in vitro study involved application of radiolabelled 2,4-DNT and 2,6-DNT solutions in acetone to excised pig skin to investigate the dermal absorption of the substance [Reifenrath et al. 2002]. The authors reported that 36% and 24% of the applied dose of the 2,4-DNT and 2,6-DNT were absorbed, respectively. Additionally, the results indicate that the substances were rapidly and extensively absorbed by viable excised pig skin. In a second study, Reinfenrath et al. [2008] determined the influence of skin surface moisture conditions on in vitro percutaneous penetration of 14C-labeled munitions including 2,6-DNT. Artificial sweat was applied to excised pig skin prior to dosing within an estimated 10 microgram per square centimeter (μg/cm^2) of radiolabeled 2,6-DNT within contaminated soil. The highest mean percentage of dermal penetration of 2,6-DNT was 17.5, which approached the value previously reported for acetone vehicle in the 2002 study (24%) [Reinfenrath et al. 2002, 2008].

The potential of DNT 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 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, an SI (skin dose to inhalation dose) ratio of 1.12 was calculated for DNT. 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.

A limited number of reviews have evaluated the systemic toxicity of DNT following dermal exposure. No dermal lethal concentration (LD_{Lo}) for humans has been identified. Following a study of guinea pigs, a dermal LD_{50} value (the dose resulting in 50% mortality in the exposed population) of greater than 1000 milligrams per kilogram body weight (mg/kg) was reported [Eastman Kodak Co. 1974]. Because the reported LD_{50} is below the critical LD_{50} value of 2000 mg/kg that identifies substances with potential for acute dermal toxicity [NIOSH 2009], DNT is considered systemically available and acutely toxic.

Studies investigating occupational exposures to DNT were identified [Perkins 1919; McGee et al. 1942, 1947; Woollen et al. 1985]. Despite the fact that DNT exposure occurred via both the dermal and inhalation routes, Woollen et al. [1985] identified skin contact with DNT and its subsequent absorption as the primary exposure pathway. McGee et al. [1942] reported hematological (anemia and cyanosis), gastrointestinal (vomiting and nausea), neurological (headache, pain/numbness in the extremities), and hepatological effects in munitions workers. In a follow-up study of male munitions workers exposed to unspecified concentrations of 2,4-DNT, 29 of 714 workers had tenderness of the liver [McGee et al. 1947]. Levine et al. [1985] investigated workers' exposures to technical-grade DNT at a DNT manufacturing plant. Biological, environmental, and surface samples were collected to assess workers exposures. This included the collection of urine over a 72 hour period, personal (breathing zone) air samples, in addition to skin and environmental wipe samples. An excess of urinary DNT metabolites within certain workers (i.e., loaders and operators) when compared to measured airborne concentrations was reported. The authors theorized that the workers were exposed to DNT via routes of exposure beyond inhalation, including dermal uptake, which may have significantly contributed to the total body burden of DNT [Levine et al. 1985]. The results of the wipe samples provided evidence of DNT on both the skin and workplace surfaces. Despite occurring through multiple exposure pathways, the reviewed studies indicate that DNT may be absorbed by the skin and contribute to systemic effects.

No data regarding dermal repeat-dose, subchronic or chronic toxicity of DNT or technical-grade dinitrotoluene in animals were identified. No standard toxicity or specialty studies evaluating biological system/function–specific effects of DNT (including reproductive and developmental effects and immunotoxicity) following dermal exposures were identified. No epidemiological investigations or experimental animal studies evaluating the carcinogenic potential of skin exposures to DNT were identified. Table 2 provides a summary of

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

Organization	Carcinogenic designation
NIOSH [1985]	Potential occupational carcinogen
NTP [2009]	No designation for DNT, 2,4-DNT, or 2,6-DNT
USEPA	No designation
IARC [1997]†	Group 2B: Possibly carcinogenic to humans
EC [2010]	R45: May cause cancer
ACGIH [2001]	Group A3: Confirmed animal carcinogen with unknown relevance to humans

Abbreviations: 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.

†IARC cancer designation applicable to 2,4-DNT and 2,6-DNT.

carcinogenic designations from multiple governmental and nongovernmental organizations for DNT.

Woollen et al. [1985]† provided evidence of the importance of dermal absorption within workers. The reviewed occupational exposure studies indicated that workers exposed to DNT via the inhalation and dermal routes may be at increased risk of numerous systemic effects, including gastrointestinal, hematological (i.e., anemia and cyanosis), neurological, and hepatological effects **[Perkins 1919; McGee 1942, 1947]**. The limited data on in vitro dermal absorption **[Reinfenrath et al. 2002, 2008]** and acute dermal toxicity **[Eastman Kodak Co. 1974]** indicate that DNT can become systemically available and toxic following dermal exposure. Therefore, on the basis of the data for this assessment, DNT is assigned the SK: SYS notation.

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

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

No in vitro tests for corrosivity of DNT in human or animal skin models or in vitro tests of skin integrity with use of cadavers were identified. Corrosivity data are limited to those from a single study, in which six albino rabbits were administered 500 milligrams (mg) of technical-grade 2,4-DNT for 4 hours under occlusion. No evidence of corrosivity was observed [E.I. DuPont de Nemours and Company 1973]. Vernot et al. [1977] compiled a list of agents possibly skin-corrosive in rabbits, but the authors did not list DNT among them. McGee et al. [1942] reported the occurrence of contact dermatitis in 6 of 154 munitions workers exposed topically to dinitrotoluene, and they attributed these effects to dermal exposure to 2,4-DNT. In a follow-up study of male munitions workers exposed to unspecified concentrations of 2,4-DNT, 32 of 714 workers had dermatitis [McGee et al. 1947]. Lee et al. [1975, 1978] indicated that 2,4-DNT and other isomers caused a slight

primary dermal irritation in rabbits. The structure activity relationship model, Deductive Estimation of Risk from Existing Knowledge (DEREK™) for Windows, did not predict DNT as a skin irritant. Although DNT produced inconsistent results in animals, it appears from case reports **[McGee et al. 1942; 1947]** and reports of positive results in rabbits **[Lee et al. 1975, 1978]** that DNT is a weak skin irritant. Therefore, on the basis of the data for this assessment, DNT is assigned the SK: DIR (IRR) notation.

4 Immune-mediated Responses (SK: SEN)

The available data regarding DNT's ability to act as a sensitizing agent or elicit an immune-mediated response are limited and conflicting. In humans, a single case study describes dermatological lesions in a rockblaster exposed to powder from dynamite operations for 10 years [Emtestam and Forsbeck 1985]. Photopatch testing was conducted. The authors interpreted the patch testing as a positive photosensitization reaction and diagnosed the rockblaster with photocontact allergy to DNT. In animals, Lee et al. [1975, 1978] investigated the sensitization potential of 2,4-DNT and 2,6-DNT using standard protocols. The authors reported negative results in guinea pig maximization tests with 2,4-DNT [Lee et al. 1975, 1978], and only mild sensitization in tests with 2,6-DNT [Lee et al. 1975]. DEREK™ did not predict DNT to be a skin sensitizer.

Overall, a single case study provided limited evidence of DNT's ability to act as a sensitizing agent or elicit an immune-mediated response. No additional human studies were identified. The results of animal tests using standard protocols, in addition to a predictive model, indicate that DNT is not a sensitizer. These findings are supported by the absence of additional reports of immune-mediated responses within exposed workers. For this reason, DNT is not identified as a skin sensitizer. Therefore, on the basis of the data for this assessment, DNT is not assigned the SK: SEN notation.

5 Summary

Limited data are available on the systemic uptake and effect of DNT in humans and animals after skin contact. Studies of workers exposed to DNT via the inhalation and dermal routes suggested an increased risk of numerous systemic effects, including hematological (i.e., methemoglobinemia, anemia and cyanosis), gastrointestinal, neurological, and hepatological effects [Perkins 1919; McGee et al. 1942, 1947]. Woollen et al. [1985] stated that skin contact and subsequent absorption of DNT was the primary exposure route. In vitro toxicokinetic data **[Reifenrath et al. 2002, 2008]** and acute dermal toxicity data **[Eastman Kodak Co. 1974]** support these findings and suggest that DNT is rapidly absorbed following dermal exposure. When these findings are coupled with those of occupational studies, it appears that DNT is readily absorbed by the skin, contributing to systemic effects and toxicity. Studies evaluating the potential for DNT to cause skin irritation have yielded inconsistent results with regard to animals; however, reports of cases in humans **[McGee et al. 1942, 1947]** and positive results in rabbits **[Lee et al. 1975, 1978]** are sufficient to demonstrate that DNT produces a mild skin irritation. Standard tests in animals showed DNT to have no sensitizing potential in animals with evidence of its effect in humans limited to a single case report. Therefore, on the basis of these

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

Organization	Skin hazard designation
NIOSH [2005]	[skin]: Potential for dermal absorption
OSHA [2009]	[skin]: Potential for dermal absorption
ACGIH [2001]	[skin] (Technical grade DNT): Based on a workplace study that indicated dermal contact may be the major route of absorption within occupational settings
EC [2010]	R24: 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.

assessments, DNT is assigned a composite skin notation of **SK: SYS-DIR (IRR)**.

Table 3 summarizes the skin hazard designations for DNT previously issued by NIOSH and other organizations. The equivalent Globally Harmonized System (GHS) for Classification and Labeling of Chemicals dermal designation for DNT is Acute Toxicity Category 3 (Hazard statement: Toxic in contact with the skin) [European Parliament 2008]. DNT has been identified as a Category 2 Mutagen (Hazard statement: Suspected of causing genetic defects), a Category 1B Carcinogen (Hazard statement: May cause cancer) and a Category 2 Reproductive toxicant (Hazard statement: Suspected of damaging fertility or the unborn child) [European Parliament 2008].

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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 DNT

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

Overview

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

1. Provide an alternative method to evaluate substances for which no clinical reports or animal toxicity studies exist or for which empirical data are insufficient to determine systemic effects.

2. Use the algorithm evaluation results to determine whether a substance poses a skin absorption hazard and should be labeled with the SYS notation.

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

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

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

Equation 1: Calculation of skin permeation coefficient (K_p)

$$K_p + \frac{1}{\frac{1}{K_{psc} + K_{pol}} + \frac{1}{K_{aq}}}$$

Where K_{psc} is the permeation coefficient in the lipid fraction of the stratum corneum, K_{pol} is the coefficient in the protein fraction of the stratum corneum, and K_{aq} is the coefficient in the watery epidermal

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

Variables used in calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path (K_{psc})	cm/hr	0.00296
Permeation coefficient of the protein fraction of the stratum corneum (K_{pol})	cm/hr	1.12552×10^{-5}
Permeation coefficient of the watery epidermal layer (K_{aq})	cm/hr	0.18524
Molecular weight (MW)*	amu	182.14
Base-10 logarithm of its octanol–water partition coefficient (Log K_{OW})*	None	1.98
Calculated skin permeation coefficient (K_p)	cm/hr	0.00292
Skin dose		
Water solubility (S_W)*	mg/cm^3	0.2
Calculated skin permeation coefficient (K_p)	cm/hr	0.00292
Estimated skin surface area (palms of hand)	cm^2	360
Exposure time	hour	8
Calculated skin dose	mg	1.68
Inhalation Dose		
Occupational exposure limit (OEL)†	mg/m^3	0.2
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	1.5
Skin dose–to–inhalation dose (SI) ratio	None	1.12

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

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 $\times$ Exposure time

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

The inhalation dose (in mg) is derived on the basis of the occupational exposure limit (OEL) of the substance—if the OEL is developed to prevent the occurrence of systemic effects rather than sensory/irritant

effects or direct effects on the respiratory tract. Assume a continuous exposure of 8 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).

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

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

Equation 3: Determination of Inhalation Dose

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 DNT. The calculated SI ratio was 1.12. On the basis of these results, DNT is predicted to represent a skin absorption hazard.

Appendix References

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