NIOSH Skin Notation Profile

Atrazine

SK

ID[SK]

[~~SK~~]

SYS

SYS (FATAL)

DIR

DIR (IRR)

DIR (COR)

SEN

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NIOSH Skin Notation Profile

Atrazine

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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 (such as irritant contact dermatitis and corrosion) to induction of immune-mediated responses (such as allergic contact dermatitis and pulmonary responses), or systemic toxicity (such as neurotoxicity and hepatotoxicity). 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 (SKs) 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 (such as skin permeation) by means of analytical or numerical methods.

This *Skin Notation Profile* provides the SK assignments and supportive data for atrazine. 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 *s*kin contact with the chemicals of interest.

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Contents

Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
amu	atomic mass unit
ATSDR	Agency for Toxic Substances and Disease Registry
CIB	Current Intelligence Bulletin
cm^2	square centimeter(s)
cm/hr	centimeter(s) per hour
cm/s	centimeter(s) per second
COR	subnotation of SK: COR indicating the potential for a chemical to be a skin corrosive following exposure to the skin
***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
FATAL	subnotation of SK: SYS indicating the potential for the chemical to be fatal following dermal absorption
G	gram(s)
g/L	gram(s) per liter
GHS	Globally Harmonized System for Classification and Labelling of Chemicals
GPMT	guinea pig maximization test
hr	hour(s)
IARC	International Agency for Research on Cancer
$ID^{(SK)}$	skin notation indicating that a chemical has been evaluated, but insufficient data exist to accurately assess the hazards of skin exposure
IPCS	International Program for Chemical Safety
IRR	subnotation of SK: DIR indicating the potential for a chemical to be a skin irritant following exposure to the skin
k_{aq}	coefficient in the watery epidermal layer
k_p	skin permeation coefficient
k_{pol}	coefficient in the protein fraction of the stratum corneum
k_{psc}	permeation coefficient in the lipid fraction of the stratum corneum
LD_{50}	lethal dose resulting in 50% mortality in the exposed population
LD_{Lo}	lowest detected lethal dose
LLNA	local lymph node assay
LOAEL	lowest-observed-adverse-effect level
log K_{OW}	base-10 logarithm of a substance's octanol-water partition
M	molarity
m^3	cubic meter(s)
mg	milligram(s)
$mg/cm^2/hr$	milligram(s) per square centimeter per hour
mg/kg	milligram(s) per kilogram body weight

mg/m³	milligram(s) per cubic meter
mL	milliliter(s)
mL/kg	milliliter(s) per kilogram body weight
MW	molecular weight
mmol	millimole
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no-observed-adverse-effect level
NTP	National Toxicology Program
OEL	occupational exposure limit
OSHA	Occupational Safety and Health Administration
ppm	parts per million
REL	recommended exposure limit
RF	retention factor
SEN	skin notation indicating the potential for immune-mediated reactions following exposure of the skin
SI ratio	ratio of skin dose to inhalation dose
SK	skin notation
~~SK~~	skin notation indicating that the reviewed data did not identify a health risk associated with skin exposure
S_W	solubility in water
SYS	skin notation indicating the potential for systemic toxicity following exposure of the skin
US EPA	United States Environmental Protection Agency
uCi	micro curies
µg	microgram(s)
µg/cm²	microgram(s) per square centimeter
µg/cm²/hr	microgram(s) per square centimeter per hour
µL	microliter(s)
µmol	micromole(s)
w/v	weight/volume

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 occur 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

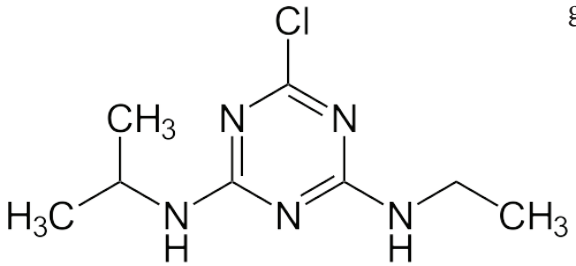
Chemical: Atrazine

CAS No: 1912-24-9

Molecular weight (MW): 215.7

Molecular formula: $C_8H_{14}ClN_5$

Structural formula:



Synonyms: 2-Chloro-4-ethyl-amino-6-isopropylamino-s-triazine; 6-Chloro-N-ethyl-N'-(1-methylethyl)-1,3,5-triazine-2,4-diamine

Uses: Atrazine is a herbicide; in 1997, an estimated 75 million pounds (34 million kilograms) of atrazine were used [ATSDR 2003].

1.2 Purpose

This skin notation profile presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with atrazine and (2) the rationale behind the hazard-specific skin notation (SK) assignment for atrazine. The SK assignment is based on the scientific rationale and logic outlined in the *Current Intelligence Bulletin 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 atrazine. A literature search was conducted through February 2018 to identify information on atrazine, 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 atrazine. The criteria for the search strategy, evaluation, and selection of data are described in Appendix E in *Current Intelligence Bulletin 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009].

1.3 Overview of SK Assignment

Atrazine may potentially be capable of causing adverse health effects following skin contact. A critical review has determined that the quantity and quality of the available data are insufficient to assign any of the skin notations so atrazine is assigned the SK notation **ID**$^{(SK)}$, indicating that atrazine has been evaluated, but insufficient data exist to accurately assess the hazards of skin exposure. Table 1 provides an overview of the critical effects and data used to develop the SK assignment for atrazine.

Table 1. Summary of the SK assignment for atrazine

Skin notation	Critical effect	Available data
ID$^{(SK)}$	—	—

2 Systemic Toxicity from Skin Exposure (SK: SYS)

Toxicokinetic studies following dermal exposure to atrazine were identified. Limited dermal absorption of atrazine has been reported in humans. Buchholz et al. [1999] measured unabsorbed radioactivity and radioactivity excreted in urine and feces over a 7-day period following application of 0.167 milligrams (mg) or 1.98 mg of [14C]-atrazine to 25 square centimeters (cm^2) of the forearms of 10 healthy male subjects for 24 hours [Buchholz et al. 1999]. These investigators reported dermal absorption of 0.3–5.1% (the percent excreted in urine and feces) of the applied dose [Buchholz et al. 1999]. In a study where atrazine exposure was evaluated in 6 workers by personal and biological monitoring, Catenacci et al. [1993] found that box cutter workers were exposed to atrazine primarily via dermal contact (4 of the 6 workers) and that 1–2% of the exposure dose of atrazine and its metabolites were detected in the urine of these workers, indicating that atrazine has limited absorption in humans following dermal absorption. Evidence of limited absorption following dermal exposure to atrazine has been provided by an animal study *in vivo* showing the presence of atrazine and its metabolites in the plasma, urine, and/or feces. In a skin penetration study conducted by Hall et al. [1988], approximately 7.7% of the applied dose (3.71 micro curies [µCi]/millimole (mmol) of 14C labeled atrazine in 100 and 200 µL of acetone for young and old rats, respectively) penetrated the clipped dorsal skin of young and adult rats. Hall et al. [1988] also reported decreasing absorption with increasing dose. Ademola et al. [1993] conducted an *in vitro* study with human skin samples exposed to [14C]-atrazine. These investigators reported that 2.1–6.2% of the dose permeated the skin and 7.3–16.4% was retained by the skin after the skin was dosed with atrazine for a 20-hour period. Brand and Mueller [2002] reported 4.47% to 8.67% was recovered when solutions of 1:10 and 1:40 of atrazine in methanol were applied to the skin of hairless mice for 24 hours.

The potential of atrazine to pose a skin absorption hazard was also evaluated, with the 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 0.01 was calculated for atrazine. An SI ratio of ≥0.1 indicates that skin absorption may significantly contribute to the overall body burden of a substance [NIOSH 2009]; therefore, atrazine is not considered to be a skin absorption hazard following dermal exposure. Additional information on the SI ratio and the variables used in its calculation are included in the appendix.

No dermal lethal doses (LD_{LO}) for humans have been identified. The reported dermal LD_{50} value in rats was greater than 2,500 mg/kg/day [Gaines and Linder 1986]. Because the reported acute dermal LD_{50} values for rats are higher 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], atrazine is not acutely toxic following dermal exposure.

No repeat-dose, subchronic, or chronic studies following dermal exposure to atrazine were identified in humans or animals.

No standard toxicity or specialty studies evaluating biological system/function specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure to atrazine were identified in animals. Epidemiological studies were identified that evaluated the reproductive toxicity of atrazine. In eligible households in the Ontario Farm Family Health Study, households with at least one member who worked on a farm, Arbuckle et al. [2001] found no increase in risk of spontaneous abortion following

preconception or postconception exposure to atrazine; however only 20% of women in the cohort reported handling pesticides and the type of exposure and if women were directly or indirectly exposed to atrazine and the exposure group is unknown [Arbuckle et al. 2001]. Using data from the same cohort, Curtis et al. [1999] reported that atrazine was not associated with any decrease in fecundity. However, an earlier study by Savitz et al. [1997] using the Ontario Farm Family Health Study, found that the use of atrazine as a yard herbicide, but not as a crop herbicide, was associated with an increase in preterm delivery. In this study male farm activities were observed in relation to miscarriage and preterm delivery [Savitz et al. 1997]. The inconsistencies in these data, and the uncertainty of exposure data (route of exposure and direct vs. indirect exposure) prevent adequate evaluation of the potential for atrazine to cause reproductive or developmental toxicity following dermal exposure.

Several case-control studies were located regarding cancer incidence and exposure of humans to atrazine [Burnmeister 1990; Cantor et al. 1992; Mills 1998]. Although these studies found correlation between atrazine use and some cancers (such as non-Hodgkin's lymphoma, leukemia, soft-tissue sarcoma, brain cancer, prostate cancer, and testicular cancer), lack of information on the exposure routes precludes estimation of the contribution of the dermal route. No standard rodent cancer bioassays following dermal exposure were identified. No agency or organization has classified atrazine as a carcinogen. Table 2 summarizes carcinogenic designations for atrazine by multiple governmental and nongovernmental organizations.

Taken together, information from human evidence, systemic toxicity studies, and toxicokinetic data are insufficient to demonstrate that atrazine is absorbed through the skin, systemically available, or toxic. Therefore, on the basis of the data for this assessment, atrazine is not assigned the SK: SYS notation.

3 Direct Effects on Skin (SK: DIR)

No human or animal *in vivo* studies on corrosivity of atrazine, *in vitro* tests for corrosivity using human or animal skin models, or *in vitro* tests of skin integrity using cadaver skin were identified. However, the limited data identified demonstrate that atrazine is not a skin irritant in humans. A case report exists of a farmer who was diagnosed with acute contact dermatitis (painful erythematous eruptions

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

Organization	Carcinogenic designation
NIOSH [2005]	No designation
NTP [2014]	No designation
US EPA [2014]	No designation
European Parliament [2008]	No GHS designation
IARC [2012]	Group 3: Not classifiable as to its carcinogenicity to humans
ACGIH [2014]	Group A3: Confirmed animal carcinogen with unknown relevance to humans

ACGIH = American Conference of Governmental Industrial Hygienists; 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; US EPA = 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.

with blistering and swelling) on his hands and forearms in the afternoon after applying atrazine to crops in the morning and cleaning the plugged nozzles of the spray rig several times with his bare hands earlier in the day [Schlicher and Beat 1972]. Because the farmer also applied a second pesticide in the afternoon of the same day, it was not possible to determine whether the dermatitis was caused by atrazine. Lisi et al. [1987] patch-tested 384 subjects (including agricultural, ex-agricultural, and non-agricultural workers) with a pesticide series of 36 substances, including 1% atrazine, which produced no skin irritation in any of the subjects patch-tested. No studies that evaluated the dermal irritation potential of atrazine in animals were available. The structure-activity relationship model, Deductive Estimation of Risk from Existing Knowledge (*DEREK™*) for Windows, predicted atrazine to be negative for skin irritation.

The available information upon which to base the potential of atrazine to cause skin irritation in humans is insufficient for adequate evaluation. Therefore, on the basis of the data for this assessment, atrazine is not assigned the SK: DIR (IRR) notation.

4 Immune-mediated Responses (SK: SEN)

There is insufficient information available to conclude that atrazine is a skin sensitizer on the basis of occupational exposure experience. Lisi et al. [1987] conducted human patch-testing on 384 subjects (including agricultural and ex-agricultural workers and others) with a pesticide series of 36 substances, including 1% atrazine. The authors reported no allergic reaction to atrazine in any of the subjects patch-tested. In other human patch tests, a 0.5% w/v suspension in water of an atrazine formulation did not cause skin sensitization on repeated application to 50 humans [Shelanski and Gittes 1965]. No studies that evaluated the potential for atrazine to cause skin sensitization were identified. The structure activity relationship model, *DEREK™* for Windows, predicted atrazine to be positive for skin sensitization.

Atrazine does not appear to be a skin sensitizer, on the basis of the limited number of studies in humans. Predictive tests (guinea pig maximization tests, Buehler tests, murine local lymph node assays, mouse ear swelling tests, etc.) in animals were not identified. Therefore, on the basis of the data for this assessment, atrazine is not assigned the SK: SEN notation.

5 Summary

The available data on both humans and animals indicate that atrazine is poorly absorbed through the skin. Although the acute dermal toxicity studies identified suggested that atrazine has low toxicity, the absence of reliable repeat-dose studies precludes adequate evaluation of the potential of atrazine to be systemically toxic following prolonged dermal exposure. No data were identified that demonstrated that atrazine was corrosive to the skin. The limited data precluded identifying whether the substance is a skin irritant. Data were also insufficient to evaluate the

Table 3. Summary of previous skin hazard designations for atrazine

Organization	Skin hazard designation
NIOSH [2005]	No designation
OSHA [2018]*	No designation
ACGIH [2014]	No designation; no sufficient data were available

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.
*Year accessed.

potential of atrazine to cause skin sensitization in humans. Additionally, sensitization predictive tests in animals were not available for review. Therefore, on the basis of these assessments, atrazine is assigned a skin notation of ID(SK).

Table 3 summarizes the skin hazard designations for atrazine previously issued by NIOSH and other organizations. The equivalent dermal designation for atrazine, according to the Globally Harmonized System (GHS) of Classification and Labelling of Chemicals, is Skin Sensitization Category 1 (Hazard statement: May cause an allergic skin reaction) [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 Atrazine

This appendix presents an overview of the SI ratio and a summary of the calculation of the SI ratio for atrazine. 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 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 [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 *kp*, 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

$$\text{Skin dose} = k_p \times S_w \times \text{Exposed skin surface area} \times \text{Exposure time}$$
$$= k_p(\text{cm/hr}) \times S_w\,(\text{mg/cm}^3) \times 360\ \text{cm}^2 \times 8\ \text{hr}$$

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 atrazine. The calculated SI ratio was 0.0114. On the basis of these results, atrazine is not predicted to represent a skin absorption hazard.

Appendix References

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

Variables used in calculation	Units	Value
Skin permeation coefficient		
Permeation coefficient of stratum corneum lipid path(k_{psc})	cm/hr	0.0044
Permeation coefficient of the protein fraction of the stratum corneum (k_{pol})	cm/hr	1.034 × 10-5
Permeation coefficient of the watery epidermal layer (k_{aq})	cm/hr	0.1702
Molecular weight (MW)*	amu	215.7
Base-10 logarithm of its octanol–water partition coefficient (Log K_{ow})*	None	2.61
Calculated skin permeation coefficient (k_p)	cm/hr	0.0043
Skin dose		
Water solubility (S_w)*	mg/cm^3	0.0347
Calculated skin permeation coefficient (k_p)	cm/hr	0.0043
Estimated skin surface area (palms of hand)[§]	cm^2	360
Exposure time	hr	8
Calculated skin dose	mg	0.4285
Inhalation Dose		
Occupational exposure limit (OEL)[†]	mg/m^3	5
Inhalation volume	m^3	10
Retention factor (RF)	None	0.75
Inhalation dose	mg	37.5
Skin dose–to–inhalation dose (SI) ratio	None	0.0114

*Variables identified from SRC [ND].
[†]The OEL used in calculation of the SI ratio for atrazine was the NIOSH recommended exposure limit (REL) [NIOSH 2005].
[§]Hayes WA [2008]. Principles and methods of toxicology. 5th ed. New York: Informa Healthcare USA.

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