

NIOSH Skin Notation Profiles

Sodium Hydroxide (NaOH)

SKK

ID^{SK}

[SK]

SYS

SYS (FATAL)

DIR

DIR (IRR)

DIR (COR)

SEN

NIOSH Skin Notation (SK) Profile

Sodium Hydroxide (NaOH)

[CAS No. 1310–73–2]

This document is in the public domain and may be freely copied or reprinted.

Disclaimer

Mention of any company or product does not constitute endorsement by the National Institute for Occupational Safety and Health (NIOSH). In addition, citations to Web sites external to NIOSH do not constitute NIOSH endorsement of the sponsoring organizations or their programs or products. Furthermore, NIOSH is not responsible for the content of these Web sites.

Ordering Information

To receive documents or other information about occupational safety and health topics, contact NIOSH at

Telephone: **1-800-CDC-INFO** (1-800-232-4636)

TTY: 1-888-232-6348

E-mail: cdcinfo@cdc.gov

or visit the NIOSH Web site at **www.cdc.gov/niosh**.

For a monthly update on news at NIOSH, subscribe to *NIOSH eNews* by visiting **www.cdc.gov/niosh/eNews**.

DHHS (NIOSH) Publication No. 2011-150

April 2011

SAFER • HEALTHIER • PEOPLE™

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 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 (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 sodium hydroxide (NaOH; CAS No. 1310–73–2). 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

Foreword	iii
Abbreviations	vi
Glossary	vii
Acknowledgments	ix
1 Introduction	1
1.1 General Substance Information	1
1.2 Purpose	1
1.3 Overview of SK Assignment for NaOH	1
2 Systemic Toxicity from Skin Exposure (SK: SYS)	1
3 Direct Effects on Skin (SK: DIR).	2
4 Immune-mediated Responses (SK: SEN).	4
5 Summary.	5
References	5

Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
ATSDR	Agency for Toxic Substances and Disease Registry
CIB	Current Intelligence Bulletin
(COR)	(COR) subnotation of SK: DIR indicating the potential for a chemical to be corrosive following exposure of the skin
DIR	skin notation indicating the potential for direct effects to the skin following contact with a chemical
EC	European Commission
GHS	Globally Harmonized System of Classification and Labeling of Chemicals
IARC	International Agency for Research on Cancer
in ²	inches
LD ₅₀	dose resulting in 50% mortality in the exposed population
LD _{Lo}	dermal lethal dose
<i>M</i>	molar concentration; molarity
mL	milliliter
MW	molecular weight
N	normality
NaOH	sodium hydroxide
NIOSH	National Institute for Occupational Safety and Health
NTP	National Toxicology Program
OEL	occupational exposure limit
OSHA	Occupational Safety and Health Administration
SEN	skin notation indicating the potential for immune-mediated reactions following exposure of the skin
SK	skin notation
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.

Acknowledgments

This document was developed by the Education and Information Division, Paul Schulte, Ph.D., Director. G. Scott Dotson, Ph.D. was the project officer for this document. Other NIOSH personnel, in particular Fredrick H. Frasch, Ph.D., Charles L. Geraci, Ph.D., Thomas J. Lentz, Ph.D., Richard Niemeier, Ph.D., and Todd Niemeier M.Sc., contributed to its development by providing technical reviews and comments. The basis for this document was a report contracted by NIOSH and prepared by Bernard Gadagbui, Ph.D., and Andrew Maier, Ph.D. (*Toxicology Excellence for Risk Assessment [TERA]*).

For their contribution to the technical content and review of this document, special acknowledgment is given to the following NIOSH personnel:

Denver Field Office

Eric Esswein, M.Sc.

Division of Applied Research and Technology

Clayton B'Hymer, Ph.D.

Division of Respiratory Disease Studies

Gregory A. Day, Ph.D.

Division of Surveillance, Hazard Evaluations, and Field Studies

Aaron Sussell, Ph.D.

Loren Tapp, M.D.

Education and Information Division

Ralph Zumwalde, M.Sc.

Health Effects Laboratory Division

Michael Luster, Ph.D.

Anna Shvedova, Ph.D.

Paul Siegel, Ph.D.

National Personal Protective Technology Laboratory

Heinz Ahlers, J.D.

Angie Shepherd

The authors thank Seleen Collins, Gino Fazio, and Vanessa B. Williams for their editorial support and contributions to the design and layout of this document. Clerical and information resources support in preparing this document was provided by Devin Baker, Daniel Echt, and Barbara Landreth.

In addition, special appreciation is expressed to the following individuals for serving as independent, external reviewers and providing comments that contributed to the development or improvement of this document:

G. Frank Gerberick, Ph.D., The Procter and Gamble Company, Cincinnati, Ohio

Dori Germolec, Ph.D., National Toxicology Program, National Institute for Environmental Health Sciences, Research Triangle, North Carolina

Ben Hayes, M.D., Ph.D., Division of Dermatology, Vanderbilt School of Medicine, Nashville, Tennessee

William Luttrell, Ph.D., CIH, Department of Chemistry & Physics, College of Arts and Sciences, Oklahoma Christian University, Edmond, Oklahoma

Howard Maibach, M.D., Department of Dermatology, School of Medicine, University of California, San Francisco, San Francisco, California

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

James Taylor, M.D., Industrial Dermatology, The Cleveland Clinic, Cleveland, Ohio

1 Introduction

1.1 General Substance Information

Chemical: Sodium hydroxide (NaOH)

CAS No: 1310–73–2

Synonyms:

NaOH; Caustic Soda; Lye; Soda
Lye; Sodium Hydrate

Molecular weight (MW): 40.0

Molecular formula: NaOH

Structural formula:

Na — OH

Uses:

Sodium hydroxide (NaOH) is used to manufacture soaps, rayon, paper, explosives, dyestuffs, and petroleum products. It is also used in processing cotton fabric, laundering and bleaching, metal cleaning and processing, oxide coating, electroplating, and electrolytic extracting [ATSDR 2002].

1.2 Purpose

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

1.3 Overview of SK Assignment for NaOH

NaOH is potentially capable of acting as a corrosive agent following skin contact. A critical review of available data has resulted in the following SK assignment for NaOH: **SK: DIR (COR)**. Table 1 provides an overview of the critical effects and data used to develop the SK assignment for NaOH.

2 Systemic Toxicity from Skin Exposure (SK: SYS)

No toxicokinetic data from human, in vivo, or in vitro studies investigating dermal exposure to NaOH were identified. No systemic effects of dermal exposure in humans or animals have been reported. No estimated values for dermal lethal dose (LD_{Lo}) in humans or dermal LD₅₀ (the dose resulting in 50% mortality in the exposed population) in animals have

Table 1. Summary of the SK assignment for NaOH

Skin notation	Critical effect	Data available
SK: DIR (COR)	Skin corrosion	Sufficient human and animal data

been identified. No epidemiological, occupational exposure, animal, or repeat-dose toxicity studies evaluating the potential of NaOH to cause systemic effects following dermal exposure were identified. However, because of the physicochemical properties of the substance, repeated applications to the skin are likely to produce increasing damage to the skin prior to systemic effects being observed. It is unlikely that exposures to nonirritating concentrations would increase the concentration of sodium in the blood or increase the pH of the blood to a significant degree. Thus, under nonirritating exposure conditions, NaOH can be considered not systemically toxic.

The literature search revealed no standard toxicity or specialty studies evaluating biological system/function-specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure to NaOH. No studies evaluating the carcinogenicity of NaOH following dermal exposure were identified. Table 2 provides a summary of carcinogenic designations from multiple governmental and nongovernmental organizations for NaOH.

No reliable data were identified upon which to evaluate the potential for NaOH to be absorbed through the skin or contribute to the onset of systemic toxic effects following dermal exposure to the substance. Therefore, on the basis of the

data for this assessment, NaOH is not assigned the SK: SYS notation.

3 Direct Effects on Skin (SK: DIR)

The direct skin effects of NaOH are caused by its strong alkalinity. NaOH solutions with a pH of 11.5 or greater should be considered corrosive to the skin [NIOSH 2009]. A 0.1-molar concentration (molarity; *M*) or 1% aqueous solution of NaOH has a pH of about 13 [Pierce 1993]. The *M* (the number of moles of a given substance per liter of solution) of NaOH associated with a pH of 11.5 is approximately 0.003 *M*, and concentrations equal to or greater than this are considered corrosive to the skin [NIOSH 2009]. Less concentrated solutions of NaOH, although not corrosive, can be irritating to the skin. The concentration-dependent corrosivity of NaOH has been demonstrated in a number of volunteer studies, dermal application tests in animals, and in vitro tests for corrosivity in human or animal skin models or of skin integrity in cadaver skin.

Reports are available from several studies of the impact of various NaOH concentrations and exposure durations on the skin of volunteers and in animal toxicity tests. Nagao et al. [1972] noted total destruction of the epidermis in 60 minutes in skin biopsies of volunteers who had 1-normal (N)* NaOH

*The document retains the unit of concentration of applied sodium hydroxide (NaOH) as “normality” as reported by the study authors. “Normality” refers to the activity of a reagent: how many moles of active species (H⁺ or OH⁻ ions) are there per liter? A normal (N) solution of a base, such as NaOH, is the number of moles of OH⁻ ions produced per liter. A 1-N NaOH solution produces 1 mole of OH⁻ ions and can react with 1 mole of an acid. For NaOH or hydrochloric acid (HCl), the normality is equal to the molarity. For NaOH, to convert from normality to percent solution, multiply the normality by the formula weight (FW [the mass of 1 mole of a compound] = 40.0) and divide by 10; that is, % solution = normality × 40.0 × 1/10.

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

Organization	Carcinogenic designation
NIOSH [2005]	None
NTP [2009]	None
USEPA [2009]	None
IARC [2009]	None
EC [2010]	None
ACGIH [2001]	None

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.

applied to their forearms for 15 to 180 minutes. A study conducted by Seidenari et al. [1995], involving a 24-hour patch test in 34 volunteers, showed that a 4% aqueous NaOH solution caused an enhanced inflammatory response with pronounced barrier function damage. Agner and Serup [1987] reported that a 2% aqueous solution of NaOH applied to the skin of volunteers under occlusion for 1 hour caused severe crusting in some volunteers but no inflammation in others up to 96 hours post-application. These results suggest significant variability in the corrosivity of NaOH to human skin and verify that concentrations at or above 1 N are corrosive. In a primary skin irritation test, 5% to 30% aqueous solutions of NaOH were corrosive to rabbit skin [United States Testing Company 1976]. A study conducted by Srikrishna and Monteiro-Riviere [1991] reported that 2-N and 4-N NaOH caused severe necrosis in all epidermal layers, whereas 6-N NaOH caused numerous and severe blisters, with necrosis extending deeper into the subcutaneous tissue, when applied on the lower abdominal region of weanling pigs. A 50% NaOH solution caused a burn that was rapid and progressive in both depth and extent when applied to 2 square inches (in²) of the clipped backs

of mice [Bromberg et al. 1965]. NaOH was found to be irritating to pig skin examined immediately after application of 1-N aqueous NaOH, as evidenced by the presence of vesicular nuclei and increased eosinophilia and a fine, dense cross-striation in polarized light [Karlsmark et al. 1988]. In rabbits, 4-hour exposure to a 2% NaOH solution caused skin corrosion, whereas a 1% solution caused no damage [Vernot et al. 1977]. The corrosivity of NaOH has also been demonstrated in a variety of in vitro assays. An aqueous solution of NaOH at pH 13.5 was corrosive in an in vitro Corrositex assay, with an average break-through time of 13 minutes [Stobbe et al. 2003]. Perkins et al. [1996] concluded that a 10% NaOH solution was corrosive to the skin, on the basis of cytotoxicity in human-skin-equivalent cultures. In another in vitro study, using isolated perfused porcine skin flaps, Srikrishna and Monteiro-Riviere [1991] reported that 4-N and 6-N NaOH caused severe necrosis of all epidermal cell layers and dermis after 8 hours of topical perfusion.

The concentration of NaOH that was demonstrated to be corrosive to the skin varied according to the test system employed and the duration of exposure. A

number of the available studies demonstrate more limited irritant responses. For example, in a patch test conducted in two different laboratories, in which a 0.5% solution (0.2 milliliter [mL]) was applied for progressively longer durations of 0.5, 1, 2, 3, and 4 hours to the skin of volunteers (treatment sites were moved for each patch application), NaOH was judged to be irritating to the skin; half of the volunteers had a reaction after just 1 hour of application [Griffiths et al. 1997]. This reaction was so vigorous that exposure for a greater duration was not undertaken at any site. Irritant contact dermatitis was also reported in volunteers after single (24-hour) or repeated (5-day) application of NaOH concentrations of 0.125% to 1.0% in aqueous medium [Park and Eun 1995]. Willis et al. [1988] reported that the 2% concentration of NaOH produced mild to moderate irritation for 75% of the 42 male volunteers, under the patch-testing conditions (1%, 2%, or 4% NaOH; closed; 48 hours). Animal studies also have identified irritant concentrations of NaOH in the absence of corrosivity. In a patch test a well-defined erythema with slight thickness of skin was observed when 2% NaOH solution in 1-propanol was applied to the shaved back of mice for 24 hours, whereas a 1% solution did not cause any reaction [Li et al. 1998]. An in vitro study conducted by Bartnik et al. [1990] indicated that NaOH dissolved in aqueous medium, applied at a dose of 500 to 5000 micrograms per square centimeter ($\mu\text{g}/\text{cm}^2$) to the skin explants of hairless mice, caused moderate to strong irritation; this was determined on the basis of the membrane-damaging effects, as assessed by lactate dehydrogenase and glutamic-oxalacetate transaminase activities.

The available data demonstrate that NaOH of sufficient concentration is corrosive to the skin, as shown by the physicochemical

properties of NaOH solutions, by tests for irritation or corrosivity in vivo in volunteers [Nagao et al. 1972; Agner and Serup 1987; Seidenari et al. 1995[†]] and experimental animals [Bromberg et al. 1965; United States Testing Company Inc. 1976; Vernet et al. 1977; Srikrishna and Monteiro-Riviere 1991], and by studies of human and animal in vitro systems [Srikrishna and Monteiro-Riviere 1991; Perkins et al. 1996; Stobbe et al. 2003]. It appears that more dilute solutions (for example, 0.5% or less) may be irritating to the skin. The transition point between corrosivity and irritation also is a function of duration of skin contact. NaOH solutions with a pH at or above 11.5 are considered corrosive [NIOSH 2009]. Therefore, on the basis of the data for this assessment, NaOH is assigned the **SK: DIR (COR)** notation.

4 Immune-mediated Responses (SK: SEN)

One study investigating the skin sensitization potential of NaOH in humans was identified. Park and Eun [1995] applied diluted NaOH solutions ranging from 0.125% to 1.0% to the backs of male volunteers. After 7 days, a challenge test was administered with a 0.125% NaOH solution. The authors reported that the observed irritation corresponded with the concentration of NaOH, but an increased response was not observed when the previously patch-tested sites were rechallenged. Park and Eun [1995] concluded that NaOH sodium hydroxide did not elicit an immune-mediated response and does not have a potential to act as a skin sensitization. No predictive tests on animals (for example, guinea pig maximization tests, Buehler tests, or

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

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

Organization	Skin hazard designation
NIOSH [2005]	None
OSHA [2009]	None
ACGIH [2001]	None
EC [2010]	R35: Causes severe burns (>5% NaOH solutions) R34: Causes burns (2%–5% NaOH solutions) R 38: Irritating to skin (<2% NaOH solutions)

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.

murine local lymph node assays) or any other studies that evaluated the potential of the substance to cause skin sensitization were identified. Therefore, on the basis of the data for this assessment, NaOH is not assigned the SK: SEN notation.

5 Summary

No reliable data were identified to assess the potential for absorption through the skin or systemic toxicity following dermal exposure to NaOH. Mathematical modeling predicts NaOH can be absorbed through the skin, but repeated applications of NaOH are more likely to produce skin damage prior to eliciting systemic effects. It is unlikely that repeated application of nonirritating concentrations of NaOH can produce systemic effects, given that such exposures would not significantly increase the concentration of sodium in the blood or increase the pH of the blood. The weight of evidence on the physicochemical properties of NaOH solutions, from several *in vivo* irritation or corrosivity tests involving volunteers [Nagao et al. 1972; Agner and Serup 1987; Seidenari et al. 1995] and experimental animals [Bromberg et al. 1965; United States Testing Company 1976; Vernot et al. 1977; Srikrishna and Monteiro-Riviere 1991], and from human and animal *in*

vitro systems [Srikrishna and Monteiro-Riviere 1991; Perkins et al. 1996; Stobbe et al. 2003] demonstrates that NaOH of sufficient concentration is corrosive to the skin. NaOH solutions with a pH of 11.5 or greater should be considered corrosive to the skin [NIOSH 2009]. Despite the wide application of NaOH in occupational settings, the literature search yielded no reports on occupational cases, diagnostic patch tests in humans, or predictive tests in animals that involved the potential of NaOH to cause skin sensitization. Therefore, on the basis of these assessments, NaOH is assigned a composite skin notation of **SK: DIR (COR)**.

Table 3 summarizes the skin hazard designations for NaOH previously issued by NIOSH and other organizations. The equivalent dermal designations for NaOH, according to the Global Harmonization System (GHS) of Classification and Labelling of Chemicals, is Skin Corrosion Category 1A (Hazard statement: Causes severe skin burns and eye damage) [European Parliament 2008].

References

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

- *ACGIH (American Conference of Governmental Industrial Hygienists) [2001]. Sodium hydroxide. In: Documentation of threshold limit values and biological exposure indices. 7th ed., Vol. 3. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.
- *Agner T, Serup J [1987]. Skin reactions to irritants assessed by polysulfide rubber replica. *Contact Dermatitis* 17(4):205–211.
- †Agner T, Serup J [1988]. Contact thermography for assessment of skin damage due to experimental irritants. *Acta Derm Venerol* 68(3):192–195.
- *ATSDR (Agency for Toxic Substance and Disease Registry) [2002]. ToxFAQ for sodium hydroxide. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, ATSDR [http://www.atsdr.cdc.gov/tfacts178.html]. Accessed 07–07–10.
- *Bartnik FG, Pittermann WF, Mendorf N, Tillman U, Kunstler K [1990]. Skin organ culture for the study of skin irritancy. *Toxicol Vitro* 4(4–5):293–301.
- *Bromberg BE, Song IC, Walden RH [1965]. Hydrotherapy of chemical burns. *Plast Reconstr Surg* 35:85–95.
- *EC (European Commission) [2010]. Sodium hydroxide. In: EINECS (European Inventory of Existing Commercial Chemical Substances) [http://ecb.jrc.ec.europa.eu/esis/]. Accessed 07–07–10.
- †ECB (European Chemical Bureau) [2007]. European Union risk assessment report: sodium hydroxide. In: Existing chemicals risk assessment report [http://ecb.jrc.ec.europa.eu/home.php?CONTENU=/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/]. 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, labeling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. *OJEU, Off J Eur Union* L353:1–1355 [http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:EN:PDF]. Accessed 07–07–10.
- *Griffiths HA, Wilhelm KP, Robinson MK, Wang XM, McFadden J, York M, Basketter DA [1997]. Interlaboratory evaluation of a human patch test for the identification of skin irritation potential/hazard. *Food Chem Toxicol* 35(2):255–260.
- *IARC (International Agency for Research on Cancer) [2009]. Agents reviewed by the IARC monographs. In: IARC monographs on the evaluation of carcinogenic risks to humans [http://monographs.iarc.fr/ENG/Classification/Listagentsalphorder.pdf]. Accessed 07–07–10.
- *Karlsmark T, Danielsen L, Thomsen HK, Aalund O, Nielsen KG, Nielsen O, Genefke IK [1988]. The effect of sodium hydroxide and hydrochloric acid on pig dermis: a light microscopic study. *Forensic Sci Int* 39(3):227–233.
- *Li L, Fiedler VC, Kumar R [1998]. Down-regulation of protein kinase C isoforms in irritant contact dermatitis. *Contact Dermatitis* 38(6):319–324.
- *Nagao S, Stroud JD, Hamada T, Pinkus H, Birmingham DJ [1972]. The effect of sodium hydroxide and hydrochloric acid on human epidermis: an electron microscopic study. *Acta Derm Venereol* 52(1):11–23.
- †Nagy-Vezekenyi K, Zs.-Nagy I, Torok E [1975]. The effects of some solvents on the epidermis. *Arch Derm Forsch* 252:53–61.
- *NIOSH [2005]. NIOSH pocket guide to chemical hazards. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2005–149 [http://www.cdc.gov/niosh/npg/]. Accessed 07–07–10.
- *NIOSH [2009]. Current intelligence bulletin 61: a strategy for assigning new NIOSH skin notations. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2009–147 [http://www.cdc.gov/niosh/docs/2009-147/pdfs/2009-147.pdf]. Accessed 07–07–10.
- *NTP (National Toxicology Program) [2009]. Eleventh report on carcinogens (RoC) [http://ntp.niehs.nih.gov/index.cfm?objectid=32BA9724-F1F6-975E-7FCE50709CB4C932]. Accessed 07–07–10.
- *OSHA (Occupational Safety and Health Administration) [2009]. Sodium hydroxide. In: OSHA/EPA occupational chemical database [http://www.osha.gov/web/dep/chemicaldata/ChemicalResult.asp?RecNo=235]. Accessed 07–07–10.
- *Park KB, Eun HC [1995]. A study of skin responses to follow-up, rechallenge and combined effects of irritants using non-invasive measurements. *J Dermatol Sci* 10(2):159–165.

- *Perkins MA, Osborne R, Johnson GR [1996]. Development of an in vitro method for skin corrosion testing. *Fund Appl Toxicol* 31(1):9–18.
- *Pierce JO [1993]. Sodium hydroxide. In: Clayton G, Clayton F (eds.), *Patty's industrial hygiene and toxicology*. 4th rev. ed., Vol. 2A. New York: John Wiley & Sons, 771–773.
- *Seidenari S, Pepe P, Di Nardo A [1995]. Sodium hydroxide-induced irritant dermatitis as assessed by computerized elaboration of 20 MHz B-scan images and by TEWL measurement: a method for investigating skin barrier function. *Acta Derm Venereol* 75(2):97–101.
- *Srikrishna V, Monteiro-Riviere NA [1991]. The effects of sodium hydroxide and hydrochloric acid on isolated perfused skin. *Toxicol Vitro* 4(3):207–216.
- *Stobbe JL, Drake KD, Maier KJ [2003]. Comparison of in vivo (Draize method) and in vitro (Corrositex assay) dermal corrosion values for selected industrial chemicals. *Int J Toxicol* 22(2):99–107.
- *UNECE (United Nations Economic Commission for Europe) [2007]. Part 3: health hazards. In: Globally harmonized system of classification and labelling of chemicals (GHS). 2nd rev. ed. [http://www.unece.org/trans/danger/publi/ghs/ghs_rev02/02files_e.html]. Accessed 07–07–10.
- *USEPA (United States Environmental Protection Agency) [2009]. Integrated Risk Information System (IRIS) [<http://www.epa.gov/iris/>]. Accessed 07–07–10.
- *United States Testing Company [1976]. *Toxicological and skin corrosion testing of selected hazardous materials*. Springfield, VA: U.S. National Technical Information Service, DOT/MTB/OHMO-76/2.
- *Vernot EH, MacEwen JD, Haun CC, Kinkead ER [1977]. Acute toxicity and skin corrosion data for some organic and inorganic compounds and aqueous solutions. *Toxicol Appl Pharmacol* 42:417–423.
- *Willis CM, Stephens JM, Wilkinson JD [1988]. Experimentally-induced irritant contact dermatitis: determination of optimum irritant concentrations. *Contact Dermatitis* 18(1):20–24.



*Delivering on the Nation's promise:
safety and health at work for all people
through research and prevention*

To receive NIOSH documents or more information about occupational safety and health topics, contact NIOSH at

1-800-CDC-INFO (1-800-232-4636)

TTY: 1-888-232-6348

E-mail: cdcinfo@cdc.gov

or visit the NIOSH Web site at www.cdc.gov/niosh.

For a monthly update on news at NIOSH, subscribe to NIOSH eNews by visiting www.cdc.gov/niosh/eNews.

DHHS (NIOSH) Publication No. 2011-150

SAFER • HEALTHIER • PEOPLE™

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health
4676 Columbia Parkway
Cincinnati, Ohio 45226-1998**

**Official Business
Penalty for Private Use \$300**