NIOSH Skin Notation Profile
Formic acid

[CAS No. 64-18-6]

External Review Draft

September 2024

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NIOSH [20XX]. NIOSH skin notation profile: formic acid. By Chen L, Hudson N. Cincinnati, OH: U.S. Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. DHHS (NIOSH) Publication No. 20XX-XXX, https://doi.org/10.26616/NIOSHPUB20XXXXX.

DHHS (NIOSH) Publication No. 20XX-XXX

DOI: https://doi.org/10.26616/NIOSHPUB20XXXXX

Month 20XX

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]. 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 with an 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 formic acid 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
CIB	Current Intelligence Bulletin
cm	centimeter
COR	subnotation of SK: DIR indicating the potential for a chemical cause corrosion or burns following exposure to the skin
DIR	skin notation indicating the potential for direct effects to the skin following contact with a chemical
ECHA	European Chemicals Agency
IARC	International Agency for Research on Cancer
LD_{50}	median lethal dose
LD_{Lo}	dermal lethal dose
mL	milliliter
mmol/L	millimoles per liter
MW	molecular weight
NIOSH	National Institute for Occupational Safety and Health
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
OSHA	Occupational Safety and Health Administration
QSAR	Quantitative structure-activity relationship
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
U.S. EPA	United States Environmental Protection Agency

Glossary

Absorption—The transport of a chemical from the outer surface of the skin into both the skin and systemic circulation (including penetration, permeation, and resorption).

Acute exposure—Contact with a chemical that occurs once or for only a short period of time.

Cancer—Any one of a group of diseases that occurs when cells in the body become abnormal and grow or multiply out of control.

Contaminant—A chemical that is (1) unintentionally present within a neat substance or mixture at a concentration less than 1.0% or (2) recognized as a potential carcinogen and present within a neat substance or mixture at a concentration less than 0.1%.

Cutaneous (or percutaneous)—Referring to the skin (or through the skin).

Dermal—Referring to the skin.

Dermal contact—Contact with (touching) the skin.

Direct effects—Localized, non-immune-mediated adverse health effects on the skin, including corrosion, primary irritation, changes in skin pigmentation, and reduction/disruption of the skin barrier integrity, occurring at or near the point of contact with chemicals.

Immune-mediated responses—Responses mediated by the immune system, including allergic responses.

Sensitization—A specific immune-mediated response that develops following exposure to a chemical, which, upon re-exposure, can lead to allergic contact dermatitis (ACD) or other immune-mediated diseases such as asthma, depending on the site and route of re-exposure.

Substance—A chemical.

Systemic effects—Systemic toxicity associated with skin absorption of chemicals after exposure of the skin.

Acknowledgments

This document was developed by the Division of Science Integration, Christine Whittaker, PhD, Director. Lilia Chen, MS, CIH, and Naomi Hudson, DrPH, were the project officers for this document. The basis for this document was a report prepared by George Holdsworth, PhD, and Lutz W. Weber, PhD (Oak Ridge Institute for Science and Education [ORISE]), and contracted by NIOSH.

Special appreciation is expressed to the following individuals for serving as internal reviewers by use of an Intergovernmental Personnel Agreement:

- Annette L. Bunge, PhD, Chemical & Biological Engineering Department, Colorado School of Mines, Golden, CO
- Youcheng Liu, MD, ScD, MPH, MS, University of North Texas Health Science Center, Fort Worth, TX

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1 Introduction

1.1 General Substance Information

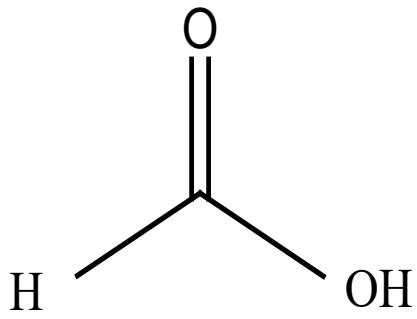
Chemical: Formic acid

CAS No: 64-18-6

Molecular weight (*MW*): 46.03

Molecular formula: CH_2O_2

Structural formula:



Source image: [NLM, no date]

General substance information was obtained from NIOSH [2007].

Synonyms: aminic acid; hydrogen carboxylic acid, methanoic acid, formisoton, formylic acid

Uses: Formic acid is used in a variety of industrial and commercial products. In the cosmetics industry, it is used as a fragrance ingredient, preservative, and pH adjuster [Johnson et al. 2016]. Formic acid has been approved by the Food and Drug Administration as a flavoring agent and preservative to food, animal feed, and animal drinking water. It is also used in washing and cleaning products, metal surface treatment products, water treatment and plant protection products, textile and paper dyeing and finishing, leather tanning, and in the manufacture of many other products [ECHA 2023].

1.2 Purpose

This *Skin Notation Profile* presents (1) a brief summary of epidemiological and toxicological data associated with skin contact with formic acid and (2) the rationale behind the hazard-specific skin notation (SK) assignment for the compound. 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 formic acid. A literature search was conducted through March 2023 to identify information on biological system/function specific effects (including reproductive and developmental effects and immunotoxicity), dermal absorption, acute toxicity, repeat-dose systemic toxicity, 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 formic acid.

1.3 Overview of SK Assignment for Formic Acid

Formic acid is potentially capable of causing adverse health effects following skin contact. A critical review of available data has resulted in the following SK assignment for the compound: **SK: SYS-DIR (COR).** Table 1 provides an overview of the critical effects and data used to develop the SK assignment for formic acid.

Table 1. Summary of the SK assignment for formic acid

Skin notation	Critical effects	Available data
SK: SYS	Metabolic acidosis, hemolysis, hemoglobinuria	Limited human data
SK: DIR(COR)	Skin corrosion	Limited human data

2 Systemic Toxicity from Skin Exposure (SK: SYS)

No studies were identified regarding the quantitative absorption of formic acid after dermal exposure in humans or animals. No human dermal lethal doses (LD_{LO}) or dermal LD_{50} (the dose resulting in 50% mortality in exposed animals) studies were identified for formic acid. There have been considerable improvements and advancements in dermal absorption studies and modeling since the publication of CIB 61 [NIOSH 2009]. In response to expert external peer reviewers' comments regarding the limitation of the skin to inhalation dose (SI) ratio information, NIOSH is no longer providing the SI ratio described in CIB 61 in the individual chemical skin notation profile documents.

Banihashemi et al. [2011] performed an animal study where formic acid with a pH of 5.5 was applied daily to a 2 centimeter (cm) × 2 cm area of shaved skin above the tail of eight Fischer 344/N female rats. These researchers observed the effects on hair growth compared to rats treated with saline or sodium formate, the monosodium salt of formic acid, for two weeks. They saw that rats treated with formic acid and sodium formate had lower numbers of hairs compared to control groups. However, the results were not statistically significant, and no systemic or local toxicity was observed by the formic acid applications [Banihashemi et al. 2011].

The rate and extent of dermal absorption and related safety concerns depend primarily on the amount of free formic acid in the formulation. Formic acid is commonly added to cosmetic formulations as a preservative or pH adjuster where it is present as neutralized formate salts, such as sodium formate. The potential for these formulations to cause adverse effects is low because the concentration of free formic acid is low [Johnson et al. 2016]. However, absorption

of the compound may be assumed from the systemic effects that result after unintended exposures to formic acid, as described in reports of human case studies [Chan et al. 1995; Sigurdsson et al. 1983]. Systemic effects were most likely a consequence of the corrosion at the skin surface that compromised the dermal barrier.

Several case reports described severe damage to the dermal barrier and systemic toxicological effects after skin exposure to concentrated formic acid. Sigurdsson et al. [1983] described the case of a 15-year-old female who spilled undiluted formic acid over her lower extremities in an agricultural incident. The patient was washed thoroughly then taken to hospital with chemical burns covering about 20% of her body surface [Sigurdsson et al. 1983]. Evidence of systemic toxicity included metabolic acidosis, manifested by a serum pH of 7.23 (normal range 7.31–7.45) and a bicarbonate concentration of 16.7 millimoles per liter (mmol/L) (normal range 18–23 mmol/L). Other physiological deficits included hemolysis and hemoglobinuria, hypopotassemia, hyponatremia, and leucocystosis. The acidosis was corrected with infusions of bicarbonate and the primary treatment thereafter centered on burn treatment. The authors concluded that the formic acid had been absorbed from the burned areas with consequent metabolic acidosis, intravascular hemolysis, and hemoglobinuria [Sigurdsson et al. 1983].

Chan et al. [1995] described another case of systemic toxicity, in which a 3-year-old girl received second- and third-degree burns over 35% of her body surface from 90% concentrated formic acid. Suffering from metabolic acidosis, the patient was put on mechanical ventilation and received intravenously administered physiologically buffered bicarbonate for rehydration and to treat acidosis [Chan et al. 1995]. With an initial serum formate level of 400 micrograms per milliliter, intravascular hemolysis, hemoglobinuria, and fluctuations in some clinical chemistry parameters, the patient underwent 2.5 hours of hemodialysis, which helped to correct the physiological imbalance. The severity of the overall impairment was such that the endotracheal tube was not removed until Day 20, and she remained hospitalized until Day 71 for skin grafts and continued wound care [Chan et al. 1995].

Table 2 summarizes carcinogenic designations of multiple governmental and nongovernmental organizations for formic acid.

Table 2. Summary of the carcinogenic designations for formic acid by numerous governmental and nongovernmental organizations

Organization	Carcinogenic designation
ACGIH [2022]	No designation
ECHA [2023]	No designation
IARC [2023]*	No designation
NIOSH [2007]	No designation
NTP [2021]	No designation
U.S. EPA [1990]	Archived (No designation)

ACGIH = American Conference of Governmental Industrial Hygienists; ECHA = European Chemicals Agency; IARC = International Agency for Research on Cancer; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; U.S. EPA = United States Environmental Protection Agency.
*Year accessed.

No studies were identified that quantitatively evaluated absorption of formic acid after dermal exposure in humans or animals. Cases of persons who suffered profound skin lesions and physiological impairment as a consequence of industrial or domestic incidents **[Chan et al. 1995; Sigurdsson et al. 1983]*** demonstrated that skin exposure to concentrated formic acid can produce systemic toxicological effects. In both cases, severe skin burns resulted in localized destruction of the dermal barrier and profound systemic effects including metabolic acidosis, intravascular hemolysis, and hemoglobinuria. Based on these data, formic acid is assigned a **SK: SYS** notation.

3 Direct Effects on Skin (SK: DIR)

Predictive models evaluating the corrosivity of formic acid were identified. Leibsch et al. [1995] evaluated the skin corrosivity of formic acid *in vitro* utilizing a three-dimensional human skin tissue model (Skin^2 ZK 1300™/ZK 1350™; Advanced Tissue Sciences, La Jolla, USA) consisting of dermal, epidermal, and corneal layers. The purpose of the Leibsch et al. study was to test the model's ability to predict phototoxicity and corrosivity classifications. Formic acid was one of the 50 chemicals used for testing, selected by a taskforce of the British chemical

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

manufacturer's association's review of human and animal data from the literature. Despite the task force's evaluation of formic acid being an *in vivo* corrosive, the Skin^2 ZK 1350 test produced a false negative result [Leibsch et al. 1995]. No tests using *in vitro* animal skin models were identified.

A multivariate quantitative structure-activity relationship (QSAR) model was developed to predict skin corrosivity for a series of carboxylic acids [Eriksson et al. 1994]. The researchers selected 45 acids based on the ADR[†] inventory, chemistry databases, and availability of physiochemical descriptors. Of these, they tested 15 carboxylic acids for cutaneous corrosion by applying patches to the shaved dorsal trunk of rabbits; however, formic acid was not one of the carboxylic acids tested on rabbits. Instead, the QSAR model was used to predict the lowest observable effect concentration of the non-*in vivo* tested acids. It predicted formic acid to have the lowest observable effect concentration of 2.3 molar. The researchers noted that the prediction error was 20% of the entire range of biological activity. They concluded that the QSAR had sound predictive capability to tentatively forecast corrosive properties of non-tested acids based on physiochemical properties [Eriksson et al. 1994].

A number of case reports of patients who suffered skin burns as a result of dermal contact with formic acid provided strong evidence for the corrosivity of formic acid [Chan et al. 1995; Karunadasa et al. 2010; Ram et al. 2010; Sigurdsson et al. 1983; Yelon et al. 1996]. Several studies have evaluated formic acid as an ingredient in hair [Banihashemi et al. 2011] and wart treatments [Bhat et al. 2001; Faghihi et al. 2010], including cases of burns that occurred after sustained contact with the treatment ointment [Balagué et al. 2014; Sjokvist et al. 2020; Tong et al. 2015]. One study used up to 7% aqueous formic acid solution to remove the stratum corneum on human subjects [Lehmann and Kligman 1983]. Irritation from formic acid was reported in an open patch test animal study performed by Sekizawa et al. [1994].

The systemic toxicity of formic acid for Chan et al. and Sigurdsson et al. were described in Section 2; however, those incidents also caused direct skin effect. The burns on the patient in the Sigurdsson et al. [1983] manuscript were reported to initially appear superficial and had a peculiar green hue. However, after a few days, blisters began to form with gross oedema resulting in heavy scarring [Sigurdsson et al. 1983]. The patient treated by Chan et al. suffered full-thickness second and third degree burns and required multiple debridements (removal of infected and/or dead skin) and skin grafts over the period of several months [Chan et al. 1995].

[†]Accord Européen pour le Transport de Marchandises Dangereuses par Route (ADR), Statens Räddningsverk, Karlstad, 1991

Both of these incidents resulted in third degree burns to such an extent that skin grafts were required to heal the wounds.

In another report [Yelon et al. 1996], a chemical delivery worker suffered burns to his face after an unintended release of 98% formic acid. This happened during a chemical transfer from his truck to a receiving container. During the transfer, a pressurized hose came loose, spraying formic acid onto his face and aerosolizing the chemical, which he inhaled. This resulted in superficial second-degree burns on his face along with a reported "burning" sensation. This was in addition to dyspnea and other inhalation injuries [Yelon et al. 1996].

More evidence for the capacity of formic acid to burn the skin has come from an account of an incident in India in which a bus collided with a tanker carrying 85% concentration of formic acid. The tanker ruptured [Ram et al. 2010]. Forty-two patients suffered various degrees of chemical injury to their eyes and skin. Over 70% of the patients suffered first-degree skin burns and 29% received deeper wounds that were designated as second-degree burns. In Sri Lanka, Karunadasa et al. [2010] performed a cross-sectional, retrospective review of acid assault patients over an 18-month period. They found that formic acid was used in 19 (41%) of 46 acid assaults. Although the exact concentrations of the acid used were unknown in almost all cases, tissue damage resulting from the chemical burn occurred [Karunadasa et al. 2010].

Banihashemi et al. [2011] investigated formic acid's effect on hair growth by topically applying formic acid daily to a 2 cm × 2 cm area of shaved skin above the tail of eight Fischer 344/N rats. The results were compared with rats treated with saline or sodium formate. After two weeks, researchers observed no evidence of redness or swelling on the skin [Banihashemi et al. 2011].

Two studies evaluating formic acid as a treatment for common warts using a needle puncture technique was reported [Bhat et al. 2001; Faghihi et al. 2010]. They both concluded the 85% formic acid was a safe, inexpensive, effective alternative for treating warts that did not require anesthesia and caused minimal scarring. Bhat et al. performed a placebo-controlled, nonrandom trial to treat common warts. Fifty patients received 85% formic acid through a formipuncture, a needle technique where the warts are punctured 5-6 times with care to not have contact with normal skin, every other day for up to 12 applications. This was compared with a control group using only water [Bhat et al. 2001]. The punctures did not produce bleeding, and contact with normal skin was avoided. After a follow-up period of 3 months, researchers reported a mild burning sensation observed in all patients at the time of application that disappeared within a few minutes with minimal scarring. No other side-effects were observed [Bhat et al. 2001].

Using a similar needle puncture technique to treat warts, Faghihi et al. [2010] performed a placebo-controlled clinical trial with 85% formic acid. Formic acid in distilled water or just distilled water was first topically applied to the warts of 34 patients with cotton swabs. The lesions were punctured every other day, 6–10 times in each lesion, without causing bleeding, for

up to 12 sessions or complete recovery. The researchers observed a keratolytic effect after formic acid was applied, where the wart became slightly white with the uppermost layer peeling off. The side effects included mild pain, bulla and ulcerations, pigment changes, bleeding and hemorrhagic crusts, and mild atrophic scars, but no systemic or severe side effects were observed [Faghihi et al. 2010].

Case reports described skin effects after formic acid was used as a treatment for warts [Sjokvist et al. 2020; Tong et al. 2015]. In these cases, the use directions were not followed, resulting in full-thickness burns. In addition, information about the ointment ingredients or formic acid concentration of the wart treatment products was not adequately provided. A 33-year-old woman applied an over-the-counter topical ointment containing formic acid to treat a wart on the little finger of her right hand. Applying the ointment on the wart for a consecutive 12 hours, including overnight, resulted in a 3 cm × 2 cm burn of the skin; subcutaneous tissue, tendon, and joint capsule requiring debridements; a reverse cross finger flap treatment; skin graft; and intensive hand therapy [Tong et al. 2015].

An 11-year-old girl used an over-the-counter topical solution containing formic acid to treat a wart on the back of her left hand [Sjökvist et al. 2020]. This treatment resulted in a 20-mm full-thickness chemical burn. The solution was applied for 8 hours with an occlusive dressing, which was advised against on the pack insert. After the initial treatment, necrosis developed after two days. The girl was advised to use aluminum acetotartrate-soaked gauze to dress the area. At Day 9, she reported to the emergency department where the necrotic area was debrided under local anesthesia. Two days later, she returned in pain and was prescribed antibiotics for wound infection. She eventually had flap surgery to close the wound. There was no evidence of local or system toxicity [Sjökvist et al. 2020].

Lehmann and Kligman [1983] used formic acid solutions of varying concentrations to develop a method for removing the horny layer of the skin, which is the chief barrier to the skin. They applied 3%, 5%, and 7% aqueous solutions of formic acid under occlusion for 24 hours on the back, forearm, and calf of 63 human subjects. They evaluated erythema in 10 volunteers where the sites were left uncovered or occluded under plastic film. Faint erythema was observed in 5 of 20 test sites immediately after the horny layer was removed. Redness developed in all sites that were left open over 6 hours, and one site developed intense erythema with a slight crust. Researchers found that occlusion moderated the reaction when only two sites showed slight erythema 24 hours after the horny later was removed. They concluded that 5%–7% formic acid could reproducibly cause complete detachment of the stratum corneum with only mild inflammation and little discomfort [Lehmann and Kligman 1983].

Formic acid was observed to be a skin irritant to animals in an open patch test by Sekizawa et al. [1994]. To test primary skin irritation, test solutions of 1 milliliter per kilogram or 1 gram per

kilogram were applied once, unoccluded, to the shaved skin on the backs of six rats (3 cm × 4 cm) and six mice (1 cm × 2 cm). Test solutions of 0.01 milliliter (mL) were applied to the shaved skin on the back of three guinea pigs (and rats for comparison) in four unoccluded circles with 1.5 cm diameters. Distilled water was applied to the control group. The researchers also performed an intradermal reaction test with a 0.01 mL solution injected into the shaved skin on the backs of rats and mice. Test solutions of 0.01 mL were injected intradermally into four spots on the shaved back skin of guinea pigs (and rats for comparison). Saline was the control used for the intradermal tests. They observed that 10%–12% formic acid was the concentration at which skin irritation was observed [Sekizawa et al. 1994].

Formic acid was observed to be a skin irritant in animal patch tests [Sekizawa et al. 1994] and in humans [Lehmann and Kligman 1983]. Case reports of burns and skin corrosion following exposure to formic acid **[Chan et al. 1995; Ram et al. 2010; Sigurdsson et al. 1983]** are supported by reports of exposure to formic acid for incorrect use on treatment of warts [Sjokvist et al. 2020; Tong et al. 2015]. On the basis of these data, formic acid is assigned the **SK: DIR (COR)** notation.

4 Immune-mediated Responses (SK: SEN)

No occupational exposure studies or diagnostic patch tests in humans that evaluated the potential of formic acid to cause skin sensitization were identified. Of the predictive tests for skin sensitization (e.g., guinea pig maximization tests, Buehler test, and murine local lymph node assays), results from only one were identified. A Buehler test of guinea pigs described in an unpublished document from BASF AG (2002) was summarized in an Organisation for Economic Co-operation and Development (OECD) report [OECD 2009] for formic acid. Following the OECD TG 406 test protocol, control animals were compared with animals treated with 0.5 mL of formic acid solution applied under occlusive patch at concentrations of 7.5% and 2% during induction and challenge phases, respectively. No skin reactions were observed in either test or control animals at 24 hours or 48 hours after the challenge.

A safety assessment was performed by members of the Research Institute for Fragrance Materials [as cited in Api et al. 2020] to determine the safety of formic acid for use as an ingredient in consumer products. They summarized maximum acceptable concentrations in finished products based on nonreactive dermal sensitivity thresholds. They determined that at concentrations below 2.7% formic acid, no appreciable risk for skin sensitization existed [as cited in Api et al. 2020]. Based on the paucity of data, this assessment does not assign a SK: SEN for formic acid.

5 Summary

No studies were identified that evaluated dermal absorption of formic acid after skin exposure in humans or animals. Two cases were reported of persons who suffered profound skin lesions and physiological impairment as a consequence of domestic or industrial incidents **[Chan et al. 1995; Sigurdsson et al. 1983]**. In both cases, severe skin burns resulted in localized destruction of the dermal barrier and profound systemic effects including metabolic acidosis, intravascular hemolysis, and hemoglobinuria. Additional cases have been documented of patients suffering burns and skin corrosion following exposure to formic acid **[Chan et al. 1995; Ram et al. 2010; Sigurdsson et al. 1983]**. Based on the lack of data, a SEN notation could not be assigned.

Negative Buehler test results in guinea pigs for dilute formic acid solutions combined with the absence of any other case reports or diagnostic patch tests in humans or predictive tests in animals preclude an adequate evaluation of the skin sensitization potential of formic acid while suggesting that skin sensitization is unlikely. Therefore, on the basis of these assessments, formic acid is assigned a composite skin notation of **SK: SYS-DIR (COR)**.

Table 3 summarizes the skin hazard designations for formic acid previously issued by NIOSH and other organizations.

Table 3. Summary of the previously issued skin hazard designations for formic acid from NIOSH and other organizations

Organization	Skin hazard designation
ACGIH [2022]	No designation
ECHA [2023]	Severe skin burns and eye damage
NIOSH [2007]	No designation
OSHA [2020]	No designation

ACGIH = American Conference of Governmental Industrial Hygienists; ECHA = European Chemicals Agency; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration.

References

ACGIH® [2022]. Formic acid. In: Documentation of threshold limit values and biological exposure indices. 9th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists.

Api AM, Belmonte F, Belsito D, Biserta S, Botelho D, Bruze M, Burton GA Jr., Buschmann J, Cancellieri MA, Dagli ML, Date M, Dekant W, Deodhar C, Fryer AD, Gadhia S, Jones L, Joshi K, Lapczynski A, Lavelle M, Liebler DC, Na M, O'Brien D, Patel A, Penning TM, Ritacco G, Rodriguez-Ropero F, Romine J, Sadekar N, Salvito D, Schultz TW, Siddiqi F, Sipes IG, Sullivan G, Thakkar Y, Tokura Y, Tsang S [2020]. RIFM fragrance ingredient safety assessment, formic acid, CAS registry number 64-18-6. Food Chem Toxicol *138*(Suppl 1):111225, https://doi.org/10.1016/j.fct.2020.111225.

Balagué N, Vostrel P, Beaulieu JY, van Aaken J [2014]. Third degree formic acid chemical burn in the treatment of a hand wart: a case report and review of the literature. Springerplus *3*:408, https://doi.org/10.1186/2193-1801-3-408.

Banihashemi M, Rad AK, Yazdi SA, Rakhshande H, Ghoyonlo VM, Zabihi Z, Yousefzadeh H [2011]. Evaluation of the effect of formic acid and sodium formate on hair reduction in rat. Clin Cosmet Investig Dermatol *4*:69–72, https://doi.org/10.2147/ccid.s20531.

Bhat RM, Vidya K, Kamath G [2001]. Topical formic acid puncture technique for the treatment of common warts. Int J Dermatol *40*(6):415–419, https://doi.org/10.1046/j.1365-4362.2001.01242.x.

Chan TC, Williams SR, Clark RF [1995]. Formic acid skin burns resulting in systemic toxicity. Ann Emerg Med *26*(3):383–386, https://doi.org/10.1016/s0196-0644(95)70091-9.

ECHA [2023]. Substance Infocard: formic acid. Helsinki, Finland: European Chemicals Agency, https://echa.europa.eu/substance-information/-/substanceinfo/100.000.527.

Eriksson L, Berglind R, Sjöström M [1994]. A multivariate quantitative structure-activity relationship for corrosive carboxylic acids. Chemometr Intell Lab Syst *23*(1):235–245, https://doi.org/10.1016/0169-7439(93)E0069-G.

Faghihi G, Vali A, Radan M, Eslamieh G, Tajammoli S [2010]. A double-blind, randomized trial of local formic acid puncture technique in the treatment of common warts. Skinmed *8*(2):70–71.

IARC [2023]. IARC monographs on the evaluation of carcinogenic hazards to humans. Agents classified by the IARC monographs, Volumes 1–134. Lyon, France: World Health Organization,

International Agency for Research on Cancer, https://monographs.iarc.who.int/agents-classified-by-the-iarc/. Date accessed: July 31, 2023.

Johnson W Jr, Heldreth B, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler DC, Marks JG Jr, Shank RC, Slaga TJ, Snyder PW, Andersen FA [2016]. Safety assessment of formic acid and sodium formate as used in cosmetics. Int J Toxicol *35*(Suppl 2):41S–54S, https://doi.org/10.1177/1091581816677716.

Karunadasa KP, Perera C, Kanagaratnum V, Wijerathne UP, Samarasingha I, Kannangara CK [2010]. Burns due to acid assaults in Sri Lanka. J Burn Care Res *31*(5):781–785, https://doi.org/10.1097/bcr.0b013e3181eed228.

Lehmann P, Kligman AM [1983]. In vivo removal of the horny layer with formic acid. Br J Dermatol *109*(3):313–320, https://doi.org/10.1111/j.1365-2133.1983.tb03547.x.

Leibsch M, Döring B, Donelly TA, Logemann P, Rheins LA, Spielmann H [1995]. Application of the human dermal model skin(2) ZK 1350 to phototoxicity and skin corrosivity testing. Toxicol In Vitro *9*(4):557–562, https://doi.org/10.1016/0887-2333(95)00042-7.

NIOSH [2007]. 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.

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 (revised 2017), https://www.cdc.gov/niosh/docs/2009-147/.

NLM [no date]. PubChem: formic acid. Summary. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, U.S. National Library of Medicine, https://pubchem.ncbi.nlm.nih.gov/compound/Formic-acid. Date accessed: August 14, 2023.

NTP [2021]. Report on carcinogens. 15th ed. Research Triangle Park, NC: U.S. Department of Health and Human Services, National Toxicology Program, https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc.

OECD [2009]. Formic acid. In: OECD Existing Chemicals Database. OED HPV chemical programme. Dossier 64186 in assessment report SIDS Formates.zip. Paris, France: Organisation for Economic Co-operation and Development, https://hpvchemicals.oecd.org/UI/SIDS_Details.aspx?id=66112e92-1ab6-48d5-aa54-8ae49cb772ea.

OSHA [2020]. Formic acid. In: OSHA Occupational Chemical Database, Washington, DC: U.S. Department of Labor, Occupational Safety and Health Administration, https://www.osha.gov/chemicaldata/468.

Ram J, Sukhija J, Behera D, Gupta A [2010]. Ocular and systemic morbidity profile in mass formic acid injuries. Ophthalmic Surg Lasers Imaging *41*(1):123–127, https://doi.org/10.3928/15428877-20091230-22.

Sekizawa J, Yasuhara K, Suyama Y, Yamanaka S, Tobe M, Nishimura M [1994]. A simple method for screening assessment of skin and eye irritation. J Toxicol Sci *19*(1):25–35, https://doi.org/10.2131/jts.19.25.

Sigurdsson J, Björnsson A, Gudmundsson ST [1983]. Formic acid burn—local and systemic effects. Report of a case. Burns Incl Therm Inj *9*(5):358–361, https://doi.org/10.1016/0305-4179(83)90084-0.

Sjökvist O, Smolle C, Jensson D, Huss F [2020]. A full-thickness chemical burn to the hand using formic acid-based anti-wart treatment: a case report and literature review. Scars Burn Heal *6*:1–5, https://doi.org/10.1177/2059513119897888.

Tong E, Dorairaj J, O'Sullivan JB, Kneafsey B [2015]. Deep full thickness burn to a finger from a topical wart treatment. Ir Med J *108*(9):283–284.

U.S. EPA [1990]. Integrated Risk Information System (IRIS): formic acid (summary, archived in 2018). Washington, DC: U.S. Environmental Protection Agency, https://iris.epa.gov/ChemicalLanding/&substance_nmbr=55.

Yelon JA, Simpson RL, Gudjonsson O [1996]. Formic acid inhalation injury: a case report. J Burn Care Rehabil *17*(3):241–242, https://doi.org/10.1097/00004630-199605000-00010.