NIOSH Skin Notation Profile
Picric Acid

[CAS No. 88-89-1]

External Review Draft

September 2024

Lilia Chen
Naomi L. Hudson

U.S. Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

Disclaimer

Mention of any company or product does not constitute endorsement by the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC). In addition, citations to websites 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 websites. All web addresses referenced in this document were accessible as of the publication date.

Get More Information

Find NIOSH products and get answers to workplace safety and health questions:

1-800-CDC-INFO (1-800-232-4636) | TTY: 1-888-232-6348
CDC/NIOSH INFO: cdc.gov/info | cdc.gov/niosh
Monthly *NIOSH eNews*: cdc.gov/niosh/eNews

Suggested Citation

NIOSH [20XX]. NIOSH skin notation profile: picric acid. By Hudson NL. 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 hepatoxicity). Understanding the hazards related to skin contact with chemicals is a critical component of modern occupational safety and health programs.

In 2009, the National Institute for Occupational Safety and Health (NIOSH) published *Current Intelligence Bulletin (CIB) 61: A Strategy for Assigning New NIOSH Skin Notations* [NIOSH 2009]. 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 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 (e.g., skin permeation) by means of analytical or numerical methods.

This *Skin Notation Profile* provides the SK assignments and supportive data for picric acid. 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 skin contact with the chemicals of interest.

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

Contents

Abbreviations

ACGIH®	American Conference of Governmental Industrial Hygienists
bw	body weight
CIB	Current Intelligence Bulletin
cm	centimeter
DIR	skin notation indicating the potential for direct effects to the skin following contact with a chemical
ECHA	European Chemicals Agency
g	gram
g/kg-bw	gram(s) per kilogram per body weight
IARC	International Agency for Research on Cancer
kg	kilogram(s)
LD_{50}	dose resulting in 50% mortality in the exposed population
LD_{LO}	dermal lethal dose
mg/kg	milligram(s) per kilogram
mL	milliliter(s)
MW	molecular weight
NIOSH	National Institute for Occupational Safety and Health
NTP	National Toxicology Program
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
U.S. EPA	United States Environmental Protection Agency
µg	microgram
µg/mL	microgram(s) per milliliter

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 (*Toxicology Excellence for Risk Assessment [TERA]*) contracted by NIOSH and prepared by Bernard Gadagbui, PhD, and Andrew Maier, PhD.

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 and 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
- The following individuals contributed to the development or improvement of the skin notation profiles:
- G. Frank Gerberick, PhD, The Procter and Gamble Company, Cincinnati, OH
- Dori Germolec, PhD, National Toxicology Program, National Institute for Environmental Health Sciences, Research Triangle, NC
- Ben Hayes, MD, PhD, Division of Dermatology, Vanderbilt School of Medicine, Nashville, TN
- Jennifer Sahmel, MSc, CIH, ChemRisk, Boulder, CO
- James Taylor, MD, Industrial Dermatology, The Cleveland Clinic, Cleveland, OH

1 Introduction

1.1 General Substance Information

Chemical: Picric acid

CAS No: 88-89-1

Molecular weight (*MW*): 229.1

Molecular formula: $C_6H_3N_3O_7$

Structural formula:

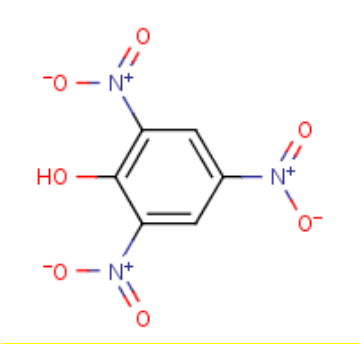

Image source: [NLM, no date]

General substance information was obtained from NIOSH [2007].

Synonyms: phenol trinitrate, 2,4,6-trinitrophenol, phenol trinitrate, picronitric acid, melinite, pertite, carbazotic acid, trinitrophenol, lyddite, shimose, phenol trinitrate, 2-hydroxy-1,3,5-trinitrobenzene

Uses: Picric acid is used in many applications, such as the making of explosives. It is also used as a component of rocket fuels; in the pharmaceutical, textile, and leather industries; in battery manufacturing; in metal etching and photographic chemicals; and as a laboratory reagent. Picric acid is usually mixed with 10%–20% water due to its explosive nature when dry [Bingham and McGowan 2012].

1.2 Purpose

This *Skin Notation Profile* presents (1) a summary of epidemiological and toxicological data associated with skin contact with picric acid and (2) the rationale behind the hazard-specific skin notation (SK) assignment for picric acid. 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 picric acid. A literature search was conducted through October 2022 to identify information on biological system/function specific effects (including reproductive and developmental effects and immunotoxicity), dermal absorption, acute toxicity, repeated-does systemic toxicity, irritation and sensitization. Information was considered from studies in humans, animals, or appropriate modeling systems that are relevant to assessing the effects of dermal exposure to picric acid.

1.3 Overview of SK Assignment for Picric Acid

Picric acid is potentially capable of causing numerous adverse health effects following skin contact. A critical review of available data has resulted in the following SK assignment for picric acid: **SK: SEN**. Table 1 provides an overview of the critical effects and data used to develop the SK assignment for picric acid.

Table 1. Summary of the SK assignment for picric acid

Skin notation	Critical effect	Available data
SK: SEN	Skin allergy (i.e., allergic contact dermatitis)	Limited animal data

2 Systemic Toxicity from Skin Exposure (SK: SYS)

No *in vivo* or *in vitro* studies evaluating toxicokinetic properties were identified that estimated the degree of absorption of picric acid through the skin of humans following dermal exposure. A historical study evaluated dog skin treated with a 5% picric acid in alcohol solution, which was then pulverized, washed, mixed with saline solution, and injected subcutaneously into live dogs. Their analysis showed substances in the dogs' urine on Days 6 and 7 that were reactive to picric acid. However, no quantitative data were provided, and the study did not describe the substances in the urine [Dennie et al. 1929]. 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.

A study evaluating evaluated dermal absorption of picric acid with animals was identified [Weeks et al. 1983]. This study measured picrate ion in the blood and urine of rabbits after 600 micrograms per kilogram (mg/kg) of picric acid was dermally applied under occluded conditions. Blood samples showed concentrations of picrate ion at 84.7, 69.7, and 0 micrograms per milliliter (µg/mL) at 6 hours, 24 hours, and 7 days, respectively. Urine concentrations of picrate ion were 12.5, 18.0, 10.3, and 1.3 µg/mL at 24, 28, 72 hours, and 7 days, respectively [Weeks et al. 1983].

No human dermal lethal doses (LD_{LO}) or dermal LD_{50} (the dose resulting in 50% mortality in exposed animals) studies were identified for picric acid. However, in 1929, Dennie et al. performed experiments on five dogs to determine lethal dose through subcutaneous injections of varying concentrations of picric acid in saline. Two dogs were given doses of 0.05 grams per kilogram of body weight (g/kg-bw) picric acid, and another two dogs were given 0.075 g/kg-bw picric acid in saline. All animals survived. The remaining dog was given subcutaneous injections of 0.1 gram (g) and 0.125 g of picric acid in saline per kg of body weight 4 days apart. This dog died [Dennie et al. 1929].

The absence of data precludes the adequate evaluation of the potential of picric acid to cause acute toxicity following dermal exposure.

No epidemiological, occupational exposure studies, or case reports, and no repeat-dose, subchronic or chronic toxicity studies in animals were identified that evaluated the potential of picric acid to cause systemic effects following dermal exposure. No toxicity or specialty studies were identified that evaluated the potential for picric acid to cause biological system/function specific effects (including reproductive and developmental effects and immunotoxicity) following dermal exposure. No epidemiological studies or animal bioassays were identified that investigated the carcinogenic potential of picric acid after dermal exposure.

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

Table 2. Summary of the carcinogenic designations for picric 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 [2020]	Inadequate information to assess carcinogenic potential

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 supporting studies evaluating toxicokinetic properties and the potential for picric acid to be absorbed through the skin and be systemically toxic were identified. No acute toxicity studies in humans or animals, epidemiological, occupational exposure studies, or case reports were identified that evaluated the potential for picric acid to be systemically toxic. A historical study by Dennie et al. [1929] indicates picric acid may be dermally absorbed and systemically toxic in large quantities; however, these data are insufficient to recommend a SYS notation. Therefore, this assessment does not assign a SK: SYS notation for picric acid.

3 Direct Effects on Skin (SK: DIR)

Historically, picric acid was used in surgery for sterilizing the skin and as an antiseptic ointment or cream (e.g., butesin picrate) to treat wounds and burns. Observations were made in the early 20th century where patients treated with picric acid solutions or butesin picrate ointment (mixture containing 63% butesin and 37% picric acid) resulted in dermatitis or erythematous, edematous, vesicular, and weeping eruptions on treated parts of the body [Fox 1932; Jackson 1930] In the 1940s and 1950s, it was reported that human contact with picric acid in the solid form resulted in distinct skin irritation and that picric acid stained the skin and the hair of workers [Schwartz 1944; Schwartz et al. 1957]; however, a detailed description of these reports was unavailable.

In animal studies, Weeks et al. [1983] exposed six rabbits to picric acid under occlusion on intact or abraded skin, which was then evaluated after 24 hours, 72 hours, and 7 days. No irritation was observed using Draize's scale for scoring skin reactions for erythema, eschar, and edema formation [Weeks et al. 1983].

Rahimi-Movaghar et al. [2008] observed no skin irritation or redness in rats when saturated picric acid solution (picric acid concentration used was not provided) was applied to the abdomen, pelvic, lower limbs, and tail postoperative once weekly, twice weekly, or every other day for 10 weeks. This study was conducted to evaluate the safety and efficacy of saturated picric acid to prevent autophagia (biting of one's own flesh) and self-mutilation in rats with spinal cord injuries [Rahimi-Moyaghar et al. 2008].

Maguire and Chase [1972] challenged sensitized guinea pigs with topically applied concentrations of 5%, 1%, 0.2%, and 0.06% picric acid in dibutyl phthalate and olive oil equally. Minor irritation was reported at the lower concentrations but was not discernable before 48 or 72 hours post application.

No human or animal *in vivo* data that evaluated the skin corrosivity of picric acid or *in vitro* tests for corrosivity using human or *in vitro* tests of skin integrity using cadaver skin

were identified. Animal studies [Rahimi-Moyaghar et al. 2008; Weeks et al. 1983] reported no skin irritation. Maguire and Chase [1972] reported minor irritation at 48 and 72 hours post-application to picric acid. These data preclude this assessment from assigning a skin notation for picric acid; therefore, this assessment does not assign a SK: DIR notation for picric acid.

4 Immune-mediated Responses (SK: SEN)

Evidence of skin sensitization following dermal exposure to picric acid has been identified in humans and animals. Picric acid is known to cause allergic contact dermatitis in the explosives industry [Hausen 1994; Schwartz 1944].

In 1929, Dennie et al. conducted skin sensitization tests on 100 students by applying a 5% alcoholic solution of picric acid on 2 squared centimeters (cm) on the skin of one arm. Four percent of the participants displayed a positive reaction. Of these, two reactions were severe and extended beyond the area of application [Dennie et al. 1929]. The researchers hypothesized that dermatitis was produced when the protein picrinate was metabolized and carried to other areas of the body. To verify this, they applied 50 mg of a 5% alcohol solution of picric acid to the intact skin of a dog. They detected and observed a positive reaction from the dog's blood to picric acid after 24 hours [Dennie et al. 1929].

Dennie et al. [1929] also reported multiple clinical observations of dermatitis on the face, hands, feet, anal, and scrotal regions when ointments containing picric acid were applied. Most skin reacted in the area where the ointment was applied, but in several cases, severely systemic reactions were observed. Because no information was provided on the other ingredients of the ointment, it is possible that other compounds may have contributed to the reactions [Dennie et al. 1929].

Another five cases of allergic dermatitis were reported after picric acid was used to treat burns or used as an analgesic. The picric acid was used in solution or in an ointment (butesin picrate) [Jackson 1930]. In all the cases, when picric acid stopped being used, the reactions subsided. Skin notations were not based on these cases since the picric acid was mixed with other compounds not listed in the article.

Several diagnostic (human patch) tests have confirmed sensitization to picric acid [Aguirre et al. 1993; Cronin 1975; Morieirty et al. 1978; Serra-Baldrich and Camarasa 1991]. In one case report, a restaurant worker applied a solution containing 1% picric acid to a burn on his hand. Afterward, a rash developed around the burn and spread to his arms [Cronin 1975]. The worker reported a similar rash during previous use of the product.

Patch test results showed a positive response to 1% picric acid in water [Cronin 1975]. Serra-Baldrich and Camarasa [1991] and Aguirre et al. [1993] reported similar circumstances of the application of a cream containing 10% picric acid and other constituents to burned skin, resulting in the development of picric acid sensitization as determined by patch testing with 1% picric acid. The patch testing was negative for the other cream components.

Morieirty et al. [1978] patch tested 536 subjects in Brazil who were suspected to have contact allergy. Patch testing was conducted with 24 contact allergens, including 5% picric acid. The study reported that 2.4% of the study population (males and females) were sensitive to picric acid [Morieirty et al. 1978].

Landsteiner and Di Somma [1940] reported the possibility of sensitization in guinea pigs following application of picric acid in oil solutions to the skin. Applications of one drop of a 5% solution of picric acid alone or butesin picrate on guinea pigs displayed dermal reactions (papulae and scaling). Of the guinea pigs receiving the application butesin picrate, eight had a positive reaction to sensitization and none were negative, and of those receiving an application of picric acid alone there were 9 guinea pigs that exhibited positive reactions to sensitization and 9 did not [Landsteiner and Di Somma 1940]. The reactions were heightened when applied to lesions caused by cantharidin, which are similar to lesions caused by burns. The authors also reported that two of six guinea pigs developed inflammation and scaling after 12 applications of two drops of 5% picric acid in a mixture of dibutyl phthalate and olive oil on the skin of the flank followed by daily intracutaneous injections of 1.0 mL of 0.1% solutions of picric acid in saline over a 2-week period [Landsteiner and Di Somma 1940]. However, a test performed 3 weeks after these applications showed that the two animals that had developed inflammation and scaling were allergic and two other animals were weakly allergic to picric acid [Landsteiner and Di Somma 1940].

Maguire and Chase [1972] and Chase and Maguire [1973, 1974] employed a "split-adjuvant" technique to investigate the skin sensitization potential of picric acid. Guinea pigs with high susceptibility to 2,4-dinitrochlrorobenzene were sensitized by injecting 2.5 µg of heat-killed tubercle bacilli in 0.05 mL paraffin oil in five intradermal sites on one flank, followed one day later by injection of 100 µg picric acid in 0.1 mL saline into each of the sites [Maguire and Chase 1972]. Animals were challenged topically with different concentrations of picric acid on Days 12, 19, 26, and 33, beginning with 1% or 5% picric acid in equal parts with dibutyl phthalate and olive oil, or with two tests of 1% and 5% picric acid [Maguire and Chase 1972]. The authors observed histological changes such as hyperkeratosis, acanthosis, and exocytosis [Maguire and Chase 1972].

Maguire and Chase [1972] also treated other groups of guinea pigs sensitized to dinitrochlorobenzene or picryl chloride using variations in the time and amount of picric acid of the split-adjuvant protocol. All 15 guinea pigs receiving 100 µg of picric acid only had mild sensitivity; however when picric acid was increased to 500 µg 9 of 16 guinea pics exhibited higher sensitivity. The authors reported that successive contact tests resulted in significant increases in the degree of hypersensitivity, with sensitivity being detected at a concentration of 0.02% [Maguire and Chase 1972]. The authors also reported that animals sensitized to picric acid gave positive contact tests with the structurally related picryl chloride (2,4,6-trinitro-1-chloro-benzene) dissolved in olive oil, indicating that picric acid cross-reacts with picryl chloride; however, animals sensitized to picryl chloride did not react to picric acid.

In a later study, Maguire and Chase [1972] and Chase and Maguire [1973] reported that picric acid was a skin sensitizer in guinea pigs and that guinea pigs sensitized with picric acid cross-reacted with picryl chloride in contact. Later, Chase and Maguire [1974] confirmed that picric acid sensitizes guinea pigs in the split-adjuvant technique, and sensitivity was boosted when additional contacts were made at intervals of 6–10 days.

Maguire [1973] tested the allergenicity of three concentrations (0.04%, 0.2%, or 1%) of picric acid in petrolatum to the clipped skin of guinea pigs. These were applied in occluded conditions on Days 1 and 2, followed by intradermal injections on either side of the sensitization site, for a total of 0.2 mL of Freund's complete adjuvant and 0.2 mL of a prospective allergen on Day 4. They received another application of picric acid on Day 7. The animals were challenged with 0.07% and 1% picric acid in dibutyl phthalate and olive oil on Day 16. [Maguire 1973]. Picric acid strongly sensitized the animals following challenges [Maguire 1973].

Several diagnostic (human patch) tests [Aguirre et al. 1993; Cronin 1975; Dennie et al. 1929; Serra-Baldrich and Camarasa 1991] indicated that picric acid is a skin sensitizer in humans. However, there is limited information in these case reports on exposure conditions.

In several predictive tests, for example, split-adjuvant techniques, application of picric acid in Freund's complete adjuvant emulsion, and others [**Chase and Maguire 1973, 1974; Landsteiner and Di Somma 1940; Maguire 1973; Maguire and Chase 1972**][*], guinea pigs developed allergic reactions following topical application of picric acid.

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

Results also indicated that picric acid cross-reacted with the structurally-related picryl chloride [Chase and Maguire 1973, 1974; Maguire and Chase 1972].

Based on the available data, this assessment concludes that picric acid induces skin sensitization in animals. Based on these available data, a **SK: SEN** notation is assigned for picric acid.

5 Summary

No studies evaluating toxicokinetic properties were identified that estimated the degree of absorption of picric acid through the skin of humans or animals following dermal exposure. No epidemiological or occupational exposure studies or case reports and no acute, repeat-dose, subchronic, or chronic toxicity studies in animals were identified that evaluated the potential for picric acid to cause acute toxicity or systemic effects following dermal exposure. Reports [Schwartz 1944; Schwartz et al. 1957] indicated that picric acid has the potential to cause skin irritation and to stain the skin; however, a detailed description of these reports was unavailable. A repeated and prolonged application of saturated solution of picric acid (dose not specified) did not produce skin irritation [Rahimi-Moyaghar et al. 2008].

Data were identified from several diagnostic (human patch) tests [Aguirre et al. 1993; Cronin 1975; Serra-Baldrich and Camarasa 1991] and predictive tests (e.g., split-adjuvant techniques, application of picric acid in Freund's complete adjuvant emulsion, and others) in animals **[Chase and Maguire 1973, 1974; Landsteiner and Di Somma 1940; Maguire 1973; Maguire and Chase 1972]** indicating that picric acid may induce skin sensitization. Based on the available data, this assessment assigns a composite skin notation of **SK: SEN** for picric acid.

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

Table 3: Summary of previous skin hazard designations for picric acid from NIOSH and other organizations

Organization	Dermal classification
ACGIH [2022]	No designation
ECHA [2023]	Skin sensitizing
NIOSH [2007]	[skin]: Potential for dermal absorption; Prevent skin contact
OSHA [2014]	[skin]: Potential for dermal absorption

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

Aguirre A, SanZde Galdeano C, Oleaga JM, Elzaguirre X, Diaz Perez JL [1993]. Allergic contact dermatitis from picric acid. Contact Dermatitis *28*(5):291–308, https://doi.org/10.1111/j.1600-0536.1993.tb03434.x.

Bingham EC, McGowan WJ, eds. [2012]. Aromatic nitro and amino compounds. In: Patty's Toxicology. 6th ed. Chapter 35, pp. 540–541. Hoboken, NJ: John Wiley & Sons, https://app.knovel.com/kn/resources/kpPTEV0011/toc?b-q=.

Chase MW, Maguire HC Jr. [1973]. Studies on the sensitization of animals with simple chemical compounds: XIV. Further studies on sensitization of guinea pigs with picric acid. Int Arch Allergy Appl Immunol *45*(4):513–542, https://doi.org/10.1159/000231098.

Chase MW, Maguire HC Jr. [1974]. Further studies on sensitization to picric acid. Monogr Allergy *8*:1–12.

Cronin E [1975]. Picric acid dermatitis. Contact Dermatitis *1*(1):64, https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1600-0536.1975.tb05327.x.

Dennie CC, McBride WL, Davis PE [1929]. Toxic reactions produced by the application of trinitrophenol (picric acid). Arch Derm Syphilol *20*(5):698–704, https://doi.org/10.1001/archderm.1929.01440050108008.

ECHA [2023]. Substance Infocard: picric acid. Helsinki, Finland: European Chemicals Agency, https://echa.europa.eu/substance-information/-/substanceinfo/100.001.696.

Fox EC [1932]. Exfoliative dermatitis from butesin picrate ointment. Arch Derm Syphilol *26*(1):44–45, https://doi.org/10.1001/archderm.1932.01450030047006.

Hausen BM [1994]. Picric acid. Contact Dermatitis *30*(1):59, https://doi.org/10.1111/j.1600-0536.1994.tb00744.x.

IARC [2023]. IARC monographs on the evaluation of carcinogenic risks to humans. Agents reviewed by the IARC monographs. Lyon, France: World Health Organization, International Agency for Research on Cancer, http://monographs.iarc.fr/ENG/Monographs/PDFs/index.phphttps://monographs.iarc.who.int/list-of-classifications/. Date accessed: July 31, 2023.

Jackson, NR [1930]. Dermatitis from picric acid solution and butesin picrate ointment. Arch Derm Syphilol *21*(1):40–41.

Landsteiner K, Di Somma AA [1940]. Studies on the sensitization of animals with simple chemical compounds: VIII. Sensitization to picric acid; Subsidiary agents and mode of sensitization. J Exp Med *72*(4):361–366, https://doi.org/10.1084/jem.72.4.361.

Maguire HC Jr. [1973]. The bioassay of contact allergens in the guinea pig. J Soc Cosmet Chem *24*:151–162.

Maguire HC Jr., Chase MW [1972]. Studies on the sensitization of animals with simple chemical compounds: XIII. Sensitization of guinea pigs with picric acid. J Exp Med *135*(2):357–375, https://doi.org/10.1084/jem.135.2.357.

Morieirty PL, Pereira C, Guimaraes NA [1978]. Contact dermatitis in Salvador, Brazil. Contact Dermatitis *4*(4):185–189, https://doi.org/10.1111/j.1600-0536.1978.tb03786.x.

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 the new NIOSH skin notations. Cincinnati, Ohio: 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: picric 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/6954. Date accessed: August 17, 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.

OSHA [2014]. OSHA technical manual: Section II: Chapter 2. Appendix A: chemicals noted for skin absorption. Washington, DC: U.S. Department of Labor, Occupational Safety and Health Administration, https://www.osha.gov/otm/section-2-health-hazards/chapter-2#Appendix_1_Skin_Absorption.

Rahimi-Movaghar V, Yazdi A, Saadat S [2008]. Saturated picric acid prevents autophagia. Acta Med Iran *46*(4):283–286, https://acta.tums.ac.ir/index.php/acta/article/view/3483/3460.

Schwartz L [1944]. Dermatitis from explosives. J Am Med Assoc *125*:186–190, https://doi.org/10.1001/JAMA.1944.02850210008002.

Schwartz L, Tulipan L, Birmingham DJ [1957]. Occupational diseases of the skin. 3rd ed., Chapter 12. Philadelphia, PA: Lea & Febiger.

Serra-Baldrich EG, Camarasa J [1991]. Allergic contact dermatitis from picric acid. Contact Dermatitis *25*(2):127, https://doi.org/10.1111/j.1600-0536.1991.tb01803.x.

U.S. EPA [2020]. Provisional peer-reviewed toxicity values for picric acid and ammonium picrate. Washington, DC: U.S. Environmental Protection Agency, EPA/690/R-20/008F, https://cfpub.epa.gov/ncea/pprtv/recordisplay.cfm?deid=349935.

Weeks MH, Asaki A, Wade J, Bongiovanni R [1983]. Health hazards associated with demilitarization products of ammonium picrate (Explosive D). In: JANNAF (Joint Army Navy NASA Air Force) safety and environmental protection subcommittee meeting. Washington, DC: U.S. Environmental Protection Agency, Health & Environmental Research Online (HERO), pp. 115–124.