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SODIUM FORMATE

(CAS #141-53-7)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: March 18, 2024

Expiration Date: March 18, 2029

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GreenScreen® Executive Summary for Sodium Formate (CAS #141-53-7)

Sodium formate is a small carboxylic acid salt that is used in personal care products as a buffering agent and preservative, and in various consumer and industrial products including paints, lacquers, varnishes, surface treatments, corrosion inhibitors, cleaning products, coloring agents, adhesives, binding agents, photographic chemicals, process regulators, tanning agents, anti-freeze agents, viscosity adjustors, flocculating agents, laboratory chemicals, and electroplating agents. It is made by reaction of sodium hydroxide and carbon monoxide heated under pressure, and also from the manufacture of pentaerythritol Sodium formate is not explosive, self-reactive, oxidizing, or flammable, and it is not a volatile organic compound (VOC).

Sodium formate was assigned a **GreenScreen Benchmark™ Score of 3** ("Use but Still Opportunity for Improvement"). This score is based on the following hazard score combinations:

- Benchmark 3c – Moderate T (Group II or II* Human)
    - Systemic Toxicity/Organ Effects incl. Immunotoxicity – single exposure (ST-s)
    - Systemic Toxicity/Organ Effects incl. Immunotoxicity – repeated exposure (ST-r)

A data gap (DG) exists for endocrine activity (E). As outlined in GreenScreen® Guidance. Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), sodium formate meets requirements for a GreenScreen Benchmark™ Score of 3 despite the hazard data gap. In a worst-case scenario, if sodium formate were assigned a High score for the data gap for endocrine activity (E), it would be categorized as a Benchmark 1 Chemical.

New Approach Methodologies (NAMs) used in this GreenScreen® include of *in vitro* assays to assess genotoxicity, and QSAR modeling to assess respiratory sensitization. The quality, utility, and accuracy of NAM predictions are greatly influenced by two primary types of uncertainties:

- Type I: Uncertainties related to the input data used
- Type II: Uncertainties related to extrapolations made

Type I (input data) uncertainties in sodium formate's NAMs dataset include lack of experimental data and lack of validated methods to assess respiratory sensitization. Sodium formate's Type II (extrapolation output) uncertainties include use of several *in vitro* assays that do not entirely mimic *in vivo* metabolism, and use of QSAR modeling to identify structural alerts for respiratory sensitization.

GreenScreen® Hazard Summary Table for Sodium Formate

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS	SnR	IrS	IrE	AA	CA	P	B	Rx	F
						s	r*	s	r*	*	*								
L	**L**	**L**	**L**	DG	**L**	**M**	*M*	**L**	**L**	**L**	**L**	**L**	**L**	**L**	*L*	**vL**	**vL**	**L**	**L**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after "repeat" for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

GreenScreen® Chemical Assessment for Sodium Formate (CAS #141-53-7)

Method Version: GreenScreen® Version 1.4
Assessment Type[1]: Certified
Assessor Type: Licensed GreenScreen® Profiler

GreenScreen® Assessment (v.1.4) Prepared By:
Name: Nancy Linde, M.S.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: January 19, 2024, March 14, 2024

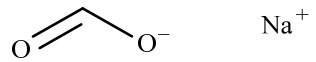
Quality Control Performed By:
Name: Jennifer Rutkiewicz, Ph.D.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: February 22, 2023, March 18, 2024

Expiration Date: March 18, 2029[2]

Chemical Name: Sodium Formate

CAS Number: 141-53-7

Chemical Structure(s):

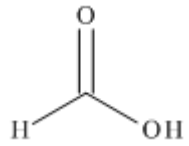


(PubChem 2024)

Also called: Formic acid, sodium salt; Salachlor; Formic acid, Na salt; Sodium formiate (PubChem 2024).

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):

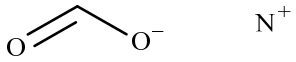
Formic acid (CAS #64-18-6), potassium hydrogen diformate (CAS #20642-05-1), ammonium formate (CAS #540-69-2), calcium formate (CAS #544-17-2), and potassium formate (CAS #590-29-4) have been evaluated in the class of formic acid and formates (OECD 2009). The formates are all expected to disocciate into formic acid and the corresponding ion in biological fluids. Therefore, as sodium, potassium, ammonium, and calcium are all ubiquitous in nature and in the human body, other formates are considered strong surrogates. It may be noted that formic acid has a lower pH which enhances its corrosivity; therefore, for some endpoints, formic acid is not a suitable surrogate.



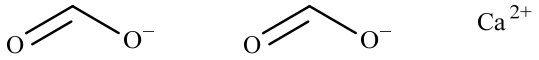
Formic acid (CAS #64-18-6)

[1] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), or "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent).
[2] Assessments expire five years from the date of completion starting from January 1, 2019. An assessment expires three years from the date of completion if completed before January 1, 2019 (CPA 2018a).

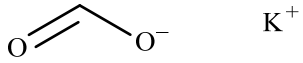
Potassium Diformate (CAS# 20642-05-1)



Ammonium formate (CAS #540-69-2),



Calcium formate (CAS #544-17-2),



Potassium formate (CAS #590-29-4)

Identify Applications/Functional Uses: (NICNAS 2020)

1. Personal care products as a buffering agent and preservative.
2. Paints, lacquers, and varnishes.
3. Surface treatments and corrosion inhibitors.
4. Cleaning products including laundry detergents.
5. Coloring agents.
6. Adhesives and binding agents.
7. Photographic chemicals.
8. Process regulators.
9. Tanning agents.
10. Anti-freeze agents.
11. Viscosity adjustors.
12. Flocculating agents.
13. Laboratory chemicals.
14. Electroplating agents.

Known Impurities[3]:

No information is available. The screen is performed on the theoretical pure substance.

GreenScreen® Summary Rating for Sodium Formate[4,5 6,7]: Sodium formate was assigned a **GreenScreen Benchmark™ Score of 3** ("Use but Still Opportunity for Improvement") (CPA 2018b). This score is based on the following hazard score combinations:

[3] Impurities of the chemical will be assessed at the product level instead of in this GreenScreen®.
[4] For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.
[5] See Appendix A for a glossary of hazard endpoint acronyms.
[6] For inorganic chemicals only, see GreenScreen® Guidance v1.4 Section 12 (Inorganic Chemical Assessment Procedure).
[7] For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen® Guidance v1.4 Annex 2.

- Benchmark 3c – Moderate T (Group II or II* Human)
    - Systemic Toxicity/Organ Effects incl. Immunotoxicity – single exposure (ST-s)
    - Systemic Toxicity/Organ Effects incl. Immunotoxicity – repeated exposure (ST-r)

A data gap (DG) exists for endocrine activity (E). As outlined in GreenScreen® Guidance (CPA 2018b) Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), sodium formate meets requirements for a GreenScreen Benchmark™ Score of 3 despite the hazard data gap. In a worst-case scenario, if sodium formate were assigned a High score for the data gap for endocrine activity (E), it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Summary Table for Sodium Formate

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS	SnR	IrS	IrE	AA	CA	P	B	Rx	F
						s	r*	s	r*	*	*								
L	**L**	**L**	**L**	DG	**L**	**M**	*M*	**L**	**L**	**L**	**L**	**L**	**L**	**L**	*L*	**vL**	**vL**	**L**	**L**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after "repeat" for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

Environmental Transformation Products

Per GreenScreen® guidance (CPA 2018b), chemicals that degrade rapidly and completely (i.e., meet criteria for a Very Low for persistence) are not likely to form persistent biodegradation intermediates because the degradation intermediates will not persist long enough to be encountered after use or release of the parent chemical (i.e., relevant). As sodium formate is readily biodegradable, it is not expected to have relevant transformation products.

Table 1: Environmental Transformation Product Summary

Life Cycle Stage	Transformation Pathway	Environmental Transformation Product	CAS #	Feasible (Yes or No)	Relevant (Yes or No)	GreenScreen® List Translator Score or GreenScreen® Benchmark™ Score[8,9]
N/A	N/A	N/A	N/A	N/A	N/A	N/A

N/A – Not Applicable.

Introduction

Sodium formate is a small carboxylic acid salt that is used in personal care products as a buffering agent and preservative, and in various consumer and industrial products including paints, lacquers, varnishes, surface treatments, corrosion inhibitors, cleaning products, coloring agents, adhesives, binding agents,

[8] The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to screen for GreenScreen Benchmark™ 1 chemicals (CPA 2018b). Pharos (Pharos 2024) is an online list-searching tool that is used to screen chemicals against the lists in the List Translator electronically.
[9] A GreenScreen® assessment of a transformation product depends on the Benchmark score of the parent chemical (see GreenScreen® Guidance).

photographic chemicals, process regulators, tanning agents, anti-freeze agents, viscosity adjustors, flocculating agents, laboratory chemicals, and electroplating agents.(NICNAS 2020). It is made by reaction of sodium hydroxide and carbon monoxide heated under pressure, and also from the manufacture of pentaerythritol (HSDB 2003).

ToxServices assessed sodium formate against GreenScreen® Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen® Hazard Assessment) (ToxServices 2021).

U.S. EPA Safer Choice Program's Safer Chemical Ingredients List

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2024a). It can be accessed at: http://www2.epa.gov/saferchoice/safer-ingredients. Chemicals on the SCIL have been assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2015). Sodium formate is on the SCIL with a full green circle, indicating it has been verified to be of low concern based on experimental and modeled data.

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen Benchmark™ 1 chemicals (CPA 2018b). Pharos (Pharos 2024) is an online list-searching tool that is used to screen chemicals against all of the lists in the List Translator electronically. ToxServices also checks the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b),[10] which are not considered GreenScreen® Specified Lists but are additional information sources, in conjunction with the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for sodium formate can be found in Appendix C.

- Sodium Formate is an LT-UNK (List Translator – Unknown) chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Sodium Formate is not listed on the U.S. DOT list.
- Sodium Formate is on the following lists for multiple endpoints (Pharos 2024, Appendix C). Specified lists for single endpoints are reported in individual hazard endpoints in the hazard assessment section below.
    - EC – CEPA DSL – Inherently Toxic to Humans (iTH)
    - German FEA – Substances Hazardous to Waters – Class 1 – Low Hazard to Waters

Hazard Statement and Occupational Control

No Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statements were identified for sodium formate, as indicated in Table 2. Additionally, the majority of notifiers in ECHA's Classification and Labeling (C&L) Inventory report that it is "not classified" (ECHA, CAS #141-53-7, 2024a). No chemical-specific recommendations for personal protective equipment (PPE) were identified; rather, generic provisions applicable to handling chemicals in general are recommended, as presented in Table 3. No occupational exposure limits (OELs) were identified which are specific to sodium formate; however, as a dust, it is subject to time weighted average (TWA) values for respirable and inhalable particles, as shown in Table 3.

[10] DOT lists are not required lists for GreenScreen® List Translator v1.4. They are reference lists only.

Table 2: GHS H Statements for Sodium Formate (CAS #141-53-7)	
H Statement	**H Statement Details**
No harmonized GHS H statements are reported by the European Chemicals Agency (ECHA). According to the majority of notifications provided to ECHA in REACH registrations, no hazards have been classified.	

Table 3: Occupational Exposure Limits and Recommended Personal Protective Equipment for Sodium Formate (CAS #141-53-7)			
Personal Protective Equipment (PPE)	**Reference**	**Occupational Exposure Limits (OEL)**	**Reference**
Wear safety glasses with side shields (or goggles). Protective gloves are not required, but rubber gloves may be used. Normal work clothes covering the legs and arms.	Perstorp 2023	ACGIH limits for PNOC: TWA: 10 mg/m^3 for inhalable particles. TWA: 3 mg/m^3 for respirable particles.	Perstorp 2023
		OSHA limits for PNOC: TWA: 15 mg/m^3 for total dust. TWA: 5 mg/m^3 for respirable fraction (vacated). TWA: 15 mg/m^3 total dust (vacated). TWA: 5 mg/m^3 respirable fraction. TWA: 15 mppcf respirable fraction TWA: 50 mppcf total dust	
		NIOSH - N/A	
		Canadian provincial limits for PNOC: Alberta, British Columbia, and Ontario: TWA: 10 mg/m^3 (inhalable) TWA: 3 mg/m^3 (respirable) Quebec: TWA: 10 mg/m^3	

Table 3: Occupational Exposure Limits and Recommended Personal Protective Equipment for Sodium Formate (CAS #141-53-7)			
Personal Protective Equipment (PPE)	**Reference**	**Occupational Exposure Limits (OEL)**	**Reference**
ACGIH: American Conference of Governmental Industrial Hygienists NIOSH: National Institute for Occupational Safety and Health PNOC: Particulates Not Otherwise Classified TWA: Time Weighted Average			

Physicochemical Properties of Sodium Formate

Sodium formate is a solid, usually present as granules or crystalline powder. It has a very low estimated vapor pressure, indicating it is unlikely to volatilize under ambient conditions. It is very soluble in water and dissociates rapidly in water into sodium and formate ions. The log K_{ow} indicates it is hydrophilic and has a low potential for bioaccumulation.

Table 4: Physical and Chemical Properties of Sodium Formate (CAS #141-53-7)		
Property	**Value**	**Reference**
Molecular formula	HCOONa	PubChem 2024
SMILES Notation	C(=O)[O-].[Na+]	PubChem 2024
Molecular weight	68.007 g/mol	PubChem 2024
Physical state	Solid	PubChem 2024
Appearance	Hygroscopic white granules, or crystalline powder	PubChem 2024
Melting point	257.8°C (OECD 102)	ECHA, CAS #141-53-7, 2024b
Boiling point	N/A – decomposes at ≥ 411°C (ASTM E 537-02)	ECHA, CAS #141-53-7, 2024b
Vapor pressure	6.57E-8 mm Hg at °C (estimated)	U.S. EPA 2017, Appendix D
Water solubility	> 1,000 g/L at 20°C (OECD 105)	ECHA, CAS #141-53-7, 2024b
Dissociation constant	pKa = 3.86 at 20°C (OECD 112)	ECHA, CAS #141-53-7, 2024b
Density/specific gravity	1.91 g/L (ISO 1183-1)	ECHA, CAS #141-53-7, 2024b
Partition coefficient	Log K_{OW} = -2.1 at pH 7 and 23°C (EU Method A.8)	ECHA, CAS #141-53-7, 2024b

Toxicokinetics

Sodium formate is absorbed from the gastrointestinal tract and is expected to dissociate into the formate and sodium ions (NICNAS 2020). It's measured dissociation constant (pKa) = 3.86 at 20°C (OECD 112) (ECHA, CAS #141-53-7, 2024), indicating rapid dissociation.

ICCA (2008) summarized that formate is a common metabolite and functions as a precursor in the biosynthesis of amino acids and nucleic acids. In studies examining the metabolism of methanol, which metabolizes to formate, elimination follows first order kinetics and formate does not bioaccumulate. Based on plasma levels, elimination half-lives are reported at 12 minutes in rats, 22 minutes in guinea pigs, 32 minutes in rabbits, 45 minutes in humans, 67 minutes in cats, 77 minutes in dogs, and 87

minutes in pigs. The differences may be attributable to species differences in the hepatic concentrations of folates and folate-dependent enzymes, which affect the rate at which formate is incorporated into other macromolecules, or the rate to which it is metabolized to carbon dioxide. It is also reported that minor quantities were excreted unchanged in the urine for all species (ICCA 2008).

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): L
Sodium formate was assigned a score of Low for carcinogenicity based on surrogate data. The surrogate potassium diformate was not carcinogenic in rats exposed orally for 2 years or mice exposed orally for 80 weeks. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate data exist and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on reliable experimental data for a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #590-29-4, 2024; OECD 2009; NICNAS 2020
  - *Oral: Surrogate: Potassium diformate (CAS #20642-05-1):* Potassium diformate was evaluated in a GLP compliant chronic toxicity study performed similar to OECD Guideline (TG) 453. Male and female Crl:HanWist(Glx:BRL)BR rats (50/sex/dose) were provided 0, 50, 400, or 2,000 mg/kg/day potassium formate (98.44-99% purity) in feed for 104 weeks. At 2,000 mg/kg, animals had decreased body weights (27% in males and 19% in females) and slightly decreased food consumption (severity not specified). Macroscopic observations identified increased incidences of raised foci and thickened walls of the stomach at ≥ 400 mg/kg/day. At ≥ 400 mg/kg/day, microscopic examinations identified basal and squamous cell hyperplasia in the limiting ridge of the stomach. Observations at 2,000 mg/kg/day included mild inflammation and foveolar epithelial hyperplasia in the stomach, Brunner's gland hypertrophy in the duodenum, and acinar cell hypertrophy in the salivary gland. No evidence of carcinogenicity in the stomach or any other tissue was reported (Klimisch 1, reliable without restrictions) (Unnamed 1999 study report).
  - *Oral: Surrogate: Potassium diformate (CAS #20642-05-1):* Potassium diformate was evaluated in a GLP compliant chronic toxicity study similar to OECD TG 453. Male and female Crl:CD-1(ICR)BR mice (51/sex/dose) were provided 0, 50, 400, or 2,000 mg/kg/day potassium formate (98.44-99% purity) in feed for 80 weeks. Body weight gain was about 15% lower in males exposed at 2,000 mg/kg/day, compared to controls. At 2,000 mg/kg/day, mucosal hyperplasia of the stomach was identified in males. No treatment-related change in incidence and nature of tumors was reported.

Mutagenicity/Genotoxicity (M) Score (H, M, or L): L
Sodium formate was assigned a score of Low for mutagenicity/genotoxicity based on surrogate data. The surrogate formic acid was not mutagenic or clastogenic in numerous *in vitro* assays or one *in vivo* mutagenicity assay. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity / genotoxicity when negative data are available for both gene mutations and chromosome aberrations, and GHS classification is not warranted (CPA 2018b). The confidence in the score is high as it is based on experimental data for a strong surrogate.

- Authoritative and Screening Lists

  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024
  - *In vitro:*
    - *Surrogate: Formic acid (CAS #64-18-6):* Formic acid was negative for mutagenicity in an Ames reverse mutation assay conducted according to OECD TG 471 (GLP status not specified). *Salmonella typhimurium* strains TA97, TA98, TA100, and TA1535 were exposed to formic acid (97.4% purity) at 0, 10, 33, 100, 333, 1,000, and 3,333 µg/plate, with and without S9 metabolic activation. Cytotoxicity was reported at ≥ 1,000 µg/plate in all strains. There were no increases in the frequency of revertants reported in any strain at any concentration with or without metabolic activation. Controls provided the expected results, and testing was performed up to cytotoxicity limits. Authors concluded the test substance was not mutagenic under the conditions of the test (Klimisch 1, reliable without restrictions) (Unnamed 1992 publication).
    - *Surrogate: Formic acid (CAS #64-18-6):* Formic acid was negative in a GLP-compliant mammalian cell gene mutation assay conducted according to OECD TG 476. Chinese hamster ovary (CHO) cells were exposed to formic acid (85.3% formic acid, 14.3% water) at concentrations of 0, 31.25, 62.5, 125, 250, and 500 µg/mL without metabolic activation, and at 0, 25, 50, 100, 200, and 400 µg/mL with S9 metabolic activation. There were no increases in mutations at the *Hprt* locus at any concentration with or without metabolic activation. The highest tested concentration was based on cytotoxicity based on relative cloning efficiency at ≥ 200 µg/mL with activation, and although no cytotoxicity was observed in cells exposed without activation, testing was conducted up to the limit concentration of 10 mM (OECD 2016). Controls provided the expected results. Authors concluded the test substance was not mutagenic under the conditions of the test (Klimisch 1, reliable without restrictions) (Unnamed 2002 study report).
    - *Surrogate: Formic acid (CAS #64-18-6):* In an *in vitro* mammalian chromosome aberration test conducted according to OECD TG 473 (GLP status not specified) CHO cells were exposed to formic acid (purity not specified) at 276, 368, 460, 552, 644, 920, 1,150, 1,266, and 1,380 µg/mL, with and without S9 metabolic activation. Cytotoxicity and an increase in aberrant cells were reported when the pH of the incubation medium was ≤ 6. When pH was adequate (7.2), no increase in aberrant cells was reported at up to 644 µg/L, and when two buffering systems were used, no increase in aberrant cells was reported at up to 920 µg/L as long as the buffer capacity was not exhausted. At the three highest concentrations, both an increase in aberrations and an increase in cytotoxicity were reported. Authors attributed the effects to low pH and high osmolarity of the medium. Similar results were reported with other (acetic and lactic) acids. As pseudo-positive results at non-physiological pH could be eliminated by neutralization of the medium or enhancement of buffer capacity, authors considered formic acid to be negative for clastogenicity (Klimisch 2, reliable with restrictions) (Unnamed 1990 publication).
  - *In vivo:*
    - *Surrogate: Formic acid (CAS #64-18-6):* Formic acid and sodium formate were evaluated in a pre-GLP sex-linked recessive lethal (SLRL) test conducted similar to OECD TG 477. Groups of male *Drosophila melanogaster* (Oregon-K strain) were exposed to the test substance at 0.1% in the feed, or as a vapor at 0.1%. For the

vapor exposures to formic acid, there was a mild but statistically significant ($p < 0.001$) increase in mutations compared to the historical controls (1.3% over 3 broods, compared to the 0.15% for historical controls). These results were not repeated when the Drosophila were exposed to neutralized formic acid, which is essentially sodium formate, as the neutralization was performed with glycine-NaOH buffer. For the feeding experiments, there were no significant increases in mutations compared to historical controls with either test substance. Based on a study of neutralized formic acid (sodium formate) with negative results at the same molar concentrations, authors concluded that effects were due to the acidic pH rather than formate, and results were considered to be negative (Klimisch 1, reliable without restrictions) (Stumm-Tegethoff BFA 1969). *ToxServices add that this test method is no longer recognized and the guideline was deleted in 2016.*

- ICCA 2008
  - *In vitro:*
    - *Surrogate: Formic acid (CAS #64-18-6):* Formic acid was negative in an SOS-Chromotest (GLP status not reported) in which *Escherichia coli* PQ37 cells were exposed to formic acid (purity not reported) up to the limit of water solubility or 100 mM with and without S9 metabolic activation. No further details were provided.
    - *Surrogate: Formic acid (CAS #64-18-6):* Formic acid was negative in a sister chromatid exchange (SCE) assay conducted similar to OECD TG 476 (GLP status not specified). Chinese hamster lung fibroblast V79 cells were exposed to formic acid (purity not specified) at concentrations of 0, 18.4, 27.6, 46.0, and 92.0 µg/mL with and without S9 metabolic activation. There was no evidence of SCE reported at any concentration with or without metabolic activation.
    - *Surrogate: Formic acid (CAS #64-18-6):* Formic acid was negative in a SCE assay conducted similar to OECD TG 476 (GLP status not specified). Human lymphocytes were exposed to formic acid (98-100% purity) at concentrations of 0.63, 1.25, 2.5, 5, and 10 mM without metabolic activation. Cytotoxicity was reported at 10 mM. Authors attributed a slight increase in SCE at the high dose to the confounding effects of pH change. No increase in SCE was reported at other concentrations, and results were considered by authors to be negative.

Reproductive Toxicity (R) Score (H, M, or L): L

Sodium formate was assigned a score of Low for reproductive toxicity based on lack of indications of reproductive toxicity in a GLP-compliant 2-generation reproductive toxicity study in rats exposed at up to 1,000 mg/kg/day (OECD TG 416). GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data exist and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on reliable measured data for the target compound.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024
  - *Oral:* Sodium formate was evaluated in a GLP-compliant 2-generation reproductive toxicity study performed according to OECD TG 416, EPA OPPTS 870.3800, and EU Method B.35. Wistar rats (25/sex/dose) were provided sodium formate (100% purity) in feed at concentrations corresponding to doses of 0, 100, 300, or 1,000 mg/kg/day, for 75 days. Exposures were started for both sexes at 2 weeks prior to mating, and continued through mating and gestation, and through postnatal day (PND) 21. There were no significant

findings based on estrous cycle, sperm measures, or reproductive parameters (mating behavior, conception, gestation, parturition, lactation and weaning, reproductive organ weight, and gross pathology) in F0 or F1 animals. There were no significant findings based on offspring viability, body weight, sexual maturation, gross pathology, or histopathology. Authors identified a NOAEL of 1,000 mg/kg/day for reproductive toxicity (Klimisch 1, reliable without restrictions) (Unnamed 2007-2008 study report).

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): L
Sodium formate was assigned a score of Low for developmental toxicity based on lack of indications of developmental toxicity in a in a GLP-compliant 2-generation reproductive toxicity study (OECD TG 416, EPA OPPTS 870.3800, and EU Method B.35) in rats and prenatal developmental toxicity studies (OECD TG 414) in rats and rabbits. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when adequate data exist and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on measured data for the target compound in two different species.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024
  - *Oral:* Sodium formate was evaluated in a GLP-compliant 2-generation reproductive toxicity study performed according to OECD TG 416, EPA OPPTS 870.3800, and EU Method B.35. Wistar rats (25/sex/dose) were provided sodium formate (100% purity) in feed at concentrations corresponding to 0, 100, 300, or 1,000 mg/kg/day, for 75 days. Exposures were started for both sexes at 2 weeks prior to mating, and continued through mating and gestation, and through PND 21. There were no significant findings based on estrous cycle, sperm measures, or reproductive parameters (mating behavior, conception, gestation, parturition, lactation and weaning, reproductive organ weight, and gross pathology) in F0 or F1 animals. There were no significant findings based on offspring viability, postnatal survival, body weight, sexual maturation, gross pathology, or histopathology. Authors identified a NOAEL of 1,000 mg/kg/day for developmental toxicity (Klimisch 1, reliable without restrictions) (Unnamed 2007-2008 study report).
  - *Oral*: Sodium formate was evaluated in a GLP compliant prenatal developmental toxicity study performed according to OECD TG 414. Pregnant Himalayan rabbits (25/dose) were administered sodium formate (100% purity) via gavage in water at 0, 100, 300, or 1,000 mg/kg/day on gestation days (GD) 6-28. There were no significant findings based on fetal weight, sex distribution, placenta weight, pre- and post-implantation loss, or external, soft tissue, or skeletal malformations. Authors identified a NOAEL of 1,000 mg/kg/day for developmental toxicity (Klimisch 1, reliable without restrictions) (Unnamed 2007-2008 study report).
  - *Oral*: Sodium formate was evaluated in a GLP compliant prenatal developmental toxicity study performed according to OECD TG 414, EU Method B.31, and EPA OPPTS 870.3700. Pregnant Wistar rats (25/dose) were administered sodium formate (> 99% purity) via gavage in water at 0, 59, 236, 945 mg/kg/day on GD 6-19. Dams were sacrificed on GD 20. There were no significant findings based on maternal toxicity, embryo/fetal toxicity, or teratogenicity at any dose. There were no significant findings based on sex distribution, weight of placenta, or fetal weight. Authors identified a NOAEL of 945 mg/kg/day for

developmental toxicity (Klimisch 1, reliable without restrictions) (Unnamed 2005 study report).

Endocrine Activity (E) Score (H, M, or L): DG
Sodium formate was assigned a score of Data Gap for endocrine activity based on lack of data. While there are no identified effects of the endocrine system, or other adverse effects plausibly related to endocrine activity across numerous studies, no data were found that specifically examine endocrine system function and/or endocrine activity *in vitro* and/or *in vivo*.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024
  - *Oral:* Sodium formate was evaluated in a GLP-compliant 2-generation reproductive toxicity study performed according to OECD TG 416, EPA OPPTS 870.3800, and EU Method B.35. Wistar rats (25/sex/dose) were provided sodium formate (100% purity) in feed at concentrations corresponding to 0, 100, 300, or 1,000 mg/kg/day, for 75 days. Exposures were started for both sexes at 2 weeks prior to mating, and continued through mating and gestation, and through PND 21. There were no significant effects on sperm parameters, estrous cycle, sexual maturation (based on vaginal opening and preputial separation), or sex ratio (Klimisch 1, reliable without restrictions) (Unnamed 2007-2008 study report).
- U.S. EPA 2024b
  - Sodium formate was predicted to be inactive for estrogen receptor agonism, antagonism, and binding by the ToxCast CERAPP Potency Level (From Literature) model (Appendix E).

<u>Group II and II* Human Health Effects (Group II and II* Human)</u>
Note: Group II and Group II* endpoints are distinguished in the v 1.4 Benchmark system (the asterisk indicates repeated exposure). For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints. See GreenScreen® Guidance v1.4, Annex 2 for more details.

Acute Mammalian Toxicity (AT) (Group II) Score (vH, H, M, or L): L
Sodium formate was assigned a score of Low for acute toxicity based on acute oral and dermal LD_{50} values for sodium formate, and other formate salts that are consistently > 2,000 mg/kg. For the inhalation route of exposure, the LC_{50} for sodium formate was > 0.67 mg/L, the highest concentration tested, and the surrogate potassium diformate has a 4-hour LC_{50} > 5.16 mg/L. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD_{50} values are > 2,000 mg/kg, and when the 4-hour LC_{50} value of a mist is > 5 mg/L (CPA 2018b). The confidence in the score is high based on numerous studies for the target compound and its closest surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2009
  - *Oral*: The mouse oral LD_{50} = 11,200 mg/kg (no further details provided).
  - *Oral: <u>Surrogate: Ammonium formate (CAS #540-69-2):</u>* In an acute toxicity study performed according to OECD TG 423, Wistar rats (6 females) were administered a single dose of

ammonium formate at 2,000 mg/kg (gavage and vehicle not specified). There were no deaths, and the LD_{50} was reported at > 2,000 mg/kg (Frey-Tox GmbH 2006).
    - *Oral: Surrogate: Ammonium formate (CAS #540-69-2):* The mouse oral LD_{50} for ammonium formate is reported at 2,250 mg/kg (no further details provided) (Malorny 1969).
    - *Oral: Surrogate: Calcium formate (CAS #544-17-2):* Ten male Wistar rats were administered calcium formate at 1,000, 2,000, 3,100, 3,500, 3,800, and 4,000 mg/kg. The LD_{50} was reported at 3,050 mg/kg (no further details provided) (Bayer AG 1978).
    - *Oral: Surrogate: Calcium formate (CAS #544-17-2):* The mouse oral LD_{50} for calcium formate is reported at 1,920 mg/kg (no further details provided) (Malorny 1969).
    - *Oral: Surrogate: Potassium hydrogen diformate (CAS #20642-05-1):* Ten Crl:CD.BR rats (males and females) were administered potassium hydrogen diformate at 2,000 mg/kg in 0.5% hydroxypropyl methylcellulose in an acute toxicity study performed according to OECD 401. The LD_{50} was reported at > 2,000 mg/kg (no further details provided) (Covance 1998).
    - *Oral: Surrogate: Potassium formate (CAS #590-29-4):* The mouse oral LD_{50} for potassium formate is reported at 5,500 mg/kg (no further details provided) (Malorny 1969).
    - *Dermal:* In a GLP-compliant acute dermal toxicity study conducted according to OECD TG 402, male and female Wistar rats (10/sex/dose) were administered 2,000 mg/kg sodium formate (100% purity) applied to clipped skin, under occlusion, for 24 hours. Animals were observed for 14 days post-administration. No mortality occurred and the LD_{50} was > 2,000 mg/kg (BASF AG 2007).
    - *Inhalation*: Sprague-Dawley rats (6/sex) were exposed to sodium formate as aerosol for 4 hours at 10 mg/L (nominal), equivalent to 0.67 mg/L (measured) in a study conducted similar to OECD TG 403. The average mass median aerodynamic diameter (MMAD) was 5.4 +/- 2.4 µm. There were no deaths and the 4-hour LC_{50} was reported at > 0.67 mg/L (measured) (Klimisch 2, reliable with restrictions) (Biodynamics 1990a).
    - *Inhalation: Surrogate: Potassium diformate (CAS #20642-05-1):* Wistar-derived rats (5/sex) were exposed to potassium diformate as aerosol for 4 hours in a nose-only inhalation chamber, at 5.16 mg/L in a GLP-compliant study performed according to OECD TG 403. The concentration in air was aerosolized using a nebulizer, and the MMAD was measured at 3.25 µm. There were no mortalities, and the 4-hour LC_{50} was assigned at > 5.16 mg/L (Klimisch 1, reliable without restrictions) (TNO 1997).
- ECHA, CAS #544-17-2
    - *Oral: Surrogate: Calcium diformate (CAS #544-17-2):* Calcium diformate was evaluated in an acute oral toxicity study performed similar to OECD TG 401. Wistar rats were administered calcium diformate by gavage in water at 1,000, 2,000, 3,100, 3,500, 3,800, and 4,000 mg/kg (10 males per dose). The post-administration observation period was 14 days. Mortality occurred at ≥ 2,000 mg/kg, and the LD_{50} was 3,050 mg/kg (no further details provided) (Klimisch 3, not reliable, based on limited reporting) (Bayer, 1978). *ToxServices notes that while authors of the REACH dossier assigned a Klimisch 3 rating to this study, it is at least as well summarized as those in the IUCLID report (ECB 2000) and SIDS report (OECD 2009). Therefore, it is considered in the weight of evidence.*
    - *Oral: Surrogate: Calcium diformate (CAS #544-17-2):* Calcium diformate was evaluated in an acute oral toxicity performed similar to OECD TG 401. Wistar rats were administered calcium diformate by gavage in water at 0, 2,000, 2,520, 3,180, 3,980, and 5,000 mg/kg (5/sex/dose). The post-administration observation period was 14 days. Mortalities occurred at ≥ 2,000 mg/kg, and the LD_{50} was calculated at 2,560 mg/kg (no

further details provided) (Klimisch 4, not assignable, as the study report was unavailable) (Degussa, 1979). *ToxServices notes that while authors of the REACH dossier assigned a Klimisch 4 rating to this study, it is at least as well summarized as those in the IUCLID report (ECB 2000) and SIDS report (OECD 2009). Therefore, it is considered in the weight of evidence.*

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-single) (Group II) Score (vH, H, M, or L): M

Sodium formate was conservatively assigned a Moderate score for systemic toxicity (single dose) based on evidence of respiratory tract irritation, including respiratory depression and bleeding in the lungs, at 5.16 mg/L in an acute inhalation toxicity study with the surrogate potassium diformate, and nasal discharge in an inhalation study with sodium formate. This corresponds to GHS Category 3 classification. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity / organ effects data support classification to GHS Category 3 (CPA 2018b). The confidence in the score is high as the classification is based on experimental data on a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.

It may be noted that all of the following studies are also summarized above under the acute toxicity section, and below under neurotoxicity – single dose:

- OECD 2009
  - *Oral: Surrogate: Ammonium formate (CAS #540-69-2):* In an acute toxicity study performed according to OECD TG 423, Wistar rats (6 females) were administered a single dose of ammonium formate at 2,000 mg/kg (gavage and vehicle not specified). Piloerection and hunched posture were observed immediately after dosing but there were no corresponding pathological findings at study termination (Frey-Tox GmbH 2006).
  - *Oral: Surrogate: Calcium formate (CAS #544-17-2):* Ten male Wistar rats were administered calcium formate at 1,000, 2,000, 3,100, 3,500, 3,800, and 4,000 mg/kg. Clinical observations included sedation, increased diuresis, and reduced general state. The LD_{50} was reported at 3,050 mg/kg (no further details provided) (Bayer AG 1978).
  - *Oral: Surrogate: Potassium hydrogen diformate (CAS #20642-05-1):* Ten Crl:CD.BR rats (males and females) were administered potassium hydrogen diformate at 2,000 mg/kg in 0.5% hydroxypropyl methylcellulose in an acute toxicity study performed according to OECD 401. Lethargy, piloerection, and tachypnea (rapid and shallow breathing) were reported. The LD_{50} was reported at > **2,000** mg/kg (no further details provided) (Covance 1998). *ToxServices notes that tachypnea may or may not be indicative of transient narcotic effects and/or general malaise. Additionally, as there was only a single dose, and no controls, this study is insufficient to assign GHS classification.*
  - *Dermal*: In a GLP-compliant acute dermal toxicity study conducted according to OECD TG 402, male and female Wistar rats (10/sex/dose) were administered 2,000 mg/kg sodium formate (100% purity) applied to clipped skin, under occlusion, for 24 hours. Animals were observed for 14 days post-administration. No mortality occurred and there were no clinical signs of toxicity. Females had reduced body weight gain during the first week of observation, but recovered during the second week. No macroscopic abnormalities were reported at necropsy (BASF AG 2007).
  - *Inhalation*: Sprague-Dawley rats (6/sex) were exposed to sodium formate as aerosol for 4 hours at 10 mg/L (nominal), equivalent to 0.67 mg/L (measured) in a study conducted similar to OECD TG 403. The average mass median aerodynamic diameter (MMAD) was

5.4 +/- 2.4 µm. There were no deaths and the 4-hour LC_{50} was reported at > 0.67 mg/L (measured). Mild clinical signs were reported including closed eyes, lacrimation, nasal discharge, slight and transient reduction in body weight gain; however, all effects subsided within one week, and there were no significant findings based on necropsy (Klimisch 2, reliable with restrictions) (Biodynamics 1990a).

- *Inhalation: Surrogate: Potassium diformate (CAS #20642-05-1):* Wistar-derived rats (5/sex) were exposed to potassium diformate as aerosol for 4 hours in a nose-only inhalation chamber, at 5.16 mg/L in a GLP-compliant study performed according to OECD TG 403. The concentration in air was aerosolized using a nebulizer, and the MMAD was measured at 3.25 µm. Signs of toxicity included severe respiratory depression in all rats throughout exposure, piloerection, moderate sluggishness in all animals, rales, blepharospasms (involuntary tight closure of the eyelids), and decreased body weight gain. Necropsy findings included discoloration and bleeding in the lungs, and air-filled, soft cecum in most animals. There were no mortalities, and the LC_{50} was assigned at >5.16 mg/L (Klimisch 1, reliable without restrictions) (TNO 1997). ***ToxServices conservatively assigned GHS Category 3 for this study based on respiratory tract irritation at a sublethal concentration.***

- ECHA, CAS #544-17-2
  - *Oral: Surrogate: Calcium diformate (CAS #544-17-2):* Calcium diformate was evaluated in an acute oral toxicity study performed similar to OECD TG 401. Wistar rats were administered calcium diformate by gavage in water at 1,000, 2,000, 3,100, 3,500, 3,800, and 4,000 mg/kg (10 males per dose). The post-administration observation period was 14 days. There were no clinical signs or mortality in animals at 1,000 mg/kg. Mortality, sedation, increased diuresis, and reduced general state were noted in the dose groups at ≥ 2,000 mg/kg. The LD_{50} was 3,050 mg/kg (no further details provided) (Klimisch 3, not reliable, based on limited reporting) (Bayer, 1978). *ToxServices notes that while authors of the REACH dossier assigned a Klimisch 3 rating to this study, it is at least as well summarized as those in the IUCLID report (ECB 2000) and SIDS report (OECD 2009). Therefore, it is considered in the weight of evidence.*

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-repeat) (Group II*) Score (H, M, or L): *M*

Sodium formate was conservatively assigned a score of Moderate for systemic toxicity / organ effects (repeated dose) based on surrogate data for the inhalation route of exposure. Two subchronic inhalation exposure studies in rats and mice exposed to the surrogate formic acid each resulted in LOAEC values of 0.174 mg/L based on histopathological changes to the respiratory tract. LOAEC values for aerosols (mists) in the range of > 0.02 and ≤ 0.2 mg/L correspond to GHS Category 2. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity / organ effects (repeated dose) when adequate data exist and GHS Category 2 classification is warranted (CPA 2018b). The confidence in the score is low because the effects on the respiratory tract may be attributed to irritation, and the surrogate formic acid is likely to be a stronger irritant than its salts. It may be noted that oral exposure data do not warrant GHS classification.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ICCA 2008
  - Rodent studies must be interpreted with caution, as rodents have high tetrahydrofolate and 10-formyl tetrafolate dehydrogenase levels that allow them to rapidly metabolize formic acid to CO_2. Humans have much lower levels of these enzymes and may be more sensitive to

formate.

- ECHA, CAS #141-53-7, 2024
    - *Oral*: *Surrogate: Potassium diformate (CAS #20642-05-1):* Potassium diformate was evaluated in a GLP compliant chronic toxicity study performed similar to OECD TG 453. Male and female Crl:HanWist(Glx:BRL)BR rats (50/sex/dose) were provided 0, 50, 400, or 2,000 mg/kg/day potassium formate (98.44-99% purity) in feed for 104 weeks. At 2,000 mg/kg, animals had decreased body weights (27% in males and 19% in females) and slightly decreased food consumption (severity not specified). Macroscopic observations identified increased incidences of raised foci and thickened walls of the stomach at ≥ 400 mg/kg/day. At ≥ 400 mg/kg/day, microscopic examinations identified basal and squamous cell hyperplasia in the limiting ridge of the stomach. Observations at 2,000 mg/kg/day included mild inflammation and foveolar epithelial hyperplasia in the stomach, Brunner's gland hypertrophy in the duodenum, and acinar cell hypertrophy in the salivary gland. No evidence of carcinogenicity in the stomach or any other tissue was reported. Authors identified a NOAEL of 400 mg/kg/day for both systemic and local toxicity based on reduced body weights and pathological changes at the high dose (Klimisch 1, reliable without restrictions) (Unnamed 1999 study report).
    - *Oral*: *Surrogate: Potassium diformate (CAS #20642-05-1):* Potassium diformate was evaluated in a GLP-compliant subchronic toxicity study conducted according to OECD TG 408. Crl:CDBR rats (10/sex/dose) were provided potassium diformate (purity not specified) in feed at 0, 600, 1,200, and 3,000 mg/kg/day, for 90 days. Satellite groups of control and high dose animals were similarly exposed, and were retained for a 4 week recovery period. There were no significant findings based on clinical signs of toxicity, mortality, or ophthalmoscopic examinations. Body weight was significantly reduced in a dose-dependent manner in males at ≥ 600 mg/kg/day, and in females at 3,000 mg/kg/day. Severity of the decreased body weights was not reported; however, the effects were noted to correspond with decreased food consumption. Some hematological and clinical chemistry parameters were significantly altered at the high dose but the authors did not consider them to be toxicologically significant due to the small magnitude of changes and lack of target organ toxicity. Localized effects (squamous cell hyperplasia) were reported in the stomachs at all doses and the authors considered them to be a response to irritation. No evidence of systemic toxicity was reported. Authors identified a LOAEL of 600 mg/kg/day for local effects, and a NOAEL of 3,000 mg/kg/day for systemic effects (Klimisch 1, reliable without restrictions) (Unnamed 1998 study report).
- HCN 2005, OECD 2009, U.S. EPA 2010, and ECHA, CAS #64-18-6, 2024
    - *Inhalation*: *Surrogate*: *Formic acid (CAS #64-18-6):* Formic acid was evaluated in a 13-week GLP-compliant inhalation toxicity study conducted according to OECD TG 413 by the National Toxicology Program (NTP). Fischer 344 rats (10/sex/dose) were administered 0, 0.015, 0.030, 0.061, 0.122, or 0.244 mg/L formic acid (95% formic acid, 5% water) vapor via whole body inhalation, 5 days/week, 6 hours/day (equivalent to 0, 0.011, 0.021, 0.044, 0.087, or 0.174 mg/L after accounting for 5 days/week exposure[11]). No mortality, clinical signs of toxicity, or effects on body weight were reported. There were no treatment-related toxicologically significant effects on hematology, clinical chemistry, or absolute/relative organ weights. At necropsy, no abnormal gross lesions were reported. The incidence of histopathological changes (squamous metaplasia of the respirators epithelium and degeneration of olfactory epithelium) was increased at the highest dose. Authors identified a NOAEC and **LOAEC** of 0.122 and 0.244 mg/L (0.087 and **0.174 mg/L** after accounting for

[11] 0.015 mg/L * 5 days/7 days = 0.01 mg/L/6h/day

5 days/week exposure) for local effects **based on histopathological changes to the respiratory tract** (Klimisch 1, reliable without restrictions) (Unnamed 1989 publication).

- The U.S. EPA (2010) used this study as the key study to derive its pRfD for formic acid, and identified the low dose of 0.015 mg/L as a LOAEC, stating that neutropenia and increased serum alkaline phosphatase were noted at higher concentrations. The U.S. EPA noted that the toxicological significance of decreased neutrophil counts is unclear, but concluded that the study indicates the potential for airborne exposure to formic acid to produce adverse effects on neutrophils. *ToxServices notes that the pRfD is "provisional" and has not been adopted. Additionally, decreased neutropenia was observed only at the lowest dose, and in the absence of corresponding adverse pathological effects, is quite possibly a spurious finding. Furthermore, although the increased serum alkaline phosphatase was noted at all dose levels, it was not dose-dependent, the severity was not reported, and in the absence of corresponding pathological findings or evidence of a functional deficit, may also be a spurious finding. Accordingly, ToxServices does not consider these findings to be toxicologically relevant; they are summarized for completeness, but are not included in the weight of evidence.*

- *Inhalation: Surrogate: Formic acid (CAS #64-18-6):* In a 13-week GLP-compliant inhalation toxicity study conducted according to OECD TG 413 by NTP, male and female B6C3F1 mice (10/sex/dose) were administered 0, 0.015, 0.030, 0.061, 0.122, or 0.244 mg/L formic acid (95% formic acid, 5% water) vapor via whole body inhalation 5 days/week, 6 hours/day (equivalent to 0, 0.011, 0.021, 0.044, 0.087, or 0.174 mg/L, respectively, after accounting for 5 days/week exposure). No treatment-related mortality or clinical signs of toxicity were reported. Body weight gain was significantly reduced in both sexes of the high dose from day 42 onwards. Terminal body weights in males and females were 84% and 80% of that of controls, respectively. Liver weights were slightly increased in males of the 0.061 and 0.122 mg/L (0.044 and 0.087 mg/L after accounting for 5 days/week exposure) dose groups. A few cases of minimal degeneration of the olfactory epithelium were reported. A NOAEC and **LOAEC** of 0.122 and 0.244 mg/L (0.087 and **0.174 mg/L** after accounting for 5 days/week exposure) for local effects was identified by the authors **based on histopathological changes to the respiratory tract.**

- HCN 2005
  - *Oral*: *Surrogate*: *Formic acid (CAS #64-18-6):* In a subchronic oral toxicity study in rats (sex and strain not specified), animals (3-6/dose) were administered 8-360 mg/kg/day formic acid in drinking water for 2-27 weeks. No signs of toxicity or effects on body weight were reported at up to 160 mg/kg/day for 15 weeks, but in rats administered 160 mg/kg/day for 17 weeks followed by 360 mg/kg/day for 90 weeks, body weight and food consumption were decreased. ToxServices identified a NOAEL of 160 mg/kg/day for this study.

Neurotoxicity (single dose, N-single) (Group II) Score (vH, H, M, or L): *L*

Sodium formate was assigned a score of Low for neurotoxicity (single dose) based on lack of frank indications of neurotoxic effects at acute oral and dermal doses greater than 2,000 mg/kg. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (single dose) when adequate data exist and GHS classification is not warranted based on a lack of effects up to 2,000 mg/kg in acute oral and dermal studies (CPA 2018b). While there are numerous acute toxicity studies for the target compound and other formate salts, the confidence in the score is low due to limited reporting, and because the available studies rely only on clinical observations and gross necropsy, with no assessment of cognitive behavior, motor skills, reflexes, strength, or other neurotoxic parameters.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.

It may be noted that all of the following studies are also summarized above under the acute toxicity and systemic toxicity/organ effects – single dose sections:

- OECD 2009
    - *Oral:* *Surrogate: Ammonium formate (CAS #540-69-2):* In an acute toxicity study performed according to OECD TG 423, Wistar rats (6 females) were administered a single dose of ammonium formate at 2,000 mg/kg (gavage and vehicle not specified). Piloerection and hunched posture were observed immediately after dosing but there were no corresponding pathological findings at study termination (Frey-Tox GmbH 2006).
    - *Oral:* *Surrogate: Calcium formate (CAS #544-17-2):* Ten male Wistar rats were administered calcium formate at 1,000, 2,000, 3,100, 3,500, 3,800, and 4,000 mg/kg. Clinical observations included sedation, increased diuresis, and reduced general state. The LD_{50} was reported at **3,050** mg/kg (no further details provided) (Bayer AG 1978). *ToxServices notes that the details are insufficient to discern if the observed sedation may or may not be an indicator of a transient narcotic effect.*
    - *Surrogate: Potassium hydrogen diformate (CAS #20642-05-1):* Ten Crl:CD.BR rats (males and females) were administered potassium hydrogen diformate at 2,000 mg/kg in 0.5% hydroxypropyl methylcellulose in an acute toxicity study performed according to OECD 401. Lethargy, piloerection, and tachypnea (rapid and shallow breathing) were reported. The LD_{50} was reported at > 2,000 mg/kg (no further details provided) (Covance 1998). *ToxServices notes that tachypnea may or may not be indicative of transient narcotic effects, general malaise, and/or respiratory tract irritation. Additionally, as there was only a single dose, and no controls, this study is insufficient to assign GHS classification.*
    - *Dermal:* In a GLP-compliant acute dermal toxicity study conducted according to OECD TG 402, male and female Wistar rats (10/sex/dose) were administered 2,000 mg/kg sodium formate (100% purity) applied to clipped skin, under occlusion, for 24 hours. Animals were observed for 14 days post-administration. No mortality occurred and there were no clinical signs of toxicity. Females had reduced body weight gain during the first week of observation, but recovered during the second week. No macroscopic abnormalities were reported at necropsy (BASF AG 2007).
    - *Inhalation*: Sprague-Dawley rats (6/sex) were exposed to sodium formate as aerosol for 4 hours at 10 mg/L (nominal), equivalent to 0.67 mg/L (measured) in a study conducted similar to OECD TG 403. The average mass median aerodynamic diameter (MMAD) was 5.4 +/- 2.4 µm. There were no deaths and the 4-hour LC_{50} was reported at > 0.67 mg/L (measured). Mild clinical signs were reported including closed eyes, lacrimation, nasal discharge, slight and transient reduction in body weight gain; however, all effects subsided within one week, and there were no significant findings based on necropsy (Klimisch 2, reliable with restrictions) (Biodynamics 1990a).
    - *Inhalation:* *Surrogate: Potassium diformate (CAS #20642-05-1):* Wistar-derived rats (5/sex) were exposed to potassium diformate as aerosol for 4 hours in a nose-only inhalation chamber, at 5.16 mg/L in a GLP-compliant study performed according to OECD TG 403. The concentration in air was aerosolized using a nebulizer, and the MMAD was measured at 3.25 µm. Signs of toxicity included severe respiratory depression in all rats throughout exposure, piloerection, moderate sluggishness in all animals, rales, blepharospasms (involuntary tight closure of the eyelids), and decreased body weight gain. Necropsy findings included discoloration and bleeding in the lungs, and air-filled, soft cecum in most

animals. There were no mortalities, and the LC_{50} was assigned at >5.16 mg/L (Klimisch 1, reliable without restrictions) (TNO 1997).

- ECHA, CAS #544-17-2
  - *Oral: Surrogate: Calcium diformate (CAS #544-17-2):* Calcium diformate was evaluated in an acute oral toxicity study performed similar to OECD TG 401. Wistar rats were administered calcium diformate by gavage in water at 1,000, 2,000, 3,100, 3,500, 3,800, and 4,000 mg/kg (10 males per dose). The post-administration observation period was 14 days. There were no clinical signs or mortality in animals at 1,000 mg/kg. Mortality, sedation, increased diuresis, and reduced general state were noted in the dose groups at ≥ 2,000 mg/kg. The LD_{50} was 3,050 mg/kg (no further details provided) (Klimisch 3, not reliable, based on limited reporting) (Bayer, 1978). *ToxServices notes that while authors of the REACH dossier assigned a Klimisch 3 rating to this study, it is at least as well summarized as those in the IUCLID report (ECB 2000) and SIDS report (OECD 2009). Therefore, it is considered in the weight of evidence.*

Neurotoxicity (repeated dose, N-repeated) (Group II*) Score (H, M, or L): DG
Sodium formate was assigned a score of Data Gap for neurotoxicity (repeated dose) based on lack of data. Specifically, none of the available repeated dose toxicity studies performed analyses for neurotoxicity beyond what would be observed in clinical observations and/or gross necropsy, such as cognitive behavior, motor activity, reflexes, and/or strength. Therefore, the data are insufficient to assign a hazard rating.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- No data were identified.

Skin Sensitization (SnS) (Group II*) Score (H, M, or L): L
Sodium formate was assigned a score of Low for skin sensitization based on surrogate data. There were no indications of skin sensitization in a guinea pig maximization test (OECD TG 406) in animals treated with potassium diformate. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data exist and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on reliable experimental data for a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024
  - *Surrogate: Potassium formate (CAS #20642-05-1):* Potassium formate was evaluated in a GLP compliant guinea pig maximization test performed according to OECD TG 406. Female Dunkin-Hartley guinea pigs (20 test animals and 10 control animals) were induced via intradermal injection at 0.5% on day 1, and epicutaneous administration at 15% in Vaseline on day 8. The challenge application was applied at 5 or 10% epicutaneously in Vaseline on day 22. There were no positive indications of skin sensitization in either challenge group, although there were numerous animals with slight erythema and/or desquamation. Control substance gave the expected results. The observed erythema and desquamation indicate the test substance was evaluated at up to irritating concentrations, in accordance with the guideline. Authors concluded the test substance was not sensitizing under the conditions of the test (Klimisch 1, reliable without restrictions) (Unnamed 1998

study report).

Respiratory Sensitization (SnR) (Group II*) Score (H, M, or L): *L*
Sodium formate was assigned a score of Low for respiratory sensitization based on extrapolation from skin sensitization data, combined with lack of structural alerts, and lack of human case studies indicating respiratory sensitization. Guidance from ECHA recommends that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when adequate data exist and GHS classification is not warranted (CPA 2018b). The confidence in the score is low as this evaluation does not account for possible non-immunologic mechanisms of respiratory sensitization, and no specific data are available.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2023
  - Sodium formate does not contain any structural alerts for respiratory sensitization (Appendix F).
- The guidance from ECHA states that the mechanisms leading to respiratory sensitization are essentially similar to those leading to skin sensitization (ECHA 2017). ECHA recommended that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. ECHA also noted that this rationale does not cover respiratory hypersensitivity caused by non-immunological mechanisms, for which human experience is the main evidence of activity (ECHA 2017). As the surrogate potassium formate was not sensitizing to the skin (see skin sensitization section above), and a literature search did not find any human evidence of respiratory sensitization by sodium formate, and sodium formate does not contain any structural alerts for respiratory sensitization (OECD 2023, Appendix F), sodium formate is not expected to be a respiratory sensitizer.

Skin Irritation/Corrosivity (IrS) (Group II) Score (vH, H, M, or L): L
Sodium formate was assigned a score of Low for skin irritation/corrosivity based on minimal irritation, below the threshold for GHS classification, that was observed in a GLP-compliant study (OECD TG 404). GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate data exist and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on reliable data for the target compound.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024
  - Sodium formate was evaluated in a GLP-compliant acute dermal irritation / corrosion test performed according to OECD TG 404. Rabbits (strain not specified) were administered the test substance (97% purity) at 500 mg in water, applied to shaved skin under semi-occlusion for 4 hours (3 animals). The test sites were rinsed after the 4-hour exposure period, and the animals were observed for 72 hours post-administration. The mean scores for erythema at 24, 48, and 72 hours post-administration was 0 in all three animals. The mean scores for edema at 24, 48, and 72 hours post-administration were 0.33 (based on a score of 1 at 24 hours, which was fully reversed by 48 hours), 0, and 0 in each of the three animals, respectively. Authors of the REACH dossier concluded the test substance was not irritating under the conditions of the test, and GHS classification is not warranted (Klimisch 1,

reliable without restrictions) (Unnamed 1988 study report).

Eye Irritation/Corrosivity (IrE) (Group II) Score (vH, H, M, or L): L
Sodium formate was assigned a score of Low for eye irritation/corrosivity based on based on minimal irritation, below the threshold for GHS classification, that was observed in a GLP-compliant study (OECD TG 405 and EU Method B.5). GreenScreen® criteria classify chemicals as a Low hazard for eye irritation/corrosivity when adequate data exist and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on reliable data for the target compound.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024
  - Sodium formate was evaluated in a GLP-compliant acute eye irritation / corrosion test performed according to OECD TG 405 and EU Method B.5. New Zealand White rabbits were administered 0.1g of the test substance (> 97% purity) instilled into one eye each (no vehicle). The animals were observed for 72 hours post-administration. Slight ocular secretion was noted in all animals at the 1-hour observation. The mean scores at 24, 48, and 72 hours for all three animals for cornea opacity, iris, conjunctivae, and chemosis were 0, 0, 0.33, and 0.11, respectively. None of the individual animals had a single conjunctivae or chemosis score greater than 1 at any time point, and the effects were fully reversed by 48 and 72 hours, respectively. Authors of the REACH dossier concluded the test substance was not irritating under the conditions of the test, and GHS classification is not warranted (Klimisch 1, reliable without restrictions) (Unnamed 1995 study report).

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): L
Sodium formate was assigned a score of Low for acute aquatic toxicity based on LC/EC_{50} values > 1,000 mg/L in fish, crustacea, and algae. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when the most sensitive trophic level has LC/EC_{50} values > 100 mg/L (CPA 2018b). The confidence in the score is high based on reliable measured data for the target compound.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024

  Fish
  - Sodium formate was evaluated in a GLP-compliant acute toxicity study performed according to EPA OTS 797.1400. *Oncorhynchus mykiss* (rainbow trout) were exposed to the test substance for 96 hours under flow-through conditions, at concentrations up to 1,000 mg/L (nominal), or 887 mg/L (measured). There were no mortalities and the 96 hour NOEC and LC_{50} were 1,000 and > 1,000 mg/L, respectively (Klimisch 1, reliable without restrictions) (Unnamed 1990 study report).
  - Sodium formate was evaluated in a GLP-compliant acute toxicity study performed according to EPA OTS 797.1400. *Pimephales promelas* (fathead minnows) were exposed to the test substance for 96 hours under flow-through conditions, at concentrations up to 1,000 mg/L (nominal), or 954 mg/L (measured). There were no mortalities and the 96 hour NOEC and LC_{50} were 1,000 and > 1,000 mg/L, respectively (Klimisch 1, reliable without restrictions) (Unnamed 1990 study report).

- Sodium formate was evaluated in a pre-GLP acute toxicity study performed according to the standard method for the determination of fish toxicity of pure substances according to Freeman (1953). *Lepomis macrochirus* (bluegill) were exposed to the test substance for 24 hours at 5,000 mg/L (nominal). The 24 hour LC_{50} was > 5,000 mg/L (no further details provided) (Klimisch 2, reliable with restrictions) (Dowden and Bennett 1965).
- Sodium formate was evaluated in non-GLP compliant acute toxicity study (guideline not specified). No fish died at 1,000 mg/L, and all fish died at 10,000 mg/L. Authors concluded the 96-hour LC_{50} was > 1,000 mg/L (Klimisch 2, reliable with restrictions) (Terhaar et al. 1972).

Crustacea

- Sodium formate was evaluated in a GLP-compliant acute toxicity study performed according to EPA 660/3-75-009. *Daphnia magna* were exposed to the test substance for 48 hours under flow-through conditions, at concentrations up to 1,000 mg/L (nominal), or 1,070 mg/L (measured). The 48-hour NOEC and EC_{50} were reported at 120 and > 1,000 mg/L, respectively (Klimisch 1, reliable without restrictions) (Unnamed 1990 study report).

Algae

- Sodium formate was evaluated in a GLP-compliant acute toxicity study performed according to the method of Miller et al. (1978), OTS Algal Acute Toxicity Test, and ASTM (1983). *Raphidocelis subcapitata* (green algae) were exposed to the test substance for 96 hours under static conditions, at concentrations up to 1,000 mg/L (nominal). The 72-hour NOEC and EC_{50} based on growth rate were reported at 500 and > 1,000 mg/L, respectively (Klimisch 1, reliable without restrictions) (Unnamed 1990 study report).

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): *L*

Sodium formate was assigned a score of Low for chronic aquatic toxicity based on a predicted ChV of 11,400 in fish, a measured 72-hour NOEC of 500 mg/L in algae exposed to sodium formate, and a measured 21-day NOEC > 100 mg/L in daphnia exposed to the surrogate formic acid. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when the most sensitive trophic level has a chronic exposure NOEC/ChV value are > 10 mg/L (CPA 2018b). The confidence in the score is low because there are no experimental data available for fish.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024

  Fish
  - No measured data found.

  Crustacea
  - *Surrogate: Formic acid (CAS #64-18-6):* Formic acid was evaluated in a GLP-compliant *Daphnia magna* Reproduction Test performed according to OECD TG 211. *Daphnia magna* were exposed to the test substance for 21 days under semi-static conditions, at concentrations up to 100 mg/L (neutralized) (neutralization agent not specified). Measured concentrations were reported to be within +/- 20% of nominal concentrations at all tested concentrations throughout the exposure period. There were no measured effects on reproduction and the 21-day NOEC was reported at > 100 mg/L (Klimisch 1, reliable without restrictions) (citation not specified).

  Algae
  - As summarized previously, sodium formate was evaluated in a GLP-compliant acute toxicity study performed according to the method of Miller et al. (1978), OTS Algal Acute

Toxicity Test, and ASTM (1983). *Raphidocelis subcapitata* (green algae) were exposed to the test substance for 96 hours under static conditions, at concentrations up to 1,000 mg/L (nominal). The 72-hour NOEC based on growth rate were reported at 500 mg/L (Klimisch 1, reliable without restrictions) (Unnamed 1990 study report).

- U.S. EPA 2022
    - Formic acid is designated to the Neutral Organics ECOSAR chemical class. The predicted ChV freshwater fish is 11,400 mg/L (Appendix G).

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): vL

Sodium formate was assigned a score of Very Low for persistence based measured data for the target substance and a surrogate. Sodium formate reached > 60/70% biodegradation in multiple tests performed similar or equivalent to OECD TG 301. The surrogate potassium formate reached 90% degradation by day 15 in a closed bottle test (OECD 301 D), and the authors reported it fulfills the criterion for the 10-day window. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when a substance partitions mainly to soil and is readily biodegradable and meets the 10-day window (CPA 2018b). The confidence in the score is high based on measured data for the target compound and a strong surrogate.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024
    - Sodium formate was evaluated in for biodegradability in a GLP-compliant closed bottle test using seawater, performed according to OECD TG 306. The test substance was added to collected seawater at 22.13 mg/L, and biodegradation was measured based on oxygen consumption, calculated as theoretical oxygen demand (ThOD) over 28 days. There was no added inoculum (this method relies on microorganisms originally present in the seawater). Biodegradation was reported at 7% on day 5, 74% on day 15, and 86% on day 28. Authors of the REACH dossier report that the test substance was readily biodegradable (Klimisch 1, reliable without restrictions) (reference not cited). ToxServices notes that is test method does not assess for ready biodegradability but rather a results of > 60% ThoD may be interpreted as having **potential for biodegradation in the marine environment** (OECD 1992a).
    - Sodium formate was evaluated in a pre-GLP study performed according to the Standard methods for the Examination of Water, Sewage, and Industrial Wastes", 11th ed. (U.S. method). The test substance was added to domestic sludge (adaptation not specified) at 40 mg/L, under aerobic conditions. Biological oxygen demand (BOD) was measured over 20 days. There were three to five replicates with 2, 4, or 6 mL of sewage per bottle. The BOD values ranged from 0.4 to 5.4 mg/L using ammonia as the nitrogen source, and 0.3 to 5.4 mg/L using nitrate as the nitrogen source. No conclusion or discussion was provided (Klimisch 2, reliable with restrictions) (Gaffney and Ingols 1961). *Due to lack of additional details, his study is included for completeness but is not included in the weight of evidence.*
    - Sodium formate was evaluated in a pre-GLP BOD5 Method using the “Standard Dilution Method.” Two replicates resulted in BOD 5 values of 0.1 g O2/g test material and 0.04 g O2/test material (no further details provided) (Klimisch 2, reliable with restrictions)

(Heukelekian and Rand 1955). *Due to lack of additional details, his study is included for completeness but is not included in the weight of evidence.*

- Sodium formate was evaluated in an Inherent Biodegradability: Zahn-Wellens/EMPA Test performed according to OECD TG 302B (GLP not specified). The test substance was added to domestic sewage (adaptation not specified) at 300 mg/L, based on dissolved organic carbon (DOC). Biodegradation was measured under aerobic conditions. Biodegradation was reported at 100% by day 9. Authors concluded the test substance is **inherently degradable** (Klimisch 4, not assignable) (Huels Investigation 2000 (unpublished) as reported in IUCLID 2000).
- Sodium formate was evaluated in a GLP-compliant Ready Biodegradability: DOC Die-Away Test performed according to EU Method C.4-A. The test substance was added to domestic activated sludge (adaptation not specified), under aerobic conditions, at 10 mg/L, based on DOC. Biodegradation was reported at 99.6% by day 28 (Klimisch 4, not assignable) (Huels Investigation 2000 (unpublished) as reported in IUCLID 2000). *ToxServices notes that this method is similar to OECD 301-A, and the results support the chemical meeting the pass level of* ***> 70% degradation in 28 days*** *(OECD 1992b).* ***Details, however, are insufficient to determine if the 10-day window was met.*** *Although there is no information on the reference substance, it is reasonable to assume method validation as the study was reported to be GLP-compliant.*
- Sodium formate was evaluated in a Ready biodegradability: Modified OECD Screening Test, performed according to OECD TG 301 E (non-GLP). The test substance was added to domestic activated sludge (adaptation not specified), under aerobic conditions, at 20 mg/L, based on DOC. Biodegradation was reported at 92% by day 21. Authors concluded the test substance was **readily biodegradable** (Klimisch 2, reliable with restrictions) (Huels (unpublished) as cited in IUCLID 2000). *ToxServices notes the results support the chemical meeting the pass level of > 70% degradation in 28 days (OECD 1992b).* ***Details, however, are insufficient to determine if the 10-day window was met.*** *As there is no information on the reference substance, there is uncertainty on whether the test was validated.*

- ECHA, CAS #590-29-4, 2024
  - *Surrogate: Potassium formate (CAS #590-29-4):* Potassium formate was evaluated in a GLP-compliant Ready Biodegradability: Closed Bottle Test performed according to OECD TG 301 D. The test substance (100% purity) was added to domestic activated sludge (adaptation not specified) at 18 mg/L under aerobic conditions for 28 days. Biodegradation was measured based on oxygen consumption. Biodegradation was 15% by day 5, 90% by day 15, and 92% by day 28. The reference substance, sodium benzoate, provided the expected results. Authors concluded the test substance was **readily biodegradable and met the 10-day window** (Klimisch 1, reliable without restrictions) (Unnamed 1992 study report).
- U.S. EPA 2017
  - The BIOWIN Ready Biodegradability predicts that sodium formate will be readily biodegradable. Fugacity modeling predicts **55.8% will partition to soil with a half-life of 17.3 days**, 36.7% will partition to water with a half-life of 8.7 days, 7.5% will partition to air with a half-life of 4,167 days, and 0.0649% will partition to sediment with a half-life of 77.9 days (Appendix D).

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL

Sodium formate was assigned a score of Very Low for bioaccumulation based on predicted BCF values of 3.162 and 0.8932, and a measured log K_{OW} of -2.1. GreenScreen® criteria classify chemicals as a

Very Low hazard for bioaccumulation when BCF values are ≤ 100 and the log K_{OW} is < 4 (CPA 2018b). The confidence in the score is high based on the measured log K_{OW}.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- U.S. EPA 2017
  - BCFBAF predicts a BCF of 3.162 using the regression based model based on a measured log K_{ow} of -2.1, and a BCF/BAF of 0.8932 using the Arnot-Gobas model for the upper trophic level, taking metabolism into consideration (Appendix D).

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): L

Sodium formate was assigned a score of Low for reactivity. Based on its molecular structure, it is not expected to be explosive, oxidizing, or self-reactive due to lack of reactive functional groups associated with these properties. Measured data indicate it is not self-heating. Based on its molecular structure it is not a peroxide. As it is not explosive, it does not require desensitization. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when GHS classification is not warranted for any of the aforementioned hazards (CPA 2018b). The confidence in the score is high based on measured data and physico-chemical properties. It may be noted that no data were found regarding corrosivity to metals.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024b
  - Sodium formate is not self-heating based on a measured self-ignition temperature of > 400°C (EU Method A.16).
- As no measured data were identified for explosivity or oxidizing potential, ToxServices used screening procedures listed in the GHS (UN 2021):
  - Based on its molecular structure, sodium formate is not considered explosive, self-reactive due to lack of functional groups associated with explosive or self-reactive properties (See Appendix G).
  - Based on its molecular structure, sodium formate is not considered to have oxidizing properties as it does not contain any structural groups known to be correlated with a tendency to react exothermally with combustible materials. Specifically, organic substances which contain oxygen, fluorine, or chlorine where these elements are chemically bonded only to carbon or hydrogen, classification as an oxidizing liquid or solid need not be applied. Therefore, as the molecular structure of sodium formate has two oxygens, which are both bonded only to carbon and hydrogen, classification is not warranted.

Flammability (F) Score (vH, H, M, or L): L

Sodium formate was assigned a score of Low for flammability as it was not flammable when tested according to EU Method A.10. GreenScreen® criteria classify chemicals as a Low hazard for flammability when adequate data exist, and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on measured data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #141-53-7, 2024b

- Sodium formate was not flammable as it did not ignite and propagate combustion either by burning with flame, or smoldering, along 200 mm of the powder train in a 2 minute test period (EU Method A.10).

Use of New Approach Methodologies (NAMs)[12] in the Assessment, Including Uncertainty Analyses of Input and Output

New Approach Methodologies (NAMs) used in this GreenScreen® include use of *in vitro* assays to assess genotoxicity, and QSAR modeling to assess respiratory sensitization. NAMs are non-animal alternative that can be used alone or in combination to provide information for safety assessment (Madden et al. 2020). At present, there is not a uniformly accepted framework on how to report and apply individual NAMs (U.S. EPA 2020, OECD 2020). The expanded application of NAMs greatly amplifies the need to communicate uncertainties associated with their use. As defined by EFSA (2018), uncertainty is "a general term referring to all types of limitations in available knowledge that affect the range and probability of possible answers to an assessment question." The quality, utility, and accuracy of NAM predictions are greatly influenced by two primary types of uncertainties (OECD 2020):

- Type I: Uncertainties related to the input data used
- Type II: Uncertainties related to extrapolations made

As shown in Table 5, Type I (input data) uncertainties in sodium formate's NAMs dataset include lack of experimental data and lack of validated methods to assess respiratory sensitization. Sodium formate's Type II (extrapolation output) uncertainties include use of several *in vitro* assays that do not entirely mimic *in vivo* metabolism, and use of QSAR modeling to identify structural alerts for respiratory sensitization. Some of sodium formate's type II uncertainties were alleviated by the use of *in vitro* test batteries and/or in combination of *in vivo* data.

Table 5: Summary of NAMs Used in the GreenScreen® Assessment, Including Uncertainty Analyses	
Uncertainty Analyses (OECD 2020)	
Type I Uncertainty: Data/Model Input	**Respiratory sensitization**: No experimental data are available and there are no validated test methods.
Type II Uncertainty: Extrapolation Output	**Genotoxicity:** The bacterial reverse mutation assay (as defined in OECD Guideline 471) only tests point-mutation inducing activity in non-mammalian cells, and the exogenous metabolic activation system does not entirely mimic *in vivo* conditions[13]. The mammalian cell gene mutation assay (as defined in OECD Guideline 476) only detects gene mutations, and the exogenous metabolic activation system does not entirely mirror *in vivo* metabolism (i.e., the liver S9 mix contains enzymes present in the endoplasmic reticulum but not the cytosol of liver cells).[14] The *in vitro* chromosome aberration assay (OECD Guideline 473) does not measure aneuploidy and it only measures structural

[12] NAMs refers to any non-animal technology, methodology, approach, or combination thereof that inform chemical hazard and risk assessments. NAMs include *in silico*/computational tools, *in vitro* biological profiling (e.g., cell cultures, 2,3-D organotypic culture systems, genomics/transcriptomics, organs on a chip), and frameworks (i.e., adverse outcome pathways (AOPs), defined approaches (DA), integrated approaches to testing and assessment (IATA).
[13] https://www.oecd-ilibrary.org/docserver/9789264071247-en.pdf?expires=1614097593&id=id&accname=guest&checksum=89925F80B9F4BD2FFC6E90F94A0EE427
[14] https://www.oecd-ilibrary.org/docserver/9789264264809-en.pdf?expires=1614097800&id=id&accname=guest&checksum=C0DE371FB9C5A878E66C9AB7F84E6BBE

	chromosomal aberrations. The exogenous metabolic activation system does not entirely mirror *in vivo* metabolism[15]. **Respiratory sensitization**: The OECD Toolbox only identifies structural alerts, and does not define applicability domains. Additionally, the ECHA guidance (2017), on which the use of OECD Toolbox structural alerts is based, does not evaluate non-immunologic mechanisms for respiratory sensitization.	
Endpoint	**NAMs Data Available and Evaluated? (Y/N)**	**Types of NAMs Data (*in silico* modeling/*in vitro* biological profiling/frameworks)**
Carcinogenicity	N	
Mutagenicity	Y	*In vitro* data: Bacterial reverse mutation assay/*in vitro* gene mutation assay/*in vitro* chromosome aberration assay
Reproductive toxicity	N	
Developmental toxicity	N	
Endocrine activity	N	
Acute mammalian toxicity	N	
Single exposure systemic toxicity	N	
Repeated exposure systemic toxicity	N	
Single exposure neurotoxicity	N	
Repeated exposure neurotoxicity	N	
Skin sensitization	N	
Respiratory sensitization	Y	*In silico* modeling: OECD Toolbox structural alerts
Skin irritation	N	
Eye irritation	N	
Acute aquatic toxicity	N	
Chronic aquatic toxicity	Y	*In silico* modeling: ECOSAR
Persistence	Y	*In silico* modeling: EPI Suite™ Non-animal testing: OECD TG 301 and 306 Biodegradation tests
Bioaccumulation	Y	*In silico* modeling: EPI Suite™

[15] https://www.oecd-ilibrary.org/docserver/9789264264649-en.pdf?expires=1614098015&id=id&accname=guest&checksum=6A4F9CE52EA974F5A74793DD54D54352

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APPENDIX A: Hazard Classification Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: Results of Automated GreenScreen® Score Calculation for Sodium Formate (CAS #141-53-7)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human								Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	**Chemical Name**	**CAS#**	**C**	**M**	**R**	**D**	**E**	**AT**	**STs**	**STr**	**Ns**	**Nr**	**SNS***	**SNR***	**IrS**	**IrE**	**AA**	**CA**	**P**	**B**	**Rx**	**F**
No	Sodium formate	141-53-7	L	L	L	L	DG	L	M	*M*	L	L	L	L	L	L	L	*L*	vL	vL	L	L

Table 3: Hazard Summary Table

Benchmark	a	b	c	d	e	f	g
1	No	No	No	No	No		
2	No	No	No	No	No	No	No
3	No	No	Yes	No			
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Sodium formate	3

Note: Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score

Table 6

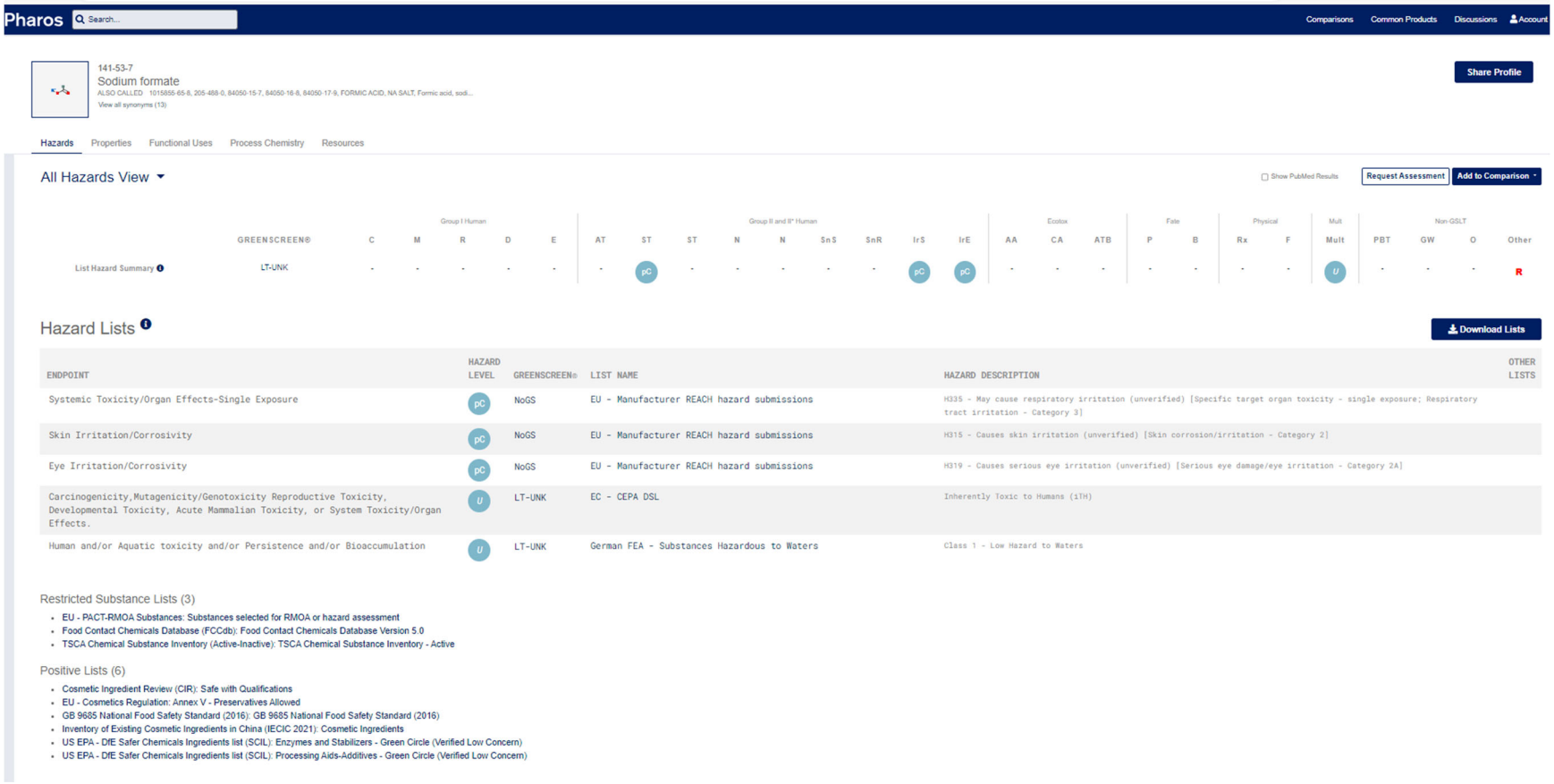
Chemical Name	Final GreenScreen® Benchmark Score
Sodium formate	3

After Data gap Assessment
Note: No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

Table 5: Data Gap Assessment Table

Datagap Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result
1												
2												
3	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes		3
4												

APPENDIX C: Pharos Output for Sodium Formate (CAS #141-53-7)



Pharos | Search... | Comparisons | Common Products | Discussions | Account

141-53-7
Sodium formate
ALSO CALLED 1015858-65-8, 205-488-0, 84050-15-7, 84050-16-8, 84050-17-9, FORMIC ACID, NA SALT, Formic acid, sodi...
View all synonyms (13)

Share Profile

Hazards | Properties | Functional Uses | Process Chemistry | Resources

All Hazards View

Show PubMed Results | Request Assessment | Add to Comparison

		Group I Human					Group II and II* Human								Ecotox			Fate		Physical		Mult	Non-GSLT			
	GREENSCREEN®	C	M	R	D	E	AT	ST	ST	N	N	SnS	SnR	IrS	IrE	AA	CA	ATB	P	B	Rx	F	Mult	PBT	GW	O	Other
List Hazard Summary	LT-UNK	-	-	-	-	-	-	pC	-	-	-	-	-	pC	pC	-	-	-	-	-	-	-	U	-	-	-	R

Hazard Lists

Download Lists

ENDPOINT	HAZARD LEVEL	GREENSCREEN®	LIST NAME	HAZARD DESCRIPTION	OTHER LISTS
Systemic Toxicity/Organ Effects-Single Exposure	pC	NoGS	EU - Manufacturer REACH hazard submissions	H335 - May cause respiratory irritation (unverified) [Specific target organ toxicity - single exposure; Respiratory tract irritation - Category 3]	
Skin Irritation/Corrosivity	pC	NoGS	EU - Manufacturer REACH hazard submissions	H315 - Causes skin irritation (unverified) [Skin corrosion/irritation - Category 2]	
Eye Irritation/Corrosivity	pC	NoGS	EU - Manufacturer REACH hazard submissions	H319 - Causes serious eye irritation (unverified) [Serious eye damage/eye irritation - Category 2A]	
Carcinogenicity,Mutagenicity/Genotoxicity Reproductive Toxicity, Developmental Toxicity, Acute Mammalian Toxicity, or System Toxicity/Organ Effects.	U	LT-UNK	EC - CEPA DSL	Inherently Toxic to Humans (iTH)	
Human and/or Aquatic toxicity and/or Persistence and/or Bioaccumulation	U	LT-UNK	German FEA - Substances Hazardous to Waters	Class 1 - Low Hazard to Waters	

Restricted Substance Lists (3)

- EU - PACT-RMOA Substances: Substances selected for RMOA or hazard assessment
- Food Contact Chemicals Database (FCCdb): Food Contact Chemicals Database Version 5.0
- TSCA Chemical Substance Inventory (Active-Inactive): TSCA Chemical Substance Inventory - Active

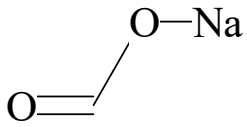
Positive Lists (6)

- Cosmetic Ingredient Review (CIR): Safe with Qualifications
- EU - Cosmetics Regulation: Annex V - Preservatives Allowed
- GB 9685 National Food Safety Standard (2016): GB 9685 National Food Safety Standard (2016)
- Inventory of Existing Cosmetic Ingredients in China (IECIC 2021): Cosmetic Ingredients
- US EPA - DfE Safer Chemicals Ingredients list (SCIL): Enzymes and Stabilizers - Green Circle (Verified Low Concern)
- US EPA - DfE Safer Chemicals Ingredients list (SCIL): Processing Aids-Additives - Green Circle (Verified Low Concern)

APPENDIX D: EPI Suite™ Modeling Results for Sodium Formate (CAS #141-53-7)

(Estimated values included in the GreenScreen® are highlighted and bolded)

EPI Suite Results For CAS 141-53-7



```
SMILES : O([Na])C=O
CHEM   : Formic acid, sodium salt
MOL FOR: C1 H1 O2 Na1
MOL WT : 68.01
------------------------------ EPI SUMMARY (v4.11) --------------------------
Physical Property Inputs:
Log Kow (octanol-water):   -2.10
Boiling Point (deg C)  :   ------
Melting Point (deg C)  :   257.80
Vapor Pressure (mm Hg) :   ------
Water Solubility (mg/L):   ------
Henry LC (atm-m3/mole) :   ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.69 estimate) =  -4.27

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C):  381.82  (Adapted Stein & Brown method)
Melting Pt (deg C):  138.01  (Mean or Weighted MP)
VP(mm Hg,25 deg C):  6.57E-008  (Modified Grain method)
VP (Pa, 25 deg C) :  8.76E-006  (Modified Grain method)
MP  (exp database):  253 deg C
Subcooled liquid VP: 2.29E-005 mm Hg (25 deg C, Mod-Grain method)
: 0.00305 Pa (25 deg C, Mod-Grain method)

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L):  1.536e+005
log Kow used: -2.10 (user entered)
melt pt used: 257.80 deg C
Water Sol (Exper. database match) =  4.34e+005 mg/L ( deg C)
Exper. Ref:  MERCK INDEX (1996); approx.

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) =  4.5449e+005 mg/L

ECOSAR Class Program (ECOSAR v1.11):
Class(es) found:
Neutral Organics

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method :   7.53E-007  atm-m3/mole  (7.63E-002 Pa-m3/mole)
Group Method:   Incomplete
For Henry LC Comparison Purposes:
```

```
User-Entered Henry LC:  not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC:  3.828E-014 atm-m3/mole  (3.878E-009 Pa-m3/mole)
VP:   6.57E-008 mm Hg (source: MPBPVP)
WS:   1.54E+005 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used:  -2.10  (user entered)
Log Kaw used:  -4.512  (HenryWin est)
Log Koa (KOAWIN v1.10 estimate):  2.412
Log Koa (experimental database):  None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model)          :   0.7983
Biowin2 (Non-Linear Model)      :   0.9525
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model):   3.4621  (days-weeks  )
Biowin4 (Primary Survey Model) :   4.1669  (days        )
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model)     :   0.7979
Biowin6 (MITI Non-Linear Model):   0.9505
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model):  1.0229
Ready Biodegradability Prediction:   YES

Hydrocarbon Biodegradation (BioHCwin v1.01):
Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled):  0.00305 Pa (2.29E-005 mm Hg)
Log Koa (Koawin est  ): 2.412
Kp (particle/gas partition coef. (m3/ug)):
Mackay model           :  0.000983
Octanol/air (Koa) model:  6.34E-011
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model     :  0.0343
Mackay model           :  0.0729
Octanol/air (Koa) model:  5.07E-009

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant =   0.0000 E-12 cm3/molecule-sec
Half-Life =   -------
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
0.0536 (Junge-Pankow, Mackay avg)
5.07E-009 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc    :  1  L/kg (MCI method)
Log Koc:  0.000       (MCI method)
Koc    :  0.09866  L/kg (Kow method)
Log Koc:  -1.006      (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
```

Rate constants can NOT be estimated for this structure!

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -2.3569 days (HL = 0.004397 days)
Log BCF Arnot-Gobas method (upper trophic) = -0.049 (BCF = 0.8932)
Log BAF Arnot-Gobas method (upper trophic) = -0.049 (BAF = 0.8932)
log Kow used: -2.10 (user entered)

Volatilization from Water:jen
Henry LC: 7.53E-007 atm-m3/mole (estimated by Bond SAR Method)
Half-Life from Model River: 642.1 hours (26.75 days)
Half-Life from Model Lake : 7073 hours (294.7 days)

Removal In Wastewater Treatment:
Total removal: 1.89 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.75 percent
Total to Air: 0.04 percent
(using 10000 hr Bio P,A,S)

Level III Fugacity Model: (MCI Method)

Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)	
Air	**7.5**	**1e+005**	**1000**
Water	**36.7**	**208**	**1000**
Soil	**55.8**	**416**	**1000**
Sediment	**0.0649**	**1.87e+003**	**0**

Persistence Time: 306 hr

Level III Fugacity Model: (MCI Method with Water percents)

Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)	
Air	7.5	1e+005	1000
Water	36.7	208	1000
water	(36.7)		
biota	(1.46e-008)		
suspended sediment	(5.5e-005)		
Soil	55.8	416	1000
Sediment	0.0649	1.87e+003	0

Persistence Time: 306 hr

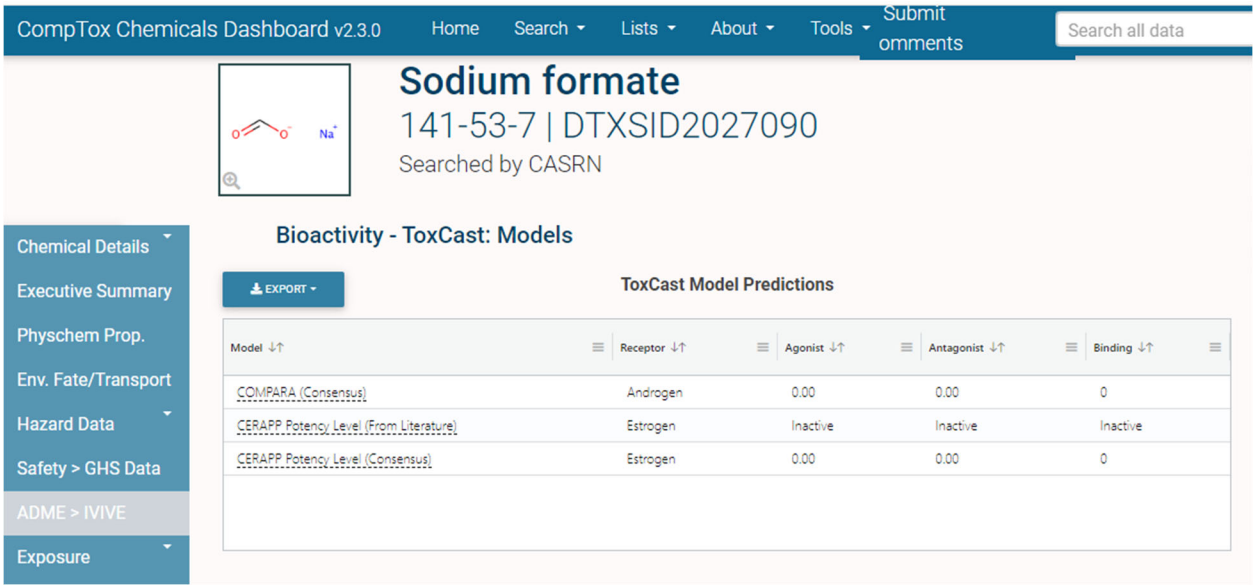
Level III Fugacity Model: (EQC Default)

Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)	
Air	7.6	1e+005	1000
Water	37.6	208	1000
water	(37.6)		
biota	(1.49e-008)		
suspended sediment	(1.83e-007)		
Soil	54.8	416	1000
Sediment	0.065	1.87e+003	0

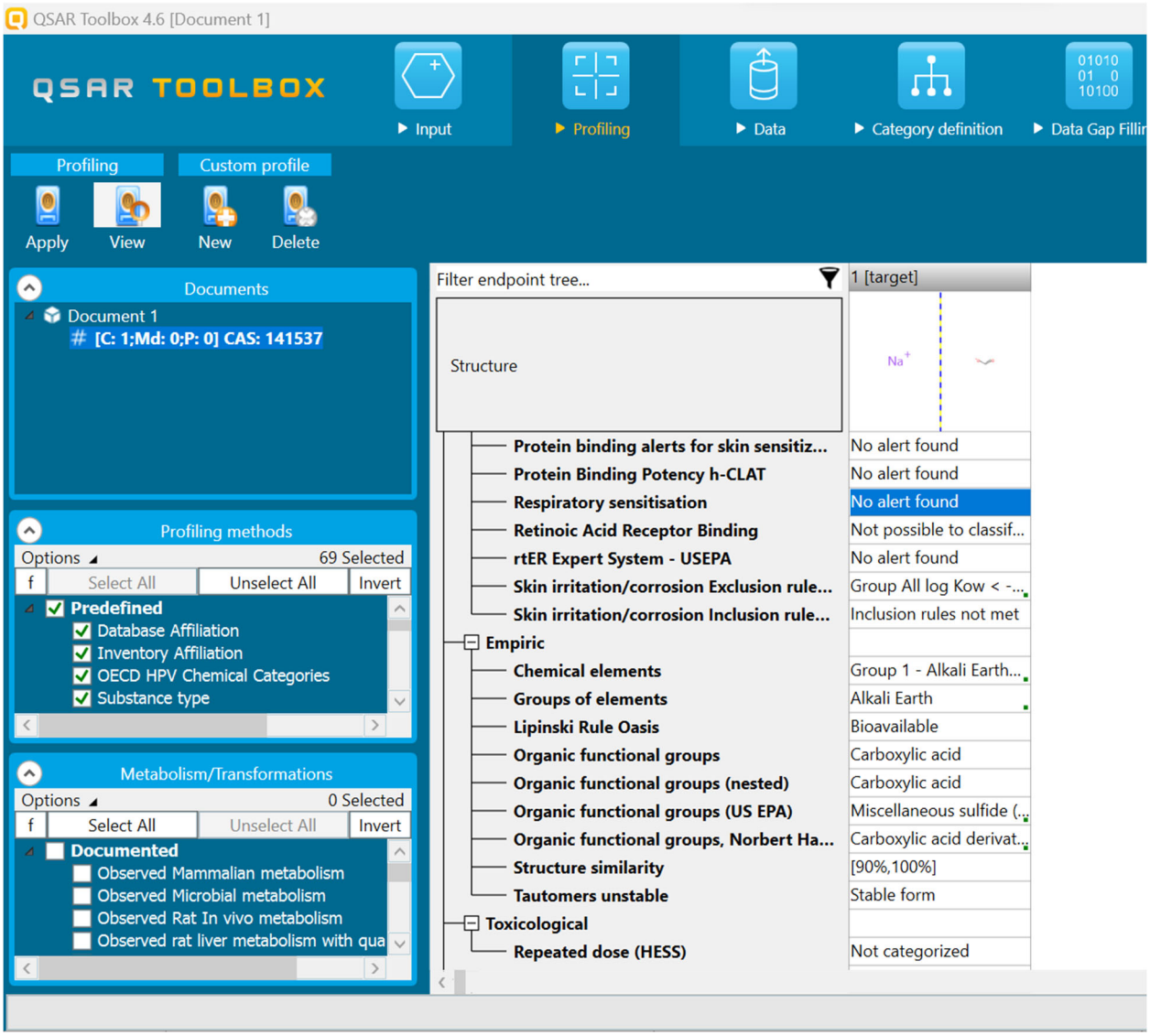
Persistence Time: 303 hr

...

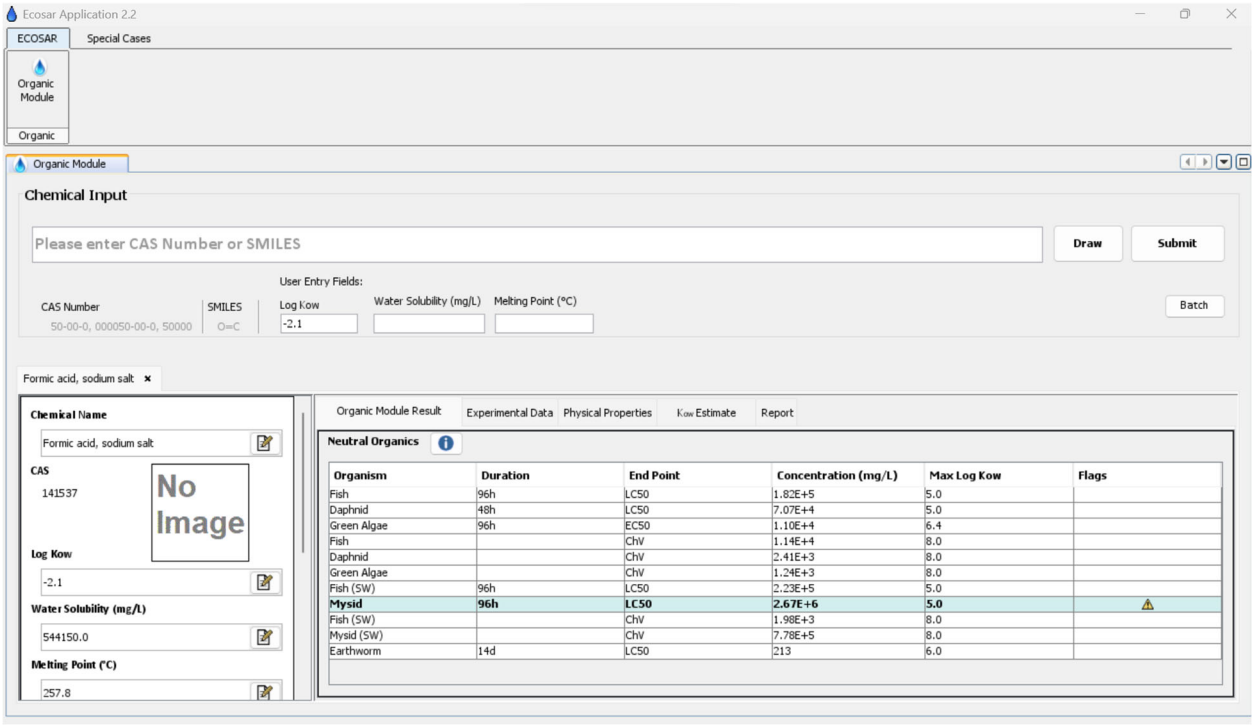
APPENDIX E: ToxCast Endocrine Activity Modeling Results for Sodium Formate (CAS #141-53-7)



APPENDIX F: OECD Toolbox Skin Sensitization Results for Sodium Formate (CAS #141-53-7)

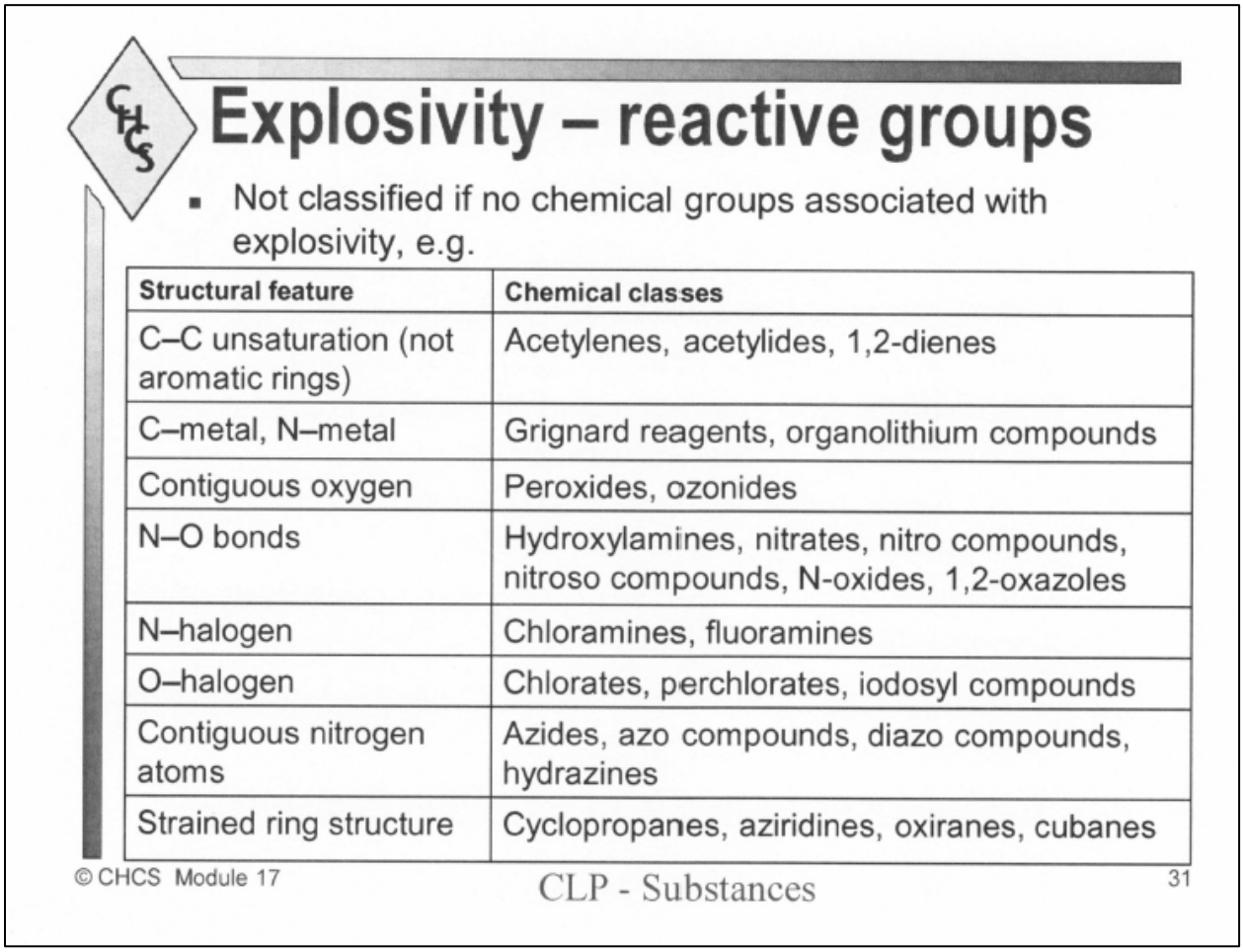


APPENDIX G: ECOSAR Modeling Results for Sodium Formate (CAS #141-53-7)



APPENDIX H: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List



Explosivity – reactive groups

- Not classified if no chemical groups associated with explosivity, e.g.

Structural feature	Chemical classes
C–C unsaturation (not aromatic rings)	Acetylenes, acetylides, 1,2-dienes
C–metal, N–metal	Grignard reagents, organolithium compounds
Contiguous oxygen	Peroxides, ozonides
N–O bonds	Hydroxylamines, nitrates, nitro compounds, nitroso compounds, N-oxides, 1,2-oxazoles
N–halogen	Chloramines, fluoramines
O–halogen	Chlorates, perchlorates, iodosyl compounds
Contiguous nitrogen atoms	Azides, azo compounds, diazo compounds, hydrazines
Strained ring structure	Cyclopropanes, aziridines, oxiranes, cubanes

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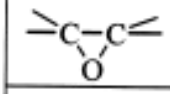
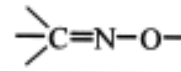
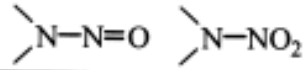
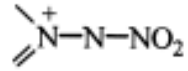
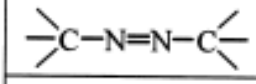
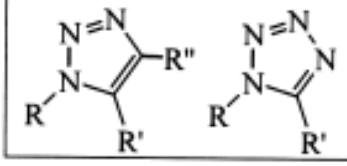
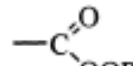
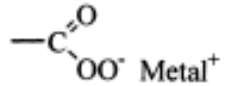
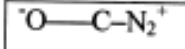
Explosivity – Full List

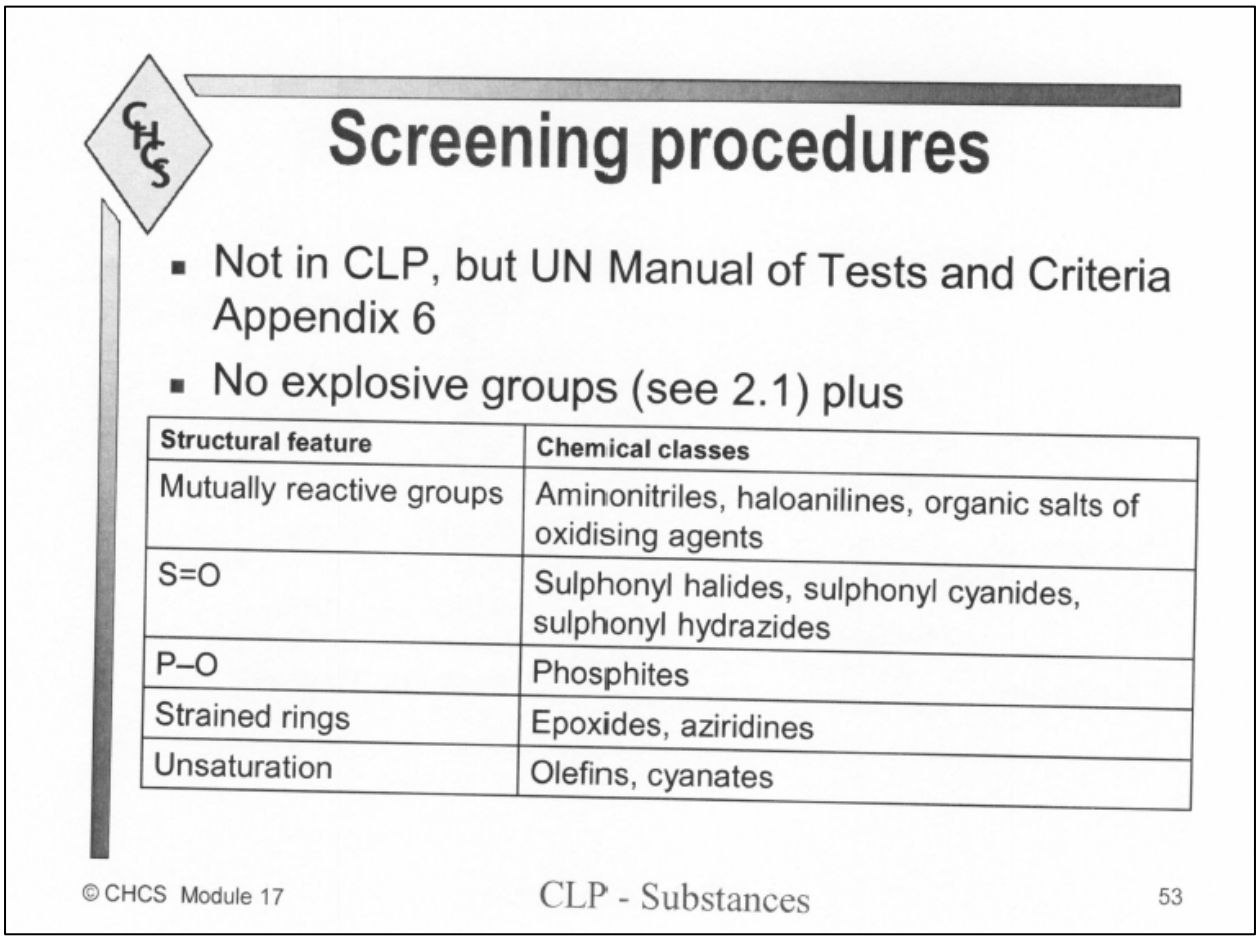
Table R.7.1-28 Chemical groups associated with explosive properties

Chemical group	Chemical Class
-C≡C- -C≡C-Metal -C≡C-Halogen	Acetylenic Compounds Metal Acetylides Haloacetylene Derivatives
	Diazo Compounds
-N=O -NO_2	Nitroso and Nitro Compounds,
R-O-N=O R-O-NO_2	Acyl or Alkyl Nitrites and Nitrates
	1,2-Epoxides
	Metal Fulminates or *aci*-Nitro Salts
	N-Metal Derivatives (especially heavy metals)
	N-Nitroso and N-Nitro Compounds
	N-Azolium Nitroimidates
	Azo Compounds
Ar-N=N-O-Ar	Arene Diazoates
$(ArN=N)_2O$, $(ArN=N)_2S$	Bis-Arenediazo Oxides and Sulfides
RN=N-NR'R''	Triazines
	High-nitrogen Compounds: e.g. Triazoles, Tetrazoles

Chemical group	Chemical Class
[1] ROOR', [2] 	Peroxy Compounds: [1] Alkyl hydroperoxides (R'=H), Peroxides (R'=organic); [2] Peroxo acids (R'=H), Peroxyesters (R'=organic)
[1] ROOMetal, [2] 	Metal peroxides, Peroxoacids salts
$-N_3$	Azides e.g. PbN_6, CH_3N_3
	Arenediazonium oxides i.e. inner diazonium salts in which the counter ion is an oxide
Ar-N=N-S- Ar-N=N-S-Ar	Diazonium sulfides and derivatives, Arenediazo Aryl Sulfides
XO_n	Halogen Oxide: e.g. percholrates, bromates, etc
NX_3 e.g. $NC1_3$, $RNC1_2$	N-Halogen Compounds

Adapted from Bretherick (Bretherick's Handbook of Reactive Chemical Hazards 6th Ed., 1999, Butterworths, London)

Self-Reactive Substances



Screening procedures

- Not in CLP, but UN Manual of Tests and Criteria Appendix 6
- No explosive groups (see 2.1) plus

Structural feature	Chemical classes
Mutually reactive groups	Aminonitriles, haloanilines, organic salts of oxidising agents
S=O	Sulphonyl halides, sulphonyl cyanides, sulphonyl hydrazides
P–O	Phosphites
Strained rings	Epoxides, aziridines
Unsaturation	Olefins, cyanates

APPENDIX I: Change in Benchmark Score

Table 5 provides a summary of changes to the GreenScreen® Benchmark™ for sodium formate. The original GreenScreen® assessment was performed in 2024 under version 1.4 criteria and ToxServices assigned a Benchmark 3_{DG} (BM-3_{DG}) score.

Table 6: Change in GreenScreen® Benchmark™ for Sodium Formate

Date	GreenScreen® Benchmark™	GreenScreen® Version	Comment
March 18, 2024	BM-3	v. 1.4	New GreenScreen® assessment.

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