Sodium Benzoate (CAS #532-32-1) GreenScreen™ Assessment

Prepared for:

Clean Production Action

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GreenScreen™ Assessment for Sodium Benzoate (CAS #532-32-1)

GreenScreen™ Version 1.2 Draft Assessment
Note: Validation Has Not Been Performed on this GreenScreen™ Assessment

Chemical Name: Sodium Benzoate

CAS Number: 532-32-1

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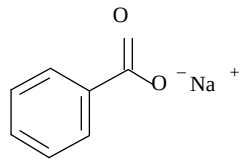
Date: December 11, 2012

Confirm application of the *de minimus* rule[1]: N/A

Chemical Structure(s):



Identify Applications/Functional Uses:
1. Preservative (HSDB 2003)
2. Antimicrobial agent (HSDB 2003)

GreenScreen™ Summary Rating for Sodium Benzoate [2]:
Sodium benzoate was assigned a GreenScreen™ Benchmark Score of 2_{DG} ("Use but Search for Safer Substitutes"). When first reviewing the hazard endpoints, sodium benzoate has Moderate (M) Skin Sensitization (SnS*) (Benchmark 3c). Additionally, it can be assigned a Benchmark Score of 3 based on Moderate (M) Eye Irritation (IrE) (Benchmark 3c). Finally, it can be assigned a Benchmark Score of 3 based on Moderate Reactivity (Rx) (Benchmark 3d). However, data gaps exist for this chemical. As outlined in CPA (2011b), Section III(1)(Benchmarking Chemicals With Data Gaps), to achieve a Benchmark Score of 3, a chemical must have data for at least 4 of 5 Group I Human Health Endpoints. The only permissible data gap is Endocrine Activity (E). Sodium benzoate meets those requirements. Additionally, a chemical must have data for at least 5 out of 7 Group II and II* Human Health Endpoints. Permissible data gaps include either skin or respiratory sensitization, or one other hazard endpoint. Sodium benzoate also meets the Group II and II* data gap rules. Data must also be available for acute and chronic aquatic toxicity, persistence, and bioaccumulation; data is available for all of these endpoints for sodium benzoate. Finally, data must be available for both physical property endpoints (Flammability (F) and Reactivity (Rx)). Data are not available for flammability; therefore, sodium benzoate is assigned a Benchmark Score of 2_{DG}. In a worst-case scenario, if sodium benzoate were assigned a High score for Endocrine Activity (E), it would be categorized as a Benchmark 1 Chemical.

[1] Every chemical in a material or formulation should be assessed if it is:
1. intentionally added and/or
2. present at greater than or equal to 100 ppm

[2] 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.

Figure 1: GreenScreen™ Hazard Ratings for Sodium Benzoate

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
						single	repeated*	single	repeated*										
L	**L**	**L**	**L**	dg	**L**	dg	**L**	dg	dg	**M**	dg	**L**	**M**	**L**	**L**	**L**	*vL*	**M**	dg

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values and lower confidence. Hazard levels in **BOLD** font reflect values based on test data (See Guidance).
Note: Please see Appendix A for a glossary of hazard acronyms.

Transformation Products and Ratings

Identify relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[3]

Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	Green Screen Rating
End of Life	Thermal Degradation	Disodium oxide	1313-59-3	Not present on CPA's Red List of Chemicals (CPA 2011d)

*The above transformation products were screened against the CPA's table of Red List chemicals (CPA 2009b).

Introduction

Sodium benzoate is a white crystalline powder. Worldwide production capacity of sodium benzoate is estimated at 100 kt per year. The major outlet for sodium benzoate is as a preservative in food and beverages (60%). The second most important market is cooling liquids (10%) (UNEP 2001).

ToxServices assessed sodium benzoate against GreenScreen™ Version 1.2 (CPA 2011a) following procedures outlined in ToxServices' SOP 1.37 (GreenScreen Hazard Assessment) (ToxServices 2012).

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 2012). Pharos (Pharos 2012) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The Pharos output for sodium benzoate can be found in Appendix B, and a summary of the results can be found below:

- German FEA – Substances Hazardous to Waters (VwVwS)
  - Class 1 Low Hazard to Waters – GreenScreen Benchmark Unspecified – occupational hazard only

[3] A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.

Physiochemical Properties of Sodium Benzoate

Table 1: Physical and Chemical Properties of Sodium Benzoate		
Property	**Value**	**Reference**
Molecular formula	$C_7H_5NaO_2$	HSDB 2003
SMILES Notation	[O-]C(=O)c1ccccc1.[Na+]	U.S. EPA 2011
Molecular weight	144.1 g/mol	HSDB 2003
Physical state	Solid	HSDB 2003
Appearance/Particle Size	White granules or crystalline powder	HSDB 2003
Vapor pressure	3.67E-09	ChemIDplus 2012
Water solubility	630 g/L	ESIS 2000
Dissociation constant	n/a	
Density/specific gravity	1.44 g/cm^3	ESIS 2000
Partition coefficient	-2.13	ESIS 2000

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M or L): L
Sodium benzoate was assigned a score of Low for carcinogenicity as no basis for concern was identified (CPA 2011c).

- Not listed as a known carcinogen by IARC, NTP, U.S. EPA, or CA Prop 65.
- In a 2-year carcinogenicity study, groups of 50 male and 52 female Fisher 344 rats, four to five weeks old, received diets containing 1 % (500 mg/kg bw/day) or 2% (1000 mg/kg bw/day) sodium benzoate for 18-24 months. Controls, consisting of 25 male and 43 female rats, received basal diet. Food intake was adequately controlled to avoid an excess; tap water was available ad libitum. Survival was very poor in all groups, due to intercurrent sialodacryoadentitis and mycoplasma infections. Al surviving animals were sacrificed between 18 and 25 months, all were autopsied, and various tissues were examined histopathologically. No adverse clinical signs directly attributable to treatment were observed, and only negligible difference in average body weight and mortality rate were seen between the treated and control groups. Although a variety of tumors occurred among treated and control rats of each sex, they were of similar type and incidence. Poor survival in all groups, due to infections, limits the usefulness of this study (UNEP 2001).
- A lifelong study using male/female Swiss Albino mice give 2% sodium benzoate continuously in drinking water showed no carcinogenic effect. In the main study, a 2% solution of sodium benzoate (purity, 99%) was administered in the drinking water to groups of 50 male and 50 female five week old mice for their lifetime. Groups of 100 males and 100 females were used as untreated controls. Both treated and control animals were 'carefully checked'; their body weights were measured weekly, and gross pathological changes were recorded. The animals were either allowed to die or were sacrifice when moribund. Complete necropsies were performed on all animals, and the liver, spleen, kidneys, bladder, thyroid, heart, pancreas, testes, ovaries, brain, nasal turbinates, at least four lobes of the lungs, and organs with gross pathological changes were examined histologically. The average daily intake of sodium benzoate was 124.0 mg for males and 119.2 mg for females on the basis of daily water consumption of 6.2 and 5.9 mL, respectively. The dose of sodium benzoate was equivalent to 6200 mg/kg bw/day for males and 5960 mg/kg bw/day for females. Treatment had no effect on survival or the incidence of tumors. This study is sufficiently reliable due to the number of animals and detailed histopathological examinations (UNEP 2001).

Mutagenicity/Genotoxicity (M) Score (H, M or L): L
Sodium benzoate was assigned a score of Low for mutagenicity/genotoxicity. Although some assays reported positive results, the weight of evidence and absence of structural alerts in sodium benzoate lead to the conclusion that sodium benzoate is not genotoxic (CPA 2011c).

- *In vitro:* Sodium benzoate was not mutagenic in Ames tests with and without metabolic activation (strains and concentration not specified) (UNEP 2001).
- *In vitro:* A cytogenetic assay using anaphase preparations of cultured human embryonic lung cells was negative – no metabolic activation was used (UNEP 2001).
- *In vitro:* An *Escherichia coli* reverse mutation assay was negative with and without metabolic activation (UNEP 2001).
- *In vitro:* A cytogenetic assay using CHL cells was positive without metabolic activation (UNEP 2001).
- *In vitro:* Sister Chromatid Exchange assays using Chinese hamster cells or human lymphocytes were positive without metabolic activation (UNEP 2001).
- *In vitro:* A recombination assay with *Bacillus subtilus* H17 and M45 was positive (reported with minimal documentation) (UNEP 2001).
- *In vitro:* Some studies reported positive results; however, these positive results are considered to be overruled by the negative results of the higher-level *in vivo* tests (UNEP 2001).
- *In vivo:* A cytogenetic assay in male rats given single or multiple gavage doses of 50, 500, or 5000 mg/kg sodium benzoate showed no significant increase in chromosomal aberration in the bone marrow (UNEP 2001).
- *In vivo:* A dominant lethal assay using male rats given single or multiple gavage doses of 50, 500, or 5000 mg/kg sodium benzoate was non-mutagenic (UNEP 2001).
- *In vivo:* A host mediated assay using male rats given multiple gavage doses of 50, 500, or 5000 mg/kg sodium benzoate showed no elevation of mutant frequencies in *Salmonella typhimurium* G46; no elevation of mutant frequencies in *Salmonella typhimurium* TA 1530; no increase in recombinant frequencies in *Saccharomyces cerevesiae* D3 (UNEP 2001).
- *In vivo:* A host mediated assay using male rats given a single gavage dose of 50, 500, or 5000 mg/kg sodium benzoate showed an elevation of mutant frequencies in *Salmonella typhimurium* TA1530 in the intermediate dose level; the other doses were negative (UNEP 2001).

Reproductive Toxicity (R) Score (H, M, or L): L
Sodium benzoate was assigned a score of Low for reproductive toxicity based on a reproductive toxicity study in rats in which no reproductive effects were observed at 1,000 mg/kg (CPA 2011c).

- *Oral:* Male and female Fischer 344 rats were fed diets containing doses of 1 or 2% (equivalent to 500 and 1,000 mg/kg/day) for 18-24 months. A NOAEL of 1,000 mg/kg/day was established, as there were no compound-related effects in the testes and ovaries of treated rats (UNEP 2001).

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): L
Sodium benzoate was assigned a score of Low for developmental toxicity based on a maternal and fetal NOAEL of >175 mg/kg in rats and mice (CPA 2011c).

- *Oral*: Pregnant Wistar rats were given doses of 1.75, 8, 38, or 175 mg/kg/day via gavage on gestation days (GDs) 6-15. A fetal and maternal NOAEL > 175 mg/kg/day was established, as there were no adverse effects seen (UNEP 2001).
- *Oral:* Pregnant Wistar rats were fed doses of 1, 2, 4, or 8% in diet (equivalent to 700, 1,400, 2,800, or 5,600 mg/kg/day) for the entire gestation period of 20 days. A fetal and maternal NOAEL of 1,400 mg/kg/day was established, based on reduced food intake and decreased body weight in the pregnant rats, perinatal death, organ abnormalities, and skeletal abnormalities. These effects were found to be due to reduced maternal feed intake, leading to malnutrition (UNEP 2001).
- *Oral*: Pregnant CD-1 mice were given doses of 1.75, 8, 38, or 175 mg/kg/day via gavage on GDs 6-15. A fetal and maternal NOAEL > 175 mg/kg/day was established, as there were no adverse effects seen (UNEP 2001).
- *Oral*: Pregnant Dutch belted rabbits were given doses of 2.5, 12, 54, or 250 mg/kg/day via gavage on GDs 6-18. A fetal and maternal NOAEL of 250 mg/kg/day was established, as there were no adverse effects seen (UNEP 2001).
- *Oral*: Pregnant golden outbred hamsters were given doses of 3, 14, 65, or 300 mg/kg/day via gavage on GDs 6-10. A fetal and maternal NOAEL of 300 mg/kg/day was established, as there were no adverse effects seen (UNEP 2001).
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006).

Endocrine Activity (E) Score (H, M or L): dg

- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- Not listed as a potential endocrine disruptor on the Red List of Chemicals (CPA 2011d).
- No relevant data were identified for sodium benzoate.

Group II and II* Human Health Effects (Group II and II* Human)

Note: Group II and Group II* endpoints are distinguished in the v 1.2 Benchmark system. For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints and test data for single or repeated exposures may be used. If data exist for single OR repeated exposures, then the endpoint is not considered a data gap. If data are available for both single and repeated exposures, then the more conservative value is used.

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M or L): L

Sodium benzoate was assigned a score of Low for acute toxicity based on an oral LD_{50} greater than 2,000 mg/kg (CPA 2011c).

- *Oral*: An LD_{50} range of 2,100-4,070 mg/kg was determined in rats (UNEP 2001).

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)

Group II Score (single dose) (vH, H, M or L): dg

- No relevant data were identified for sodium benzoate.

Group II* Score (repeated dose) **(H, M, L): L**

Sodium benzoate was assigned a score of Low for systemic toxicity (repeated dose) based on studies in rats and mice with no adverse effects observed at doses of >3,000 mg/kg (CPSC 2011c).

- A 90-day study with male/female Sherman rats given 640, 1280, 3145, or 6290 mg/kg/day USP sodium benzoate continuously in feed showed no adverse effects at ≤3145 mg/kg bw. There was increased mortality (4/8 died); reduced weight gain; increased weight of livers and kidneys; pathological lesions (not specified) in livers and kidneys at 6290 mg/kg bw. The NOAEL was determined to be 3145 mg/kg bw/day (UNEP 2001).
- According to a 35 day study (by drinking water) in mice (strain not specified), no effects were observed at 3000 mg/kg bw. At this dose level also in a chronic study, no toxic effects were found in histopathological examinations (UNEP 2001).

Neurotoxicity (N)

Group II Score (single dose) **(vH, H, M or L):** dg

- No relevant data were identified for sodium benzoate.

Group II* Score (repeated dose) **(H, M, and L):** dg

- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006).
- Not listed as a potential neurotoxicant on the Red List of Chemicals (CPA 2011d).
- No relevant data were identified for sodium benzoate.

Skin Sensitization (SnS) Group II* Score (H, M or L): M

Sodium benzoate was assigned a score of Moderate for skin sensitization based on positive skin reactions in humans (CPA 2011c).

- A clinical dermatological study showed positive test patch test reactions in 0.2% of the patients treated with 5% sodium benzoate in petrolatum. It has been suggested that this very low potential of sodium benzoate to elicit a non-immunologic contact urticaria may be due to the formation of benzoic acid at kin contact (UNEP 2001).
- Sodium benzoate is not sensitizing in animals. No other study details were provided (UNEP 2001).

Respiratory Sensitization (SnR) Group II* Score (H, M or L): dg

- No relevant data were identified for sodium benzoate.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): L
Sodium benzoate was assigned a score of Low for skin irritation/corrosivity as sodium benzoate was determined to be non-irritating to the skin of rabbits (CPA 2011c).

- Sodium benzoate was not irritating on the skin of rabbits according to OECD Guideline 404. No other study details were provided (UNEP 2001).

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): M
Sodium benzoate was assigned a score of Moderate for eye irritation/corrosivity as it was slightly irritating to the eyes of rabbits (CPA 2011c).

- Sodium benzoate was slightly irritating to the eyes of rabbits according to OECD Guideline 405. No other study details were provided (UNEP 2001).

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): L
Sodium benzoate was assigned a score of Low for acute aquatic toxicity based on aquatic toxicity values greater than 100 mg/L in fish, aquatic invertebrates and green algae (CPA 2011c).

- An LC_{50} of 484 mg/L was identified in *Pimephales promelas* (freshwater fish, 96 hour) (UNEP 2001).
- An LC_{50} of 100-650 mg/L was identified in *Daphnia magna* (aquatic invertebrate, 48 and 96 hour) (UNEP 2001).
- An EC_{50} of 430 mg/L was identified in green algae (96 hour) (UNEP 2001).
- An LC_{50} of 6.34×10^5 mg/L is predicted in fish (96 hour). However, the chemical may not be soluble enough to measure this predicted effect (U.S. EPA 2009).
- An LC_{50} of 1.9×10^5 mg/L is predicted in daphnid (48 hour). However, the chemical may not be soluble enough to measure this predicted effect (U.S. EPA 2009).
- An EC_{50} of 14,136 mg/L is predicted in green algae (96 hour). However, the chemical may not be soluble enough to measure this predicted effect (U.S. EPA 2009).

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): L
Sodium benzoate was assigned a score of Low for chronic aquatic toxicity based on chronic aquatic toxicity values greater than 10 mg/L (CPA 2011c).

- A ChV of 49,605 mg/L was identified in fish (20 day) (U.S. EPA 2009).
- A ChV of 11,209 mg/L was identified in daphnia (length of time not specified) (U.S. EPA 2009).
- A ChV of 2,651 mg/L was identified in green algae (length of time not specified) (U.S. EPA 2009).

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): L
Sodium benzoate was assigned a score of Low for persistence as it is readily biodegradable (CPA 2011c).

- Sodium benzoate is readily biodegradable, with 90-93% biodegradation occurring in 7 days and 88-97% occurring in 28 days (UNEP 2001).

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL
Sodium benzoate was assigned a score of very Low for bioaccumulation based on a predicted bioconcentration factor less than 100.

- The octanol/water partition coefficient of sodium benzoate (log K_{ow}= -2.13) indicates a low potential for bioaccumulation. This is also supported by the rapid biotransformation and/or excretion of benzoate compounds in urine in animals (UNEP 2001).
- BCFBAF predicts a bioconcentration factor (BCF) of approximately 3 and a log K_{ow} of -2.27 (U.S. EPA 2009).

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M or L): M
Sodium benzoate was assigned a score of Moderate for reactivity as it has the potential to form explosive mixtures in air (CPSC 2011c).

- Can form explosive mixtures in air (UNEP 2001).

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

- No relevant data were identified for sodium benzoate.

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APPENDIX A: Hazard Benchmark Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(Cr) Corrosion/ Irritation (Skin/ Eye)

(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

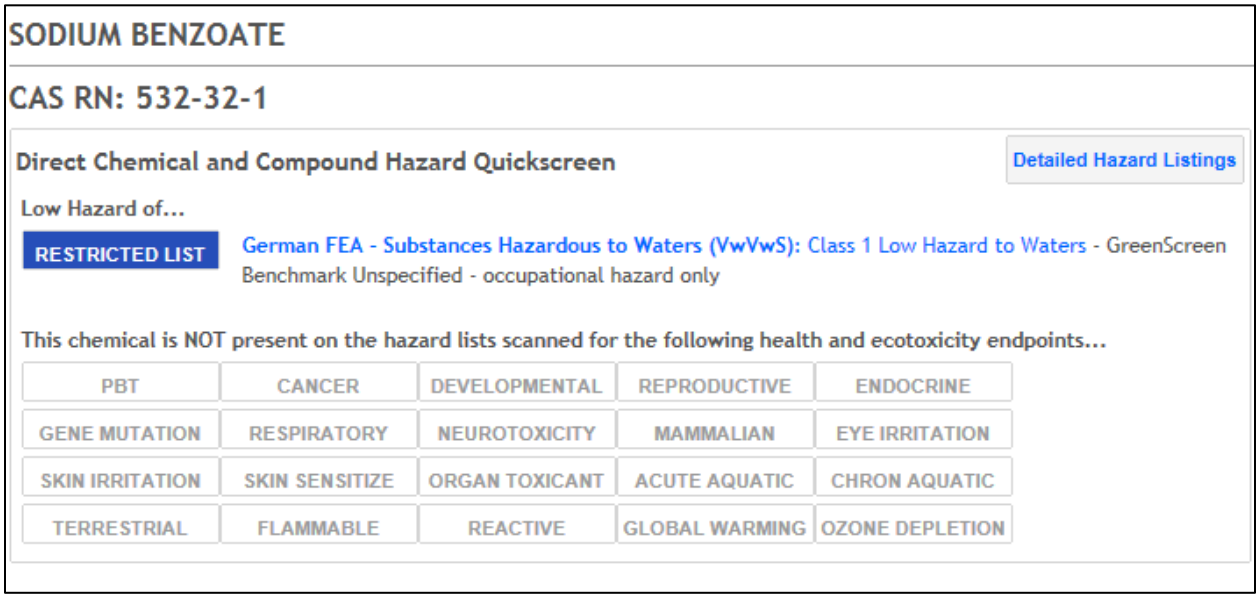
(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: Pharos List Translator Results



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