Dossier for Candidate Low-Priority Substance D-gluco-Heptonic acid, sodium salt (1:1), (2.xi.)- (CASRN 31138-65-5) (Sodium Glucoheptonate)

For Release at Proposal

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1. Introduction

In the Lautenberg amendments to the Toxic Substances Control Act (TSCA) (section 6(b)(1)(B)) and implementing regulations (40 CFR 702.3), a low-priority substance is described as a chemical substance that the Administrator concludes does not meet the statutory criteria for designation as a high-priority substance, based on information sufficient to establish that conclusion, without consideration of costs or other non-risk factors. A high-priority substance is defined as a chemical substance that the Administrator concludes, without consideration of costs or other non-risk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to potentially exposed or susceptible subpopulations identified as relevant by the Administrator. D-gluco-Heptonic acid, sodium salt (1:1), (2.xi.)-, referenced as sodium glucoheptonate for the remainder of this document, is one of the 40 chemical substances initiated for prioritization as referenced in a March 21, 2019 notice (84 FR 10491).[1]

Before determining low or high prioritization status, under EPA's regulations at 40 CFR 702.9[2] and pursuant to section 6(b)(1)(A) of the statute, EPA will generally use reasonably available information to screen the candidate chemical substance under its conditions of use against the following criteria and considerations:

- the hazard and exposure potential of the chemical substance;
- persistence and bioaccumulation;
- potentially exposed or susceptible subpopulations;
- storage near significant sources of drinking water;
- conditions of use or significant changes in the conditions of use of the chemical substance;
- the chemical substance's production volume or significant changes in production volume; and
- other risk-based criteria that EPA determines to be relevant to the designation of the chemical substance's priority.

Designation of a low-priority substance indicates that the chemical substance does not meet the statutory criteria for a high-priority substance and that a risk evaluation is not warranted at the time.

This risk-based, screening-level review is organized as follows:

- *Section 1 (Introduction):* This section explains the requirements of the Lautenberg amendments to the Toxic Substances Control Act (TSCA) and implementing regulations – including the criteria and considerations -- pertinent to prioritization and designation of low-priority substances.

[1] https://www.federalregister.gov/documents/2019/03/21/2019-05404/initiation-of-prioritization-under-the-toxic-substances-control-act-tsca

[2] The prioritization process is explained in the *Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act* (82 FR 33753).

- *Section 2 (Background on the Proposed Low-Priority Substance):* This section includes information on attributes of the chemical substance, including its structure, and relates them to its functionality.

- *Section 3 (Physical-Chemical Properties):* This section includes a description of the physical-chemical properties of the chemical substance and explains how these properties lead to the chemical's fate, transport, and exposure potential.

- *Section 4 (Relevant Assessment History):* This section includes an overview of the outcomes of other governing entities' assessments of the chemical substance.

- *Section 5 (Conditions of Use):* This section presents the chemical substance's known, intended, and reasonably foreseen conditions of use under TSCA.

- *Section 6 (Hazard Characterization):* This section summarizes the reasonably available hazard information and benchmarks the information against low-concern thresholds.

- *Section 7 (Exposure Characterization):* This section includes a qualitative summary of potential exposures to the chemical substance.

- *Section 8 (Summary of Findings):* In this section, EPA presents information pertinent to prioritization against each of the seven statutory and regulatory criteria and considerations, and proposes a conclusion based on that evidence.

- *Section 9 (Proposed Designation):* In this section, EPA presents the proposed designation for this chemical substance.

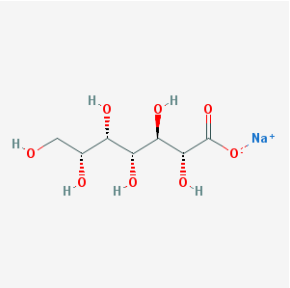
- *Appendix A (Conditions of Use Characterization):* This appendix contains a comprehensive list of TSCA and non-TSCA uses for the chemical substance from publicly available databases.

- *Appendix B (Hazard Characterization):* This appendix contains information on each of the studies used to support the hazard evaluation of the chemical substance.

- Appendix C (Literature Search Outcomes): This appendix includes literature search outcomes and rationales for studies that were identified in initial literature screening but were found to be off-topic or unacceptable for use in the screening-level review.

2. Background on Sodium Glucoheptonate

Table 1 below provides the CAS number, synonyms, and other information on sodium glucoheptonate.

Table 1: Sodium Glucoheptonate at a Glance	
Chemical Name	Sodium Glucoheptonate (D-gluco-Heptonic acid, sodium salt (1:1), (2.xi.)-)
CASRN	31138-65-5
Synonyms	alpha-D-Glucoheptonic acid sodium salt; D-Gluco-heptonic acid, monosodium salt; D-glycero-D-gulo-Heptonic acid sodium salt; D-glycero-D-gulo-Heptonic acid, monosodium salt; Gluceptate Sodium; Glucoheptonic Acid Sodium Salt; Glucosecarboxylic Acid Sodium Salt; Glucosecarboxylic acid sodium salt hydrate; Glucosemonocarboxylic acid; MolPort-006-120-012; Monosodium D-glycero-D-gulo-heptonate; potassium (2R,3R,4S,5R,6R)-2,3,4,5,6,7-hexahydroxyheptanoate; sodium (2R,3R,4S,5R,6R)-2,3,4,5,6,7-hexahydroxyheptanoate; sodium (2R,3R,4S,5R,6R)-2,3,4,5,6,7-hexakis(oxidanyl)heptanoate; Sodium Alpha-Glucoheptonate; Sodium D-glycero-D-gulo-heptonate; sodium glucopentonate; Monosodium D-glucoheptonate; Sodium glucoheptonate dihydrate
Trade Name(s)	SEQLENE 540; SEQLENE ES-50; H-Quest L-50 LA; Milco 150
Molecular Formula	$C_7H_{13}NaO_8$
Representative Structure	

Sodium glucoheptonate belongs to the hydroxycarboxylic acid salt family. The chemical structure of sodium glucoheptonate consists of a seven-carbon chain with hydroxyl (-OH) groups terminating in a carboxylic acid group. The close proximity of the oxygen atoms within the chemical structure lends to its function as a highly efficient chelating agent, by binding to positively charged metal ions in solution and thereby prevent these ions from forming insoluble precipitates with other ions that may be present. Sodium glucoheptonate functions as a chelating agent over a wide pH range due to its efficiency in forming stable chelates with divalent and trivalent metal ions such as calcium, magnesium, iron, aluminum, and other metals, thereby reducing the adverse effects these metals can have on systems. These properties contribute to the use of sodium glucoheptonate as a high performing chelating agent in a variety of applications and product sectors. Section 5 includes conditions of use for this chemical.

3. Physical-Chemical Properties

Table 2 lists physical-chemical properties for sodium glucoheptonate. A chemical's physical-chemical properties provide a basis for understanding a chemical's behavior, including in the environment and in living organisms. These endpoints provide information generally needed to assess potential environmental release, exposure, and partitioning as well as insight into the potential for adverse toxicological effects.

Table 2: Physical-Chemical Properties for Sodium Glucoheptonate

Source/Model	Data Type	Endpoint	Endpoint Value	Notes
Sigma-Aldrich 2019	Experimental	State at room temperature	Solid	
ECHA 2018	Experimental	Molecular weight	248 g/mol	
EPISuite v.4.11[3]	Calculated	Molecular weight	248.17 g/mol	
ECHA 2018	Experimental	Molar volume	220 cm^3/mol	
ECHA 2018	Experimental	Water solubility	$12.63x10^5$ to $13.87x10^5$ mg/L at 20°C and pH 9.7 (55.8 to 58.1% w/w)	
EPISuite v.4.11	Estimated	Water solubility	$1.0x10^6$ mg/L	K_{ow} method
ECHA 2018	Experimental	Water solubility	5.09 mol/L	
EPISuite v.4.11	Estimated	Log K_{ow}	-6.44	
EPISuite v.4.11	Estimated	Log K_{oa}	5.59	
EPISuite v.4.11	Estimated	Log K_{oc}	1.0(MCI); -4.23 (K_{ow})	
EPISuite v.4.11	Estimated	Vapor pressure	$1.20x10^{-19}$ mm Hg	
EPISuite v.4.11	Estimated	Henry's Law	$2.31x10^{-14}$ atm-m^3/mol	Bond method
EPISuite v.4.11	Estimated	Volatilization	$1.66x10^9$ days (river) $1.82x10^{10}$ days (lake)	
EPISuite v.4.11	Estimated	Photolysis (indirect)	2.64h min ($T_{1/2}$)	OH rate constant 4.85E-11 cm^3/molecules-sec (12 hour day; 1.5E6 OH/cm^3)
EPISuite v.4.11	Estimated	Hydrolysis	Rate constants cannot be estimated	No hydrolysable functional groups
EPISuite v.4.11	Estimated	Biodegradation potential	Ready prediction: Yes	
EPISuite v.4.11	Estimated	BAF	0.89	
EPISuite v.4.11	Estimated	BCF	3.16	Based on regression equation

[3] EPI Suite Physical Property Inputs – Water solubility= 1263000 mg/L, SMILES: [O-]C(=O)C(O)C(O)C(O)C(O)C(O)CO.[Na+]

EPA's Sustainable Futures/P2 Framework Manual[4] was used to interpret the physical-chemical properties provided in Table 2. Based on its reported physical state, sodium glucoheptonate is a solid at ambient temperatures (Sigma-Aldrich, 2019). In the solid form, sodium glucoheptonate has the potential for exposure via direct dermal exposure, through ingestion or through inhalation of dust particles if they are generated. Since it is a salt, sodium glucoheptonate is expected to be non-volatile at ambient temperatures (US EPA, 2019). Based on measured solubility data (ECHA, 2018), sodium glucoheptonate is considered water soluble, indicating the potential for this substance to dissolve in water and form an aqueous solution. The estimated Henry's Law constant (US EPA, 2019) for sodium glucoheptonate indicates volatilization from water and aqueous solutions is not expected to occur, and therefore exposure via inhalation of vapors under ambient conditions is expected to be minimal. Water soluble substances have an increased potential for absorption through the lungs; therefore, if exposed to the chemical in dust form, absorption through the lungs is likely. Oral exposure to this chemical could result in absorption through the gastrointestinal tract based on experimental evidence in closely-related analogs (discussed in Section 6.1.1). However, based on its estimated log K_{ow} (US EPA, 2019), sodium glucoheptonate is unlikely to sequester in fatty tissues (also discussed in Section 6.3.2). The estimated log K_{oc} (US EPA, 2019) indicates this substance is highly mobile in soils, increasing its potential for leaching into, and transport in, groundwater, including well water. Sodium glucoheptonate is expected to have low persistence (US EPA, 2019). Experimental biodegradation data for sodium glucoheptonate are not available; however, the measured biodegradation data for, sodium gluconate, a closely-related analog, indicate it can be considered readily biodegradable, and ultimately degradable anaerobically (OECD SIDS, 2004, 2072857), meaning that if it were to enter groundwater, it is likely to be broken down into carbon dioxide and water.

3.1 References

European Chemicals Agency (ECHA). (2018). Sodium glucoheptonate. Retrieved from https://echa.europa.eu/registration-dossier/-/registered-dossier/8874

Sigma-Aldrich. (2019). Sodium glucoheptonate. Retrieved from. https://www.sigmaaldrich.com/catalog/buildingblock/product/chemimpexinternationalinc/ch6h11e4f2d5?lang=en&region=US

U.S. EPA. (2019). Estimation Programs Interface Suite, v 4.11. United States Environmental Protection Agency, Washington, DC, USA

[4] https://www.epa.gov/sites/production/files/2015-05/documents/05.pdf

4. Relevant Assessment History

EPA assessed the toxicological profile of sodium glucoheptonate and added the chemical to the Safer Choice Program's Safer Chemical Ingredients List (SCIL) in September 2012 under the functional classes of chelating agents. The SCIL[5] is a continuously updated list of chemicals that meet low-concern Safer Choice criteria.[6]

In 2011, EPA included sodium glucoheptonate in a test rule under TSCA section 4(a)(1)(B), based on the potential for exposures of workers and consumers to these chemicals, that required manufacturers and processors of this and other high production volume (HPV) chemical substances to develop screening-level health, environmental, and fate data.[7] HPV chemicals are chemicals produced or imported in the United States in quantities of 1 million pounds or more per year. Relevant data submitted to the agency under this test rule has been incorporated in the Agency's screening review. EPA also reviewed international assessments of sodium glucoheptonate. EPA identified assessments by Canada's and Germany's government agencies.

The Canadian Government, through an assessment of toxicity and exposure as part of its categorization of the Domestic Substance List, found that sodium glucoheptonate did not meet its criteria for further attention.[8]

The German Environment Agency (UBA) designated sodium glucoheptonate as "low hazard to waters" in August 2017 based on an assessment of ecotoxicity and environmental fate.[9]

[5] https://www.epa.gov/saferchoice/safer-ingredients

[6] https://www.epa.gov/sites/production/files/2013-12/documents/dfe_master_criteria_safer_ingredients_v2_1.pdf

[7] https://www.federalregister.gov/documents/2011/10/21/2011-26894/certain-high-production-volume-chemicals-test-rule-and-significant-new-use-rule-fourth-group-of

[8] https://canadachemicals.oecd.org/ChemicalDetails.aspx?ChemicalID=D7922D37-A1B8-4327-9E58-47D212E52C0B

[9] https://webrigoletto.uba.de/rigoletto/public/searchDetail.do?kennummer=7009

5. Conditions of Use

EPA assembled information on conditions of use for sodium glucoheptonate. Per TSCA section 3(4), the term "conditions of use" means the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of. One source of information that EPA used to understand conditions of use is 2016 Chemical Data Reporting (CDR). The CDR rule (previously known as the Inventory Update Rule, or IUR), under TSCA section 8, requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S., generally above a reporting threshold of 25,000 lb. per site per year. CDR includes information on the manufacturing, processing, and use of chemical substances with information dating to the mid-1980s. CDR may not provide information on other life-cycle phases such as chemical substance's end-of-life after use in products (i.e., disposal).

According to CDR, sodium glucoheptonate is manufactured domestically and imported. Based on CDR reporting, it is used in processing (incorporation into formulation, mixture or reaction) for use as a raw material in internal blending of construction materials; soap, cleaning compound, and toilet preparation manufacturing; plating agents and surface treating agents. Additionally, the commercial use of sodium glucoheptonate for cleaning and furnishing care products was identified. Based on the known manufacturing, processing, and uses of this chemical substance, EPA assumes distribution in commerce. According to CDR, sodium glucoheptonate was recycled by one facility. No information on disposal is found in CDR or through EPA's Toxics Release Inventory (TRI) Program[10] since sodium glucoheptonate is not a TRI-reportable chemical. Although reasonably available information did not specify additional types of disposal, for purposes of this proposed prioritization designation, EPA assumed end-of-life pathways that include releases to air, wastewater, surface water, and land via solid and liquid waste based on the conditions of use (e.g., incineration, landfill).

To supplement CDR, EPA conducted research through the publicly available databases listed in Appendix A (Table A.2) and performed additional internet searches to clarify conditions of use or find additional occupational[11] and consumer uses. This research improved the Agency's understanding of the conditions of use for sodium glucoheptonate. Although EPA identified uses of sodium glucoheptonate in personal care products, this screening review covers TSCA conditions of use for the chemical substance and personal care products are not considered further in EPA's assessment. Exclusions to TSCA's regulatory scope regarding "chemical substance" can be found at TSCA section 3(2). Table 3 lists the conditions of use for sodium glucoheptonate considered for chemical substance prioritization, per TSCA section 3(4). Table 3 reflects the TSCA uses determined as conditions of use listed in Table A.3 (Appendix A).

[10] https://www.epa.gov/toxics-release-inventory-tri-program

[11] Occupational uses include industrial and/or commercial uses

Table 3: Conditions of Use for Sodium Glucoheptonate			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
Manufacturing	Domestic manufacture	Domestic manufacture	EPA (2017b)
	Import	Import	EPA (2017b)
Processing	Processing- incorporation into formulation, mixture or reaction	Plating agents and surface treating agents – resale of chemicals	EPA (2017b)
		Construction – used as a raw material in internal blending of construction materials	
		Solids separation agents – All other chemical product and preparation manufacturing	
		Plating agents and surface treating agents – miscellaneous manufacturing	
		Processing aids, not otherwise listed – soap, cleaning compound, and toilet preparation manufacturing	
		Ion exchange agents - Nonmetallic mineral product manufacturing (includes clay, glass, cement, concrete, lime, gypsum, and other nonmetallic mineral product manufacturing, Soap, cleaning compound, and toilet preparation manufacturing, Pesticide,[12] fertilizer, and other agricultural chemical manufacturing, Oil and gas drilling, extraction, and	

[12] EPA's 2016 CDR reports use of sodium glucoheptonate as an ion exchange agent during the processing phase (incorporation into formulation, mixture, or reaction product) of manufacturing. Sodium glucoheptonate is not registered with the California Department of Pesticide Regulation or the National Pesticide Information Retrieval System.

Table 3: Conditions of Use for Sodium Glucoheptonate			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
		support activities	
	Processing repackaging	Solids separation agents - All other chemical product and preparation manufacturing	
	Primary metal manufacturing	Manufacture of metal products, treatment and coating of metals	CPCat (2019); ECHA (2018b)
	Plastics product manufacturing	Manufacture of plastics products, including compounding and conversion	ECHA (2018b)
	Furniture and related product manufacturing	Manufacture of furniture	ECHA (2018b)
	Rubber product manufacturing	Manufacture of rubber products	ECHA (2018b); Synapse Information Resources (n.d.)
	Textiles, apparel, and leather manufacturing	Manufacture of textiles, leather and fur	CPCat (2019); ECHA (2018b)
	All other chemical product and preparation manufacturing	Printing and reproduction of recorded media	All other chemical product and preparation manufacturing
	Electrical and electronic products	Manufacture of computer, electronic and optical products, electrical equipment	ECHA (2018b); ECHA (2018c); Synapse Information Resources (n.d.)
	Recycling	Recycling	EPA (2017b)[13]
Distribution	Distribution	Distribution	EPA (2017b)
	Agriculture, forestry, fishing and hunting[14]	Chelating agent	CPCat (2019), ECHA (2018b)

[13] According to CDR reports, at least one manufacturer recycles the chemical substance. No other information on recycling was identified.

[14] Assumed to be a mix of TSCA and non-TSCA products. It is expected that more specifically defined uses in the table are representative of the uses that fall into this category.

Table 3: Conditions of Use for Sodium Glucoheptonate			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
	Mining (except oil and gas) and support activities	Mining	ECHA (2018b)
Industrial/Commercial uses	Oil and Gas Exploration	Oil and gas drilling, extraction, and support activities; extraction agents	EPA (2017b); ECHA (2018c); ECHA (2018b)
	Odor Agents	Air care products	ECHA (2018c); ECHA (2018b)
	Laundry and dishwashing care products	Laundry booster	Alco-Chem Inc. (2015b); Alco-Chem Inc. (2015a)
	Agricultural products (non-pesticidal)	Plant protection products	ECHA (2018c); ECHA (2018b)
	Adsorbents	Chelating agent	ECHA (2018c); ECHA (2018b)
	Anti-freeze and de-icing products	Anti-freeze and de-icing products	ECHA (2018c); ECHA (2018b)
	Explosive materials	Explosives	ECHA (2018c); ECHA (2018b)
	Fuels and related products	Fuels, Heat transfer fluids, Hydraulic fluids	ECHA (2018c); ECHA (2018b)
	Other	Laboratory chemicals, intermediates	ECHA (2018c); ECHA (2018b)
Industrial/commercial/consumer uses	Fabric, textile, and leather products not covered elsewhere	Leather treatment products	ECHA (2018a); ECHA (2018c); ECHA (2018b)
	Cleaning and furnishing care products	Degreaser, Polishes and wax blends[15]	EPA (2017b); CPCat (2019); ECHA (2018a); ECHA (2018c); ECHA (2018b)
	Laundry and dishwashing care products	Cleaning/washing agents for dish washing machines	CPCat (2019)

[15] One manufacturer reported 100% commercial use for cleaning and furnishing care products to the 2016 CDR (EPA (2017b)). While specific products are not identified on the CDR, other sources seem to suggest use in degreasers, polishes, and wax blends.

Table 3: Conditions of Use for Sodium Glucoheptonate			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
	Paints and coatings	Coatings and paints, thinners, paint removers,	ECHA (2018a); ECHA (2018c); ECHA (2018b); Synapse Information Resources (n.d.)
	Adhesives and sealants	Chelating agent	ECHA (2018)
	Lubricants and greases	Lubricants, greases, release products	ECHA (2018a); ECHA (2018c); ECHA (2018b)
	Lawn and garden products	Fertilizers	ECHA (2018a); ECHA (2018b); ECHA (2018c)
	Odor Agents	Fragrances	ECHA (2018); CPCat (2019)
	Other	Fluid property modulator, Food-contact paper/paperboard manufacturing, Electricity, steam, gas, water supply and sewage treatment	CPCat (2019), Synapse Information Resources (n.d.); ECHA (2018a); ECHA (2018c); ECHA (2018b)
	Ink, toner, and colorant products	Ink and toners	ECHA (2018a); ECHA (2018c); ECHA (2018b)
	Photographic supplies, film, and photo chemicals	Photo-chemicals	ECHA (2018a); ECHA (2018c); ECHA (2018b)
Commercial/consumer uses	Plating agents and surface treating agents	C909 the product is used as a cleaner in plating processes. The processes are diverse, examples of final uses are: automotive, machinery, basically all applications of plating	EPA (2017b)

Table 3: Conditions of Use for Sodium Glucoheptonate			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
	Other metal products	Metal products not covered elsewhere	
	Arts, crafts, and hobby materials	Finger paints	ECHA (2018a); ECHA (2018b); ECHA (2018c)
Consumer	Laundry and dishwashing products	Color-safe bleach, stain remover	DeLima Associates (2017); Walmart (2018)
	Automotive care products	Automotive wheel and tire cleaner	DeLima Associates (2012)
Disposal	Releases to air, wastewater, solid and liquid wastes		Though not explicitly identified, releases from disposal are assumed to be reasonably foreseen[16]

[16] See Section 5 for a discussion on why releases are assumed to be reasonably foreseen for purposes of this proposed prioritization designation.

6. Hazard Characterization

EPA reviewed primary literature and other data sources to identify reasonably available information. This literature review approach[17] is tailored to capture the reasonably available information associated with low-hazard chemicals. EPA also used this process to verify the reasonably available information for reliability, completeness, and consistency. EPA reviewed the reasonably available information to identify relevant, quality studies to evaluate the hazard potential for sodium glucoheptonate against the endpoints listed below. EPA's New Chemicals Program has used these endpoints for decades to evaluate chemical substances under TSCA[18] and EPA toxicologists rely on these endpoints as key indicators of potential human health and environmental effects. These endpoints also align with internationally accepted hazard characterization criteria, such as the Globally Harmonized System of Classification and Labelling of Chemicals[19] as noted above in Section 4 and form the basis of the comparative hazard assessment of chemicals.

Human health endpoints evaluated: Acute mammalian toxicity, repeated dose toxicity, carcinogenicity, mutagenicity/genotoxicity, reproductive and developmental toxicity, neurotoxicity, skin sensitization, and eye and skin irritation.

Environmental fate and effects endpoints evaluated: Aquatic toxicity, environmental persistence, and bioaccumulation.

The low-concern criteria used to evaluate both human health and environmental fate and effects are included in Table 4 below.

Table 4: Low-Concern Criteria for Human Health and Environmental Fate and Effects

Human Health				
Acute Mammalian Toxicity[20]	**Very High**	**High**	**Moderate**	**Low**
Oral LD_{50} (mg/kg)	≤ 50	> 50 – 300	> 300 - 2000	> 2000
Dermal LD_{50} (mg/kg)	≤ 200	> 200 – 1000	> 1000 - 2000	> 2000
Inhalation LC_{50} (vapor/gas) (mg/L)	≤ 2	> 2 – 10	> 10 - 20	> 20
Inhalation LC_{50} (dust/mist/fume) (mg/L)	≤ 0.5	> 0.5 - 1.0	> 1.0 - 5	> 5
Repeated Dose Toxicity (90-day study)[21]		**High**	**Moderate**	**Low**

[17] Discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA", also released at proposal.

[18] https://www.epa.gov/sustainable-futures/sustainable-futures-p2-framework-manual

[19] https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev07/English/ST_SG_AC10_30_Rev7e.pdf

[20] Values derived from GHS criteria (*Chapter 3.1: Acute Toxicity.* 2009, United Nations).

[21] Values from GHS criteria for Specific Target Organ Toxicity Repeated Exposure (*Chapter 3.9: Specific Target Organ Toxicity Repeated* Exposure. 2009, United Nations).

Table 4: Low-Concern Criteria for Human Health and Environmental Fate and Effects				
Oral (mg/kg-bw/day)		< 10	10 - 100	> 100
Dermal (mg/kg-bw/day)		< 20	20 - 200	> 200
Inhalation (vapor/gas) (mg/L/6h/day)		< 0.2	0.2 - 1.0	> 1.0
Inhalation (dust/mist/fume) (mg/L/6h/day)		< 0.02	0.02 - 0.2	> 0.2
Reproductive Toxicity[22]		**High**	**Moderate**	**Low**
Oral (mg/kg/day)		< 50	50 - 250	> 250
Dermal (mg/kg/day)		< 100	100 - 500	> 500
Inhalation (vapor, gas, mg/L/day)		< 1	1 - 2.5	> 2.5
Inhalation (dust/mist/fume, mg/L/day)		< 0.1	0.1 - 0.5	> 0.5
Developmental Toxicity[26]		**High**	**Moderate**	**Low**
Oral (mg/kg/day)		< 50	50 - 250	> 250
Dermal (mg/kg/day)		< 100	100 - 500	> 500
Inhalation (vapor, gas, mg/L/day)		< 1	1 - 2.5	> 2.5
Inhalation (dust/mist/fume, mg/L/day)		< 0.1	0.1 - 0.5	> 0.5
Mutagenicity/ Genotoxicity[23]	**Very High**	**High**	**Moderate**	**Low**
Germ cell mutagenicity	GHS Category 1A or 1B: Substances known to induce heritable mutations or to be regarded as if they induce heritable mutations in the germ cells of humans.	GHS Category 2: Substances which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans.	Evidence of mutagenicity support by positive results *in vitro* OR *in vivo* somatic cells of humans or animals	Negative for chromosomal aberrations and gene mutations, or no structural alerts.
Mutagenicity and genotoxicity in somatic cells		OR Evidence of mutagenicity		

[22] Values derived from the U.S. EPA's Office of Pollution Prevention & Toxics criteria for HPV chemical categorizations (*Methodology for Risk-Based Prioritization Under ChAMP*), and the EU REACH criteria for Annex IV (2007).

[23] From GHS criteria (*Chapter 3.5: Germ Cells Mutagenicity.* 2009, United Nations) and supplemented with considerations for mutagenicity and genotoxicity in cells other than germs cells.

Table 4: Low-Concern Criteria for Human Health and Environmental Fate and Effects				
		supported by positive results in *in vitro* AND *in vivo* somatic cells and/or germ cells of humans or animals.		
Carcinogenicity[24]	**Very High**	**High**	**Moderate**	**Low**
	Known or presumed human carcinogen (GHS Category 1A and 1B)	Suspected human carcinogen (GHS Category 2)	Limited or marginal evidence of carcinogenicity in animals (and inadequate[25] evidence in humans)	Negative studies or robust mechanism-based structure activity relationship (SAR)
Neurotoxicity (90-day study)[215]		**High**	**Moderate**	**Low**
Oral (mg/kg-bw/day)		< 10	10 - 100	> 100
Dermal (mg/kg-bw/day)		< 20	20 - 200	> 200
Inhalation (vapor/gas) (mg/L/6h/day)		< 0.2	0.2 - 1.0	> 1.0
Inhalation (dust/mist/fume) (mg/L/6h/day)		< 0.02	0.02 - 0.2	> 0.2
Sensitization[26]		**High**	**Moderate**	**Low**
Skin sensitization		High frequency of sensitization in humans and/or high potency in animals (GHS Category 1A)	Low to moderate frequency of sensitization in human and/or low to moderate potency in animals (GHS Category 1B)	Adequate data available and not GHS Category 1A or 1B
Respiratory sensitization		Occurrence in humans or evidence of sensitization in humans based on animal or other tests (equivalent to GHS Category 1A or 1B)	Limited evidence including the presence of structural alerts	Adequate data available indicating lack of respiratory sensitization

[24] Criteria mirror classification approach used by the IARC (*Preamble to the IARC Monographs: B. Scientific Review and Evaluation: 6. Evaluation and rationale.* 2019*)* and incorporate GHS classification scheme (*Chapter 3.6: Carcinogenicity*. 2009, United Nations).

[25] EPA's approach to determining the adequacy of information is discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA", also released at proposal.

[26] Incorporates GHS criteria (*Chapter 3.4: Respiratory or Skin Sensitization.* 2009, United Nations).

Table 4: Low-Concern Criteria for Human Health and Environmental Fate and Effects				
Irritation/ Corrosivity[27]	**Very High**	**High**	**Moderate**	**Low**
Eye irritation/ corrosivity	Irritation persists for >21 days or corrosive	Clearing in 8-21 days, severely irritating	Clearing in 7 days or less, moderately irritating	Clearing in less than 24 hours, mildly irritating
Skin irritation/ corrosivity	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours
Environmental Fate and Effects				
Acute Aquatic Toxicity Value ($L/E/IC_{50}$)[28]	**Chronic Aquatic Toxicity Value ($L/E/IC_{50}$)[28]**	**Persistence (Measured in terms of level of biodegradation)[29]**		**Bioaccumulation Potential[30]**
May be low concern if ≤10 ppm…	…and ≤1 ppm…	…and the chemical meets the 10-day window as measured in a ready biodegradation test…		…and BCF/BAF < 1000.
Low concern if >10 ppm and <100 ppm…	…and >1 ppm and <10 ppm…	…and the chemical reaches the pass level within 28 days as measured in a ready biodegradation test		
Low concern if ≥100 ppm…	…and ≥ 10 ppm…	… and the chemical has a half-life < 60 days…		

6.1 Human Health Hazard

Below is a summary of the reasonably available information that EPA included in the hazard evaluation of sodium glucoheptonate. In many cases, EPA used analogous chemicals to make findings for a given endpoint. Where this is the case, use of the analog is explained. If the chemical studied is not named, the study is for sodium glucoheptonate. Appendix B contains more information on each study.

Sodium glucoheptonate is the sodium salt of glucoheptanoic acid, which is a 7-carbon aldonic acid (oxidized sugar) derived from glucoheptose. EPA used best professional judgement to select analogs for sodium glucoheptonate based on similarity in structure and functionality, with the assumption that these chemicals will have similar environmental transport and persistence characteristics, and bioavailability and toxicity profiles. All of the analogs presented in Table 4 are either salts or esters of aldonic acids containing 5-7 carbon atoms. D-gluconic acid, an aldonic acid containing 6 carbon atoms, some of its corresponding salts, and one ester derivative. The sodium, potassium and calcium salts of D-gluconic acid are expected to readily dissociate under environmentally and biologically

[27] Criteria derived from the Office of Pesticide Programs Acute Toxicity Categories (U.S. EPA. *Label Review Manual.* 2010).

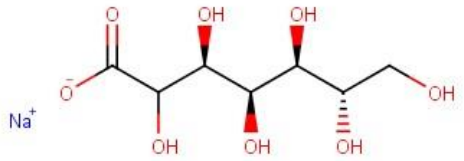
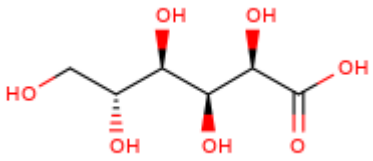
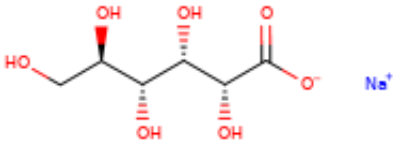
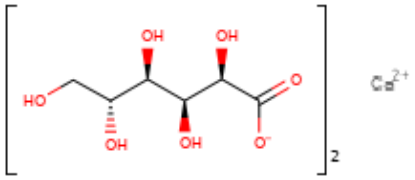
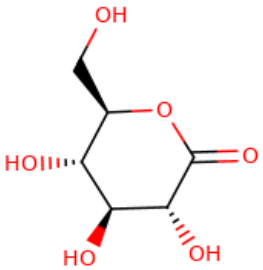
[28] Derived from GHS criteria (*Chapter 4.1: Hazards to the Aquatic Environment.* 2009, United Nations), EPA OPPT New Chemicals Program (*Pollution Prevention (P2) Framework,* 2005*)* and OPPT's criteria for HPV chemical categorization (*Methodology for Risk Based Prioritization Under ChAMP. 2009).*

[29] Derived from OPPT's New Chemicals Program and DfE Master Criteria and reflects OPPT policy on PBTs (*Design for the Environment Program Master Criteria for Safer Chemicals, 2010).*

[30] Derived from OPPT's New Chemicals Program and Arnot & Gobas (2006) [Arnote, J.A. and F.A. Gobas, *A review of bioconcentration factor (BCF) and bioaccumulation factor (BAF) assessments for organic chemicals* in aquatic organisms. Environmental Reviews, 2006. 14: p. 257-297.]

relevant conditions to release gluconic acid and/or gluconate anion, depending on the ambient pH. As a result, the environmental and health effects of these compounds are expected to be very similar to those of sodium glucoheptonate. In addition, glucono-delta-lactone is an analog for the target compound. Glucono-delta-lactone is a cyclic ester (lactone) of D-gluconic acid. The lactone and acid are interconverted to each other and exist in equilibrium in aqueous solution. Based on these factors, the environmental and toxicological effects of glucono-delta-lactone and D-gluconic acid are expected to be very similar to each other, and to sodium glucoheptonate.

Table 5: Sodium Glucoheptonate and Analog Structures

CASRN	Name	Structure
31138-65-5	Sodium glucoheptonate	
526-95-4	D-Gluconic acid	
527-07-1	Sodium gluconate	
299-28-5	Calcium gluconate	
90-80-2	Glucono-delta-lactone	

6.1.1 Absorption, Distribution, Metabolism, and Excretion

Absorption

Sodium glucoheptonate has limited potential for inhalation exposure under environmental conditions and if incorporated in a water or aqueous solution (based on its solid state and low Henry's Law constant, Section 3). If sodium glucoheptonate is present as dust and inhaled, absorption from the lungs is likely based on its high water solubility (Section 3).

The potential for dermal absorption of sodium glucoheptonate is predicted to be low when in the neat form and in a water-based product formulation based on its low log K_{ow} (Section 3).

An oral gavage study on rats in closely-related analogs provided evidence that sodium glucoheptonate is likely to be absorbed through the intestine. Rats dosed with U-^{14}C labeled glucono-delta-lactone or sodium gluconate via oral gavage displayed evidence of distribution into blood and the intestine within 5 hours of exposure (discussed further below in Excretion), indicating the chemical is rapidly absorbed through the gastrointestinal tract (ECHA, 1979a, b). Based on these data, sodium glucoheptonate is expected to be absorbed through the intestine following an oral exposure.

Distribution

Sodium glucoheptonate is considered water soluble (Section 3) and is likely to be distributed mainly in aqueous compartments in an organism. This prediction is supported by experimental evidence. Following an oral gavage dose of U-^{14}C labeled glucono-delta-lactone or sodium gluconate in rats, radioactivity was measured in blood, feces, and the intestine within 5 hours of exposure, indicating rapid absorption and distribution occurred (discussed further in Excretion) (ECHA, 1979a, b).

Metabolism

Because quality experimental data[31] on sodium glucoheptonate metabolite formation were limited, the Quantitative Structure-Activity Relationship (QSAR) toolbox[32] was used to run the rat liver S9 metabolism simulator, the skin metabolism simulator, and the *in vivo* rat metabolism simulator. The QSAR toolbox was used to identify putative sodium glucoheptonate metabolites. Sodium glucoheptonate is expected to be metabolized by oxidation in the liver to sodium hydroxide and sugar, sugar acids, and a sugar alcohol, and metabolized to a number of highly oxidized metabolites in the skin. *In vivo* metabolites are expected to include some carbohydrate acids, and derivatives of tetrahydro-furan-2-carbaldehyde and tetrahydro-2-furancarboxylic acid.

Excretion

To assess sodium glucoheptonate's excretion pathways, EPA used experimental data from analogs. An oral study in rats dosed with glucono-delta-lactone found 25% was exhaled as carbon dioxide, 23% remained in the whole body (excluding the gastrointestinal tract), 29.5% in the intestine and feces, and 7% in urine (ECHA, 1979a, b). For animals orally dosed with sodium gluconate, 12.1,

[31] Discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances under TSCA."

[32] https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm

19.7, 44.9, and 5% was recovered from exhaled carbon dioxide, whole body (excluding gastrointestinal tract), intestine and feces, and in urine, respectively (ECHA, 1979a, b).

In a human study, approximately 7.7% to 15% of an administered oral dose of glucono-delta-lactone was reported in urine following exposure (JECFA, 1986). In another human study, there was no recovery in the urine following a single oral dose of glucono-delta-lactone (JECFA, 1986).

Based on these data, it is expected that sodium glucoheptonate will be primarily excreted through feces and exhaled breath.

6.1.2 Acute Toxicity

EPA assessed the mammalian toxicity potential from acute exposure to sodium glucoheptonate using experimental data. An OECD Guideline 425 study exposed rats via oral gavage to sodium glucoheptonate and indicated no mortality in rats at the highest dose tested, 2000 mg/kg (ECHA, 2013b; Harlan Laboratories, 2013a). An OECD Guideline 402 study for acute dermal exposure to rats also indicated no mortality at the highest dose tested, 2000 mg/kg (ECHA, 2013a). These studies indicated low concern for acute toxicity with expected LD_{50}s above the low-concern threshold of 2000 mg/kg for dermal and oral exposures.

6.1.3 Repeated Dose Toxicity

EPA assessed the potential for mammalian toxicity from repeated exposure using experimental data. An OECD Guideline 422 (combined repeated dose toxicity study and reproduction/developmental toxicity screening test) oral gavage study exposed rats to sodium glucoheptonate beginning two weeks prior to mating and continued the exposure through gestation to lactation day 5 (for females), for a total of 8 weeks (ECHA, 2013e). The no observed adverse effect level (NOAEL) was determined to be 1000 mg/kg-day. The NOAEL identified in this study indicated low concern for toxicity resulting from sub-chronic exposure by far exceeding the low-concern threshold of 100 mg/kg-day for a 90-day exposure (the threshold is 200 mg/kg-day for a 45-day exposure).

6.1.4 Reproductive and Developmental Toxicity

In the previously mentioned OECD Guideline 422 oral gavage study on rats (Section 6.1.3), no adverse reproductive effects were noted at the highest dose, resulting in a NOAEL of 1000 mg/kg-day. The study also examined a subset of developmental endpoints, such as litter parameters and assessment of surface righting reflexes. No adverse effects were noted for these developmental endpoints (ECHA, 2013e).

EPA further examined the potential for developmental toxicity using data from an analog, glucono-delta-lactone. Oral gavage studies on several species, including mice (JECFA, 1986; ECHA, 1973b; Inc, 1973), hamsters (JECFA, 1986; ECHA, 1979a; Inc, 1973), rabbits (JECFA, 1986; ECHA, 1973c; Inc, 1973), and rats (JECFA, 1986; ECHA, 1973a; Inc, 1973), indicated no adverse effects at the highest dose tested in each study. For these studies, the NOAELs ranged from 560 to 780 mg/kg-day. These results, taken with the low-concern criteria oral threshold of 250 mg/kg-day, indicate low concern for reproductive and developmental toxicity.

6.1.5 Genotoxicity

EPA assessed the potential for genotoxicity using an OECD Guideline 474 *in vivo* DNA damage study (Harlan Laboratories, 2013c). Mice exposed to sodium glucoheptonate by intraperitoneal injection resulted in no reported increases in DNA damage and repair effects. EPA also considered several *in vitro* and *in vivo* gene mutation and chromosomal aberration studies on closely-related analogs. All studies resulted in negative findings, providing further evidence these results indicate low concern for genotoxicity from sodium glucoheptonate.

6.1.6 Carcinogenicity

Because quality experimental data on sodium glucoheptonate were limited, EPA relied on publicly available quantitative structure activity relationship (QSAR) models and structural alerts (SA) to assess the carcinogenic potential for sodium glucoheptonate. Structural alerts represent molecular functional groups or substructures that are known to be linked to the carcinogenic activity of chemicals. The most common structural alerts are those for electrophiles (either direct acting or following activation). Modulating factors that will impact the carcinogenic potential of a given electrophile will include its relative hardness or softness, its molecular flexibility or rigidity, and the balance between its reactivity and stability.[33] For this chemical, there is an absence of the types of reactive structural features that are present in genotoxic carcinogens. Sodium glucoheptonate is not an electrophile. ISS profiler, a QSAR model,[34] identified an aldehyde metabolite alert; however, this aldehyde metabolite is formed in the first oxidation transformation during metabolism and will rapidly be transformed to the corresponding carboxylic acid. Further, the Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA) models'[35] results indicate sodium glucoheptonate has low potential to be carcinogenic or mutagenic.

Sodium glucoheptonate is a multi-hydroxy acid that is likely to be metabolized through oxidation. Sodium glucoheptonate and its metabolites are expected to be rapidly excreted from the body (discussed in Section 6.1.1). Therefore, it is anticipated that this chemical will not remain in the body for a long period of time, reducing concern for carcinogenicity.

Sodium glucoheptonate's metabolism, a lack of structural alerts, and experimental genotoxicity studies indicates that this chemical is unlikely to be carcinogenic or mutagenic.

6.1.7 Neurotoxicity

EPA assessed the potential for neurotoxicity from exposure to sodium glucoheptonate on a subset of the exposed rats from the OECD Guideline 422 described in Section 6.1.3 were used for the neurotoxicity assessments. No adverse neurological effects on behavior (motor activity, grip strength,

[33] "Fundamental and Guiding Principles for (Q)SAR Analysis of Chemical Carcinogens with Mechanistic Considerations: Series on Testing and Assessment, No. 229." 2015. Environment Directorate, Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology.

[34] Carcinogenicity alerts by ISS 2.4 profiler as encoded in the QSAR Toolbox 4.3 (qsartoolbox.org). A summary of the results from these models is provided in Appendix B.

[35] There are four carcinogenicity models housed within the VEGA 1.1.4 software tool available from https://www.vegahub.eu. A summary of the results from these models is provided in Appendix B.

sensory reactivity) or histology (brain, spinal cord and sciatic nerve) were observed at the highest dose tested, 1000 mg/kg-day (ECHA, 2013c, d). The results from this study indicate low concern for neurotoxicity by exceeding the 100 mg/kg-day threshold.

6.1.8 Skin Sensitization

EPA assessed the potential for sodium glucoheptonate to cause skin sensitization using an OECD Guideline 429 study in mice (ECHA, 2013i). Sodium glucoheptonate was negative for dermal sensitization. This negative result indicated low concern to skin sensitization for sodium glucoheptonate.

6.1.9 Skin Irritation

EPA assessed the potential for sodium glucoheptonate to cause dermal irritation effects using a study on EPISKINTM tissues (ECHA, 2013h). This study identified sodium glucoheptonate as non-irritating. EPA also reviewed *in vivo* data on D-gluconic acid. D-gluconic acid was non-irritating in two rabbit studies (ECHA, 2009b; OECD, 2004). These results indicated low concern for skin irritation from sodium glucoheptonate.

6.1.10 Eye Irritation

To assess potential for eye irritation, EPA used read-across from sodium glucoheptonate's analogs, glucono delta-lactone and D-gluconic acid. An *in vitro* bovine corneal opacity and permeability assay found glucono-delta-lactone to be a severe irritant (Gautheron et al., 1994). D-gluconic acid had moderate results for eye irritation using *in vivo* studies. One study in rabbits indicated D-gluconic acid was mildly irritating to the eyes with all effects fully reversible in 72 hours (OECD, 2004), while another study in rabbits concluded D-gluconic acid was irritating with most effects reversed by the study's end at 72 hours (ECHA, 2009a). While the *in vitro* study provided evidence of irritation, EPA weighed the outcome of the *in vivo* effects to determine that the reversible results indicated moderate concern for eye irritation from sodium glucoheptonate.

6.1.11 Hazards to Potentially Exposed or Susceptible Subpopulations

The above information supports a low human health hazard finding for sodium glucoheptonate based on low-concern criteria. This finding includes considerations such as the potential for developmental toxicity, reproductive toxicity, and acute and repeated dose toxicity that may impact potentially exposed or susceptible subpopulations. Based on the hazard information discussed in Section 6, EPA did not identify populations with greater susceptibility to sodium glucoheptonate.

6.2 Environmental Hazard

EPA assessed environmental hazard for sodium glucoheptonate based on available acute toxicity experimental data and estimated chronic toxicity values using the Ecological Structure Active Relationships (ECOSAR) Predictive Model.[36] Appendix B contains a summary of the reasonably available environmental hazard data.

[36] https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model

6.2.1 Acute Aquatic Toxicity

EPA assessed ecological hazard from acute exposures to sodium glucoheptonate. No adverse effects were observed in aquatic invertebrates and aquatic vertebrates exposed to sodium glucoheptonate at the highest doses tested (100 mg/L), resulting in no effects expected at concentrations less than 100 mg/L for aquatic vertebrates (Harlan Laboratories, 2015b; ECHA, 2013g) and 100 mg/L for invertebrates (Harlan Laboratories, 2015a; ECHA, 2013f). Algae exposed to sodium glucoheptonate resulted in an acute EC50 of 790 mg/L based on growth rate and 190 mg/L based on biomass (ECHA, 2013j; Harlan Laboratories, 2013b). These aquatic toxicity studies indicate low concern for acute aquatic exposure by exceeding the low-concern threshold of 100 mg/L.

6.2.2 Chronic Aquatic Toxicity

Chronic toxicity values estimated using ECOSAR for aquatic vertebrates, aquatic invertebrates, and algae are 860,000 mg/L, 175,000 mg/L, and 83,000 mg/L, respectively. These toxicity values indicated that sodium glucoheptonate is expected to have low environmental hazard based on the low-concern criteria chronic aquatic toxicity threshold of 10 mg/L.

6.3 Persistence and Bioaccumulation Potential

6.3.1 Persistence

EPA assessed the environmental persistence for sodium glucoheptonate. An experimental OECD Guideline 301F biodegradation study demonstrated this substance biodegraded under aerobic conditions by greater than 60 percent in 10 days, confirming it is readily biodegradable in a sewage sludge inoculum (ECHA, 2012). Based on read-across from sodium gluconate, sodium glucoheptonate is expected to anaerobically biodegrade completely (OECD, 2004). No degradation products of concern were identified for sodium glucoheptonate. Given the low aquatic toxicity concern for this chemical, meeting the low-concern criteria means that the chemical did not produce degradation products of concern and has a half-life less than 60 days. Further, using read-across from sodium gluconate, sodium glucoheptonate is expected to anaerobically biodegrade completely after 35 days (OECD, 2004). The available biodegradation results meet the low-concern threshold and indicate this chemical will have low potential for persistence.

6.3.2 Bioaccumulation Potential

Based on the estimated bioaccumulation factor (BAF) value of 3.16 using the Estimation Programs Interface (EPI) Suite models,[37] sodium glucoheptonate has low potential for bioaccumulation in the environment based on the low-concern threshold of less than 1000.

[37] https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface

7. Exposure Characterization

EPA considered reasonably available information on exposure for sodium glucoheptonate. In general, there is limited information on exposure for low-hazard chemicals. EPA determined the CDR database and certain other sources of sodium glucoheptonate use information are sources of information relevant to sodium glucoheptonate's exposure potential. Of these sources, EPA determined that the CDR database contained the primary source of information on the conditions of use for this exposure characterization. EPA also consulted sources of use information from other databases and public sources (listed in Table A.2). EPA used these sources only where they augmented information from the CDR database to inform intended, known, or reasonably foreseen uses (Section 5).

As shown in Tables 3 and A.3, sodium glucoheptonate is used in processing (incorporation into formulation, mixture or reaction) for use as a raw material in internal blending of construction materials; detergents, cleaning compounds, and toilet preparation manufacturing; plating agents and surface treating agents. Non-TSCA uses are beyond the scope of this assessment because of the exclusions under TSCA section 3(2). (See Table A.3)

Under the conditions of use identified in Table 3, EPA assessed the potential exposure to the following categories: the environment, the general population, and potentially exposed or susceptible subpopulations including workers, consumers, and children.

7.1 Production Volume Information

Production volume information for sodium glucoheptonate is based on an analysis of CDR data reported from 1986 to 2015.[38] The CDR database indicates that, for reporting year 2015, six companies manufactured or imported sodium glucoheptonate at six sites. For all reporting years aggregate production volume for sodium glucoheptonate was between 1,000,000 and 10,000,000 lbs. The exact amount is available for one year, 2011, in which 9,880,022 lbs. of sodium glucoheptonate was produced or imported. In general, since 1986, production volume has remained relatively stable.

7.2 Exposures to the Environment

EPA expects most exposures to the environment to occur during the manufacturing, processing, and industrial, consumer, and commercial uses of sodium glucoheptonate. Exposure is also possible from other uses, such as distribution and disposal. These activities could result in releases of sodium glucoheptonate to media including surface water, landfills, and air.

EPA expects high levels of removal of sodium glucoheptonate during wastewater treatment (either directly from the facility or indirectly via discharge to a municipal treatment facility or Publicly Owned Treatment Works (POTW)). Further, sodium glucoheptonate is expected to have low persistence (aerobic and anaerobic biodegradation are discussed in Section 6.3.1) and has the

[38] The CDR requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S. generally above 25,000 lb. per site.

potential to be broken down in the environment to carbon dioxide and water. Therefore, any release of the chemical to surface water is expected to break down, reducing exposure to aquatic organisms in the water column, benthic organisms, and groundwater sources of drinking water, including well water.

If disposed of in a landfill, this chemical is expected to degrade under aerobic and anaerobic conditions (aerobic and anaerobic biodegradation are discussed in Section 6.3.1).

If incineration releases during manufacturing and processing occur, EPA expects significant degradation of sodium glucoheptonate to the point that it will not be present in air.

7.3 Exposures to the General Population

EPA expects the general population is unlikely to be exposed to sodium glucoheptonate from the environmental releases described above. The general population is unlikely to be exposed to sodium glucoheptonate via inhalation of ambient air because sodium glucoheptonate is a solid, has a low vapor pressure, and will break down if incinerated. Sodium glucoheptonate is also unlikely to be present in surface water because it will degrade (discussed in Section 6.3.1), reducing the potential for the general population to be exposed by oral ingestion or dermal exposure. Given the low bioconcentration and bioaccumulation potential of sodium glucoheptonate, oral exposure to sodium glucoheptonate via fish ingestion is unlikely.

7.4 Exposures to Potentially Exposed or Susceptible Subpopulations

EPA identified workers, consumers, and children as potentially exposed or susceptible subpopulations. EPA identified workers based on greater exposure to sodium glucoheptonate than the general population during manufacturing and processing. EPA identified children (including any adults working closely with children) as a population that may experience greater exposure to sodium glucoheptonate than the general population during use of arts and crafts products. EPA also identified consumers as a population that may experience greater exposure to sodium glucoheptonate than the general population through use of cleaning products or arts and craft products, for example. EPA did not identify populations with greater susceptibility to sodium glucoheptonate.

7.4.1 Exposures to Workers

Based on its reported physical form and measured melting point, sodium glucoheptonate is a solid under ambient conditions. Based on sodium glucoheptonate's conditions of use (Table 3), workers may be exposed to solids via ingestion or inhalation of dust if generated. Sodium glucoheptonate is a salt and therefore not expected to be a volatile substance, meaning workers are unlikely to be exposed through inhalation of vapors. Workers may be exposed to sodium glucoheptonate in manufacturing, processing, distribution, use and disposal.

7.4.2 Exposures to Consumers

Consumers could be exposed to sodium glucoheptonate through the use of arts, crafts, and hobby materials (e.g., finger paints), laundry and dishwashing products, automotive care products, or other uses as specified in Table 3. For all these uses, if dermal contact does occur, sodium glucoheptonate is expected to be minimally absorbed through the skin (see Section 6.1.1). If the chemical is in an

aerosol product and inhalation exposure occurs, sodium glucoheptonate's absorption from the lungs is likely based on its high level of water solubility (Section 6.1.1). Consumer exposure is likely through inhalation or incidental ingestion of dust if using consumer products in a powdered form, such as powdered laundry and dishwashing products and automotive care products. EPA does not include intentional misuse, such as people drinking products containing this chemical, as part of the known, intended or reasonably foreseen conditions of use that could lead to an exposure (82 FR 33726). Thus, oral exposures will be incidental (meaning inadvertent and low in volume). Sodium glucoheptonate is expected to be rapidly metabolized and excreted, further reducing the duration of exposure.

7.4.3 Exposures to Children

Children may have dermal contact with sodium glucoheptonate through use of arts and crafts products, such as finger paints. Given the molecular weight, water solubility, and partitioning coefficients in Section 3, this chemical is expected to be poorly absorbed through the skin. Based on its Henry's Law constant (Section 3), sodium glucoheptonate is not expected to be volatile from these liquid products, reducing the potential for inhalation exposures to children. If arts and crafts products are in a powdered form, inhalation of dust is likely. Children may also rub their eyes or incidentally ingest the product. Sodium glucoheptonate is expected to be rapidly metabolized and excreted (Section 6.1.1), reducing the duration of exposure.

8. Summary of Findings

EPA has used reasonably available information on the following statutory and regulatory criteria and considerations to screen sodium glucoheptonate against each of the priority designation considerations in 40 CFR 702.9(a) and discussed individually in this section, under its conditions of use:

- the hazard and exposure potential of the chemical substance (See Sections 6 and 7);
- persistence and bioaccumulation (See Section 6.3);
- potentially exposed or susceptible subpopulations (See Section 7.4);
- storage near significant sources of drinking water (See Section 8.4);
- conditions of use or significant changes in the conditions of use of the chemical substance (See Section 5);
- the chemical substance's production volume or significant changes in production volume (See Section 7.1); and
- other risk-based criteria that EPA determines to be relevant to the designation of the chemical substance's priority.

EPA conducted a risk-based, screening-level review based on the criteria and other considerations above and other relevant information described in 40 CFR 702.9(c) to inform the determination of whether the chemical substance meets the standard of a high-priority substance. High-priority substance means a chemical substance that EPA determines, without consideration of costs or other non-risk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to potentially exposed or susceptible subpopulations identified as relevant by EPA (40 CFR 702.3). This section explains the basis for the proposed designation and how EPA applied statutory and regulatory requirements, addressed issues, and reached conclusions.

8.1 Hazard and Exposure Potential of the Chemical Substance

Approach: EPA evaluated the hazard and exposure potential of sodium glucoheptonate. EPA used this information to inform its proposed determination of whether sodium glucoheptonate would meet the statutory criteria and considerations for proposed designation as a low-priority substance.

- **Hazard potential:**

For sodium glucoheptonate's hazard potential, EPA gathered information for a broad set of human health and environmental endpoints described in detail in Section 6 of this document. EPA benchmarked this information against the low-concern thresholds explained in Section 6. EPA found that sodium glucoheptonate is of low concern for human health and environmental hazard across the range of endpoints in these low-concern criteria.

- **Exposure potential:**

To understand exposure potential, EPA gathered information on physical-chemical properties, production volumes, and the types of exposures likely to be faced by workers, the general population, consumers, and children (discussed in Sections 3 and 7). EPA also gathered information on environmental releases. EPA identified workers, the general population, consumers, children, and the

environment as most likely to experience exposures. EPA determined that while the general population, consumers, children and workers may be exposed to sodium glucoheptonate, exposure by dermal, inhalation, and ingestion pathways are limited by sodium glucoheptonate's physical-chemical properties. If sodium glucoheptonate is released into the environment, its exposure potential will be reduced through biodegradation under aerobic and anaerobic conditions.

Rationale: Although sodium glucoheptonate may cause moderate eye irritation, the effects are expected to be reversible, reducing concern for longer-term or chronic effects. Workers could be exposed during processing, manufacturing, distribution, use, and disposal, splashing of solutions, or hand-to-face and eye contact. Other uses covered under TSCA, especially consumer uses in cleaning and furnishing care products and laundry and dishwashing products, would be unlikely to result in more than incidental eye exposure. Eye irritation resulting from exposure in an occupational and consumer setting is mitigated by the reversible nature of the effect and addressed by rinsing with water.

Proposed conclusion: Based on an initial analysis of reasonably available hazard and exposure information, EPA proposes to conclude that the risk-based, screening-level review under 40 CFR 702.9(a)(1) does not support a finding that sodium glucoheptonate meets the standard for a high-priority substance. The reasonably available hazard and exposure information described above provides sufficient information to support this proposed finding.

8.2 Persistence and Bioaccumulation

Approach: EPA has evaluated both the persistence and bioaccumulation potential of sodium glucoheptonate based on a set of EPA and internationally accepted measurement tools and thresholds that are sound indicators of persistence and bioaccumulation potential (described in Section 6). These endpoints are key components in evaluating a chemical's persistence and bioaccumulation potential.

Rationale: EPA review of experimental data indicates sodium glucoheptonate is readily biodegradable under aerobic conditions, with greater than 60 percent biodegradation expected within 10 days, and expected to be biodegradable under anaerobic conditions based on a closely-related analog (Section 6.3.1). EPA's EPI Suite models indicate a low potential for bioaccumulation (Section 6.3.2).

Proposed conclusion: Based on an initial screen of reasonably available information on persistence and bioaccumulation, EPA proposes to conclude that the screening-level review under 40 CFR 702.9(a)(2) does not support a finding that sodium glucoheptonate meets the high-priority substance. The reasonably available persistence and bioaccumulation information described above provides sufficient information to support this proposed finding.

8.3 Potentially Exposed or Susceptible Subpopulations

Approach: TSCA Section 3(12) states that the "term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the

Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." EPA identified workers engaged in the manufacturing, processing, distribution and use, and disposal of sodium glucoheptonate as a potentially exposed or susceptible subpopulation (described in more detail in Section 7). EPA also identified children (and any adults working closely with children) as a population that may experience greater exposure to sodium glucoheptonate than the general population during use of arts and crafts products. Consumers are also a potentially exposed subpopulation because of their use of products such as arts, crafts, and hobby materials, laundry and dishwashing products, and automotive care products.

Rationale: EPA did not identify hazard effects for this chemical that would make any population susceptible. EPA expects workers, consumers, and children to have a higher exposure to sodium glucoheptonate than the general population. Higher exposure to children could result from use of finger paints containing sodium glucoheptonate, which might lead to inadvertent eye contact. Because of the chemical's low-concern hazard properties and reversibility of the effects, this exposure does not pose a significant increase in risk for children, consumers, or workers.

Proposed conclusion: Based on the Agency's understanding of the conditions of use and expected users such as potentially exposed or susceptible subpopulations, EPA proposes to conclude that the screening-level review under 40 CFR 702.9(a)(3) does not support a finding that sodium glucoheptonate meets the standard for a high-priority substance. While the conditions of use will result in an increase in exposures to certain populations, the consistently low-hazard profile of sodium glucoheptonate provides sufficient evidence to support a finding of low concern. The reasonably available information on conditions of use, hazard and exposure described above provides sufficient information to support this proposed finding.

8.4 Storage Near Significant Sources of Drinking Water

Approach: In Sections 6 and 7, EPA explains its evaluation of the elements of risk relevant to the storage of sodium glucoheptonate near significant sources of drinking water. For this criterion, EPA focused primarily on the chemical substance's potential human health hazards, including to potentially exposed or susceptible subpopulations, and environmental fate properties, and explored a scenario of a release to a drinking water source. EPA also investigated whether the chemical was monitored for and detected in a range of environmental media. The requirement to consider storage near significant sources of drinking water is unique to prioritization under TSCA Section 6(b)(1)(A) and 40 CFR 702.9(a)(4).

Rationale: In terms of health hazards, sodium glucoheptonate is expected to present low concern to the general population, including susceptible subpopulations, across a spectrum of health endpoints.

In the event of an accidental release into a surface drinking water source, though sodium glucoheptonate is water soluble (see Section 3), it is not expected to persist (see Section 6.3.1) in the drinking water supply. In the event of an accidental release to land, its biodegradability (aerobically

and anaerobically, section 6.3.1) reduces its potential for leaching into groundwater, including well water. Fate and transport evaluation indicated sodium glucoheptonate is unlikely to partition into sediment, predicted to biodegrade under aerobic and anaerobic conditions (see Section 3), and unlikely to bioaccumulate (see Section 6), minimizing the likelihood that the chemical would be present in sediment or groundwater to pose a longer-term drinking water contamination threat.

A sudden release of large quantities of the chemical near a drinking water source could have immediate effects on the usability of a surface drinking water source. If such a release were to occur, two primary factors would operate together to reduce concern. First, the chemical would be expected to present low concern to the general population, including susceptible subpopulations, across a spectrum of health endpoints (see section 6). Second, sodium glucoheptonate would degrade in aerobic and anaerobic environments (see section 6). Together, these factors mean that any exposures to this chemical through drinking water sources would be short-lived, and that if ingestion were to take place, concern for adverse health effects would be low.

EPA also explored whether the chemical had been identified as a concern under U.S. environmental statutes in the past. EPA searched lists of chemicals and confirmed that sodium glucoheptonate does not appear on these lists. The lists reviewed include EPA's List of Lists (https://www.epa.gov/sites/production/files/2015-03/documents/list_of_lists.pdf). EPA also searched the lists of chemicals included in the National Primary Drinking Water Regulations and the Unregulated Contaminant Monitoring Rule (UCMR) under the Safe Drinking Water Act (SDWA).

Proposed conclusion: Based on a qualitative review of a potential release near a significant source of drinking water, EPA proposes to conclude that the screening-level review under 40 CFR 702.9(a)(4) does not support a finding that sodium glucoheptonate meets the standard for a high-priority substance. The reasonably available information on storage near significant sources of drinking water described above provides sufficient information to support these proposed findings.

8.5 Conditions of Use or Significant Changes in Conditions of Use of the Chemical Substance

Approach: EPA evaluated the conditions of use for sodium glucoheptonate and related potential exposures and hazards.

Rationale: EPA assessed the conditions of use of sodium glucoheptonate (see Section 5 and Appendix A) and found it to have a broad range of conditions of use. EPA expects that even if the conditions of use were to expand beyond activities that are known, intended, or reasonably foreseen, the exposure outcome of the screening review would likely not change and would not alter the Agency's conclusion of low concern. EPA bases this expectation on sodium glucoheptonate's consistently low-concern hazard characteristics across the spectrum of hazard endpoints and regardless of a change in the nature or extent of its use and resultant increased exposures.

Proposed conclusion: EPA's qualitative evaluation of potential risk does not support a finding that sodium glucoheptonate meets the high-priority substance based on its low-hazard profile under the

current conditions of use. EPA proposes to find that even if conditions of use broaden, resulting in an increase in the frequency or amount of exposures, the analysis conducted to support the screening-level review under 40 CFR 702.9(a)(5) would not change significantly. In particular, the analysis of concern for hazard, which forms an important basis for EPA's findings, would not be impacted by a change in condition of use. Therefore, such changes would not support a finding that sodium glucoheptonate meets the standard for a high-priority substance. The reasonably available information on conditions of use, or significant changes in conditions of use, described above provides sufficient information to support this proposed finding.

8.6 The Volume or Significant Changes in Volume of the Chemical Substance Manufactured or Processed

Approach: EPA evaluated the current production volumes of sodium glucoheptonate (Section 7.1) and related potential exposures (Sections 7.2 through 7.4).

Rationale: EPA used reasonably available information on production volume (see Appendix A) in considering potential risk. It is possible that designation of sodium glucoheptonate as a low-priority substance could result in increased use and higher production volumes. EPA expects, however, that any changes in sodium glucoheptonate's production volume would not alter the Agency's assessment of low concern given the chemical's low-hazard profile. EPA bases this expectation on sodium glucoheptonate's consistently low-concern hazard characteristics across the spectrum of hazard endpoints. This expectation would apply, even with a significant change in the volume of the chemical substance manufactured or processed and resultant increased exposures.

Proposed conclusion: Based on this screening criteria under 40 CFR 702.9(a)(6), EPA proposes to find that even if production volumes increase, resulting in an increase in the frequency or level of exposure, sodium glucoheptonate does not meet the standard for a high-priority substance. The reasonably available information on production volume, or significant changes in production volume described above provides sufficient information to support this proposed finding.

8.7 Other Considerations

EPA did not identify other considerations for the screening review to support the proposed designation of sodium glucoheptonate as a low-priority substance.

9. Proposed Designation

Based on a risk-based, screening-level review of the chemical substance and, when applicable, relevant information received from the public and other information as appropriate and consistent with TSCA section 26(h) and (i), EPA is proposing to designate sodium glucoheptonate as a low-priority substance as it does not meet the statutory criteria for a high-priority substance.

Appendix A: Conditions of Use Characterization

EPA gathered information on and related to conditions of use including uses of the chemical, products in which the chemical is used, types of users, and status (e.g., known, regulated).

A.1 CDR Manufacturers and Production Volume

The Chemical Data Reporting (CDR) rule (previously known as the Inventory Update Rule), under TSCA section 8, requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S., generally above a reporting threshold of 25,000 lb. per site per year. According to the 2016 CDR database, six companies manufactured or imported sodium glucoheptonate for reporting year 2015. Individual production volumes were withheld, but may be available in later releases of the 2016 CDR.

Table presents the historic production volume of sodium glucoheptonate from the CDR from 1986-2015. For all reporting years aggregate production volume for sodium glucoheptonate was between 1,000,000 and 10,000,000 lbs. The exact amount is available for one year, 2011, in which 9,880,022 lbs. of sodium glucoheptonate was produced or imported.

Table A.1: 1986-2015 National Production Volume Data for Sodium Glucoheptonate (Non-Confidential Production Volume in Pounds)

1986	1990	1994	1998	2002	2006	2011	2012	2013	2014	2015
1 M – 10 M	1 M – 10 M	1 M – 10 M	1 M – 10 M	1 M – 10 M	1 M – 10 M	9,880,022	1 M – 10 M	1 M – 10 M	1 M – 10 M	1 M – 10 M

Source(s):
EPA (2018a; 2017b; 2006; 2002)

Note(s):
K = Thousand; M = Million; NDR = No data reported

A.2 Uses

A.2.1 Methods for Uses

Section A.2 provides a list of known uses of sodium glucoheptonate, organized by category of use. To compile the uses, EPA searched publicly available databases listed in Table A.2 and conducted additional Google searches to clarify uses. Search terms differed among databases because of different search term requirements for each database (i.e., some databases search by CASRN while others search by chemical name).

Table A.2: Sources Searched for Uses of Sodium Glucoheptonate

Title	Author and Year	Search Term(s)	Found Use Information? [1]
Sources search for all use reports			
California Links to Pesticides Data	California Dept of Pesticide Regulation (2013)	31138-65-5	No
Canada Chemicals Management Plan information sheets	Government of Canada (2018)	D-gluco-Heptonic acid; Sodium glucoheptonate	No
Chemical and Product Categories (CPCat)	Dionisio et al. (2015)	31138-65-5	Yes
ChemView [2]	EPA (2018a)	31138-65-5	Yes
Children's Safe Product Act Reported Data	Washington State Dept. of Ecology (2018)	31138-65-5	No
Consumer Product Information Database (CPID)	DeLima Associates (2018)	31138-65-5	Yes
Danish surveys on chemicals in consumer products	Danish EPA (2018)	N/A, There is no search, but report titles were checked for possible information on the chemical	No
Datamyne	Descartes Datamyne (2018)	Sodium glucoheptonate	Yes
DrugBank	DrugBank 2018	31138-65-5; Sodium glucoheptonate	No
European Chemicals Agency (ECHA) Registration Dossier	ECHA (2018b)	31138-65-5	Yes
eChemPortal [2]	OECD (2018)	31138-65-5	Yes
Envirofacts [2]	EPA (2018b)	31138-65-5	No
Functional Use Database (FUse)	EPA (2017a)	31138-65-5	Yes
Kirk-Othmer Encyclopedia of Chemical Technology	Kirk-Othmer (2006)	31138-65-5; Sodium glucoheptonate	No
Non-Confidential 2016 Chemical Data Reporting (CDR)	EPA (2017b)	31138-65-5	Yes
PubChem Compound	Kim et al. (2016)	31138-65-5	Yes

Table A.2: Sources Searched for Uses of Sodium Glucoheptonate			
Title	**Author and Year**	**Search Term(s)**	**Found Use Information? [1]**
Safer Chemical Ingredients List (SCIL)	EPA (2018d)	31138-65-5	Yes
Synapse Information Resources [2]	Synapse Information Resources (n.d.)	31138-65-5	Yes
Resource Conservation and Recovery Act (RCRA)	EPA (2018c)	Sodium glucoheptonate; D-gluco-Heptonic	No
Scorecard: The Pollution Information Site	GoodGuide (2011)	31138-65-5	No
Skin Deep Cosmetics Database	EWG (2018)	31138-65-5; Sodium glucoheptonate; Sodium gluceptate	No
Toxics Release Inventory (TRI)	EPA (2018e)	31138-65-5	No
TOXNET [2]	NLM (2018)	31138-65-5	No
Ullmann's Encyclopedia of Industrial Chemistry	Ullmann's (2000)	Sodium glucoheptonate	No
Additional sources identified from reasonably available information			
Alco-Chem Inc.	Alco-Chem Inc. (2015a)	Identified while reviewing details of this chemical's uses and products.	Yes
Harcros Chemicals Inc.	Harcros Chemicals Inc. (2014)		
TCI America	TCI America (2014)		
Walmart	Walmart (2018)		

Note(s):
1. If use information was found in the resource, it will appear in **Error! Reference source not found.** unless otherwise noted.
2. This source is a group of databases; thus, the exact resource(s) it led to will be cited instead of the database as whole.

The U.S. Patent and Trademark Office has an online database that shows 398 patents referencing "sodium glucoheptonate" (USPTO 2018). Although patents could be useful in determining reasonably foreseen uses, it is difficult to confirm whether any of the patented technologies are currently in use. Uses inferred from patents containing sodium glucoheptonate were not included in Table A.3. Note that the uses in Table A.3 that are covered under TSCA are included in Section 5, Table 3 of this document.

A.2.2 Uses of Sodium Glucoheptonate

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Cleaning Products		
Air care products	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in air care products. ECHA does not expand on this use, however this category generally includes products such as air fresheners, candles, and scented gels. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.
Automotive wheel and tire cleaner	Consumer	DeLima Associates (2012) CPID lists one automotive cleaner containing sodium glucoheptonate. CPID generally includes products for consumer use; therefore, the expected user is a consumer.
Cleaning and furnishing care products	Commercial	EPA (2017b); Harcros Chemicals Inc. (2014); Synapse Information Resources (n.d.) CDR reports use of liquid sodium glucoheptonate in commercial cleaning and furnishing care products, with a concentration of 30-60 percent by weight. Synapse Information Resources identifies use of sodium glucoheptonate in dairy cleaners and bottle cleaners. Expected users are commercial based on CDR's user classification.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Cleaning/washing agents for dish washing machines	Consumer, commercial, industrial	Dionisio et al. (2015) CPCat identifies use of sodium glucoheptonate in cleaning/washing agents in Nordic countries. This use could not be confirmed by the SPIN databases. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial.
Coatings and paints, thinners, paint removers	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c); Synapse Information Resources (n.d.) The ECHA registration dossier identifies use of sodium glucoheptonate in coatings, paints, thinners, and paint removers. Synapse Information Resources identifies use of sodium glucoheptonate in paint stripping. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Degreaser	Consumer, commercial, industrial	Dionisio et al. (2015) CPCat identifies use of sodium glucoheptonate in cold degreasing, de-waxing, and de-polishing in Nordic countries. This use could not be confirmed by the Substances in Preparations in Nordic Countries (SPIN) databases. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Laundry booster	Commercial, industrial	Alco-Chem Inc. (2015b); Alco-Chem Inc. (2015a) An SDS from Alco-Chem identifies the product Liquid Laundry Break containing <5 percent sodium glucoheptonate. According to the manufacturer, the product is a heavy-duty alkaline builder that improves detergent performance by emulsifying soils. Expected user is not identified in the source but is likely commercial and industrial based on the fact that the product is sold in five and fifteen-gallon pails.
Polishes and wax blends	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier reports use of sodium glucoheptonate in polishes and wax blends. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Stain remover	Consumer	DeLima Associates (2017); Walmart (2018) CPID lists one stain remover containing sodium glucoheptonate. This product is currently for sale. CPID generally includes products for consumer use; therefore, the expected user is a consumer.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Manufacturing		
Chemical manufacturing	Industrial	EPA (2017b); ECHA (2018c); TCI America (2014) CDR reports use of sodium glucoheptonate as a solid's separation agent during the repackaging and processing (incorporation into formulation, mixture, or reaction product) phases of all other chemical product and preparation manufacturing. TCI identifies use of sodium glucoheptonate in lab chemicals. The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in the manufacture of fine chemicals and bulk, large-scale chemicals including petroleum products. Expected users are industrial based on CDR's industrial processing and use report and reporting under ECHA's uses at industrial sites.
Fluid property modulator	Consumer, commercial, industrial	Dionisio et al. (2015) CPCat identifies use of sodium glucoheptonate as a complexing, sequestering, surface treatment, and chelating agent in Nordic countries. Use could not be confirmed by SPIN databases. Expected users are consumer, commercial, and industrial.
Manufacture of computer, electronic and optical products, electrical equipment	Commercial, industrial	ECHA (2018c); ECHA (2018d); Synapse Information Resources (n.d.) The ECHA registration dossier reports use of sodium glucoheptonate as a chelating agent in manufacturing of computer, electronic and optical products and electrical equipment and as a component of semiconductors. Synapse Information Resources identifies use of sodium glucoheptonate in aluminum etching. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Manufacture of furniture	Industrial	ECHA (2018c) The ECHA registration dossier reports use of sodium glucoheptonate as a chelating agent in the manufacture of furniture. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on reporting under ECHA's uses at industrial sites.
Manufacture of metal products	Industrial	Dionisio et al. (2015); ECHA (2018c) CPCat reports use of sodium glucoheptonate in the manufacture of fabricated metal products (except machinery) in Nordic countries. Use could not be confirmed by SPIN databases. The ECHA registration dossier identifies use of sodium glucoheptonate in the manufacture of basic metals, including alloys. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on CPCat's class of chemical category and reporting under ECHA's uses at industrial sites.
Manufacture of plastics products, including compounding and conversion	Industrial	ECHA (2018c) The ECHA registration dossier reports use of sodium glucoheptonate as a chelating agent in plastic products manufacturing. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on reporting under ECHA's uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Manufacture of rubber products	Industrial	ECHA (2018c); Synapse Information Resources (n.d.) Synapse Information Resources identifies use of sodium glucoheptonate as a latex stabilizer. The ECHA registration dossier reports use of sodium glucoheptonate in rubber product manufacturing. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on reporting under ECHA's uses at industrial sites.
Manufacture of textiles, leather and fur	Industrial	Dionisio et al. (2015); ECHA (2018c) CPCat identifies use of sodium glucoheptonate in Nordic textile manufacturing; however, use could not be confirmed by SPIN databases. The ECHA registration dossier reports use of sodium glucoheptonate as a chelating agent in the manufacture of textiles, leather, and fur. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on reporting under ECHA's uses at industrial sites.
Manufacture of wood and wood products	Industrial	ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in the manufacture of wood and wood products. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on reporting under ECHA's uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Manufacturing (general)	Industrial	ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in general manufacturing (machinery, equipment, etc.). No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on reporting under ECHA's uses at industrial sites.
Nonmetallic mineral product manufacturing (includes clay, glass, cement, concrete, lime, gypsum, and other nonmetallic mineral product manufacturing)	Industrial	EPA (2017b) CDR reports use of sodium glucoheptonate as an ion exchange agent during the processing phase (incorporation into formulation, mixture, or reaction product) of manufacturing. Expected users are industrial based on CDR's industrial processing and use report.
Plating agents and surface treating agents	Consumer, commercial, industrial	EPA (2017b) CDR reports use of sodium glucoheptonate as an industrial plating/surface treating agent in the processing phase (incorporation into formulation, mixture, or reaction product) of resale of chemicals and miscellaneous manufacturing. CDR also identifies use of sodium glucoheptonate as a cleaner in multiple consumer and commercial plating processes, including automotive and machinery applications. Cleaners in plating processes contain 30-60 percent sodium glucoheptonate by weight, according to CDR. Expected users are consumer, commercial, and industrial.
Soap, cleaning compound, and toilet preparation manufacturing	Industrial	EPA (2017b) CDR reports use of sodium glucoheptonate as an ion exchange agent and processing aid during the processing phase (incorporation into formulation, mixture, or reaction product) of manufacturing. Expected users are industrial based on CDR's industrial processing and use report.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Treatment and coating of metals	Industrial	Dionisio et al. (2015); Synapse Information Resources (n.d.) CPCat identifies use of sodium glucoheptonate in treatment and coating of metals, metals workshops, and metal machining in Nordic Countries. Use could not be confirmed by SPIN databases. Synapse Information Resources identifies use of sodium glucoheptonate in metal cleaning. Expected users are industrial based on CPCat's class of chemical category.
TSCA Conditions of Use: Food, Agriculture, and Horticulture		
Agriculture, forestry, and fishing[1]	Industrial	ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in agriculture, forestry, and fishing. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on CPCat's class of chemical category.
Crop and animal production, hunting and related service activities[1]	Industrial	Dionisio et al. (2015) CPCat reports use of sodium glucoheptonate in crop and animal production, hunting, and related service activities in Nordic countries, however this use could not be verified by SPIN databased. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on CPCat's class of chemical category.
Fertilizers	Consumer, Commercial, Industrial	ECHA (2018a); ECHA (2018c); ECHA (2018d) The ECHA registration dossier reports use of sodium glucoheptonate in fertilizers. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Food-contact paper/paperboard manufacturing	Consumer, commercial, industrial	Synapse Information Resources (n.d.) Synapse identifies use of sodium glucoheptonate in the manufacture of food-contact paper/paperboard. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial.
Pesticide, fertilizer, and other agricultural chemical manufacturing	Industrial	EPA (2017b) EPA's 2016 CDR reports use of sodium glucoheptonate as an ion exchange agent during the processing phase (incorporation into formulation, mixture, or reaction product) of manufacturing. Sodium glucoheptonate is not registered with the California Department of Pesticide Regulation or the National Pesticide Information Retrieval System. Expected users are industrial based on CDR's industrial processing and use report.
Plant protection products	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier reports use of sodium glucoheptonate as a chelating agent in plant protection products. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Media and Printing		
Finger paints	Consumer, commercial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in finger paints. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses and uses by professional workers. ECHA also indicated industrial use; however, this is likely referring to its manufacture for this use as finger paints are not likely used industrially.
Fragrances[2]	Consumer, commercial, Industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in fragrances. No relevant products containing sodium glucoheptonate could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Ink and toners	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in ink and toners. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Photo-chemicals	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in photo-chemicals. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Printing and reproduction of recorded media	Industrial	ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in printing and reproduction of recorded media. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on reporting under ECHA's uses at industrial sites.
TSCA Conditions of Use: Miscellaneous		
Adhesives, sealants	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in adhesives, sealants. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Adsorbents	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in adsorbents. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.
Anti-freeze and de-icing products	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in anti-freeze and de-icing products. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.
Construction	Industrial	EPA (2017b); ECHA (2018c); Harcros Chemicals Inc. (2014) CDR reported use of sodium glucoheptonate as a raw material in internal blending of construction materials. Expected users are industrial based on identification in CDR's industrial processing and use report.
Electricity, steam, gas, water supply and sewage treatment	Consumer, Commercial, industrial	Dionisio et al. (2015); ECHA (2018a); ECHA (2018d); ECHA (2018c) CPCat identifies use of sodium glucoheptonate as an ion exchange agent in industrial water treatment. The ECHA registration dossier lists sodium glucoheptonate as an ingredient in consumer, commercial and industrial water treatment chemicals. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Explosives	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in explosives. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.
Extraction agents	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in extraction agents. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.
Fuels	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in fuels. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.
Heat transfer fluids	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in heat transfer fluids. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Hydraulic fluids	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in hydraulic fluids. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.
Intermediate	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in intermediates. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.
Laboratory chemicals	Commercial, industrial	ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in lab chemicals. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are commercial and industrial based on reporting under ECHA's uses by professional workers and uses at industrial sites.
Leather treatment products	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in leather treatment products. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Lubricants, greases, release products	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in lubricants, greases, and release products. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Mining	Industrial	ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in mining activities. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on identification under ECHA's uses at industrial sites.
Offshore industries	Industrial	ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in offshore industries. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on identification under ECHA's uses at industrial sites.
Oil and gas exploration, drilling, extraction, and support activities	Commercial, industrial	EPA (2017b) CDR reported use of Sodium Glucoheptonate in commercial and industrial oil and gas exploration and as an ion exchange agent in industrial oil and gas drilling, extraction and support activities. Expected users are commercial based on CDR's user classification, and industrial based on identification in CDR's industrial processing and use report.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Other metal products	Consumer, commercial	EPA (2017b) CDR reports use of sodium glucoheptonate in metal products not covered elsewhere. These products contain less than one percent sodium glucoheptonate by weight, according to CDR. Expected users are consumer and commercial based on CDR's user classification.
Paper and board treatment products	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c); Synapse Information Resources (n.d.) Synapse Information Resources identifies use of sodium glucoheptonate in kier boiling (used to bleach or scour cotton or process paper pulp) and caustic boiloff (possibly referring to boil-out which is the removal of excess fibers and minerals in paper treatment). The ECHA registration dossier reports use of sodium glucoheptonate in paper and board treatment products as well as the manufacture of pulp, paper, and paper products. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Products such as pH-regulators, flocculants, precipitants, neutralization agents	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in products such as pH-regulators, etc. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Non-TSCA Uses		
Biocidal products (e.g. disinfectants, pest control)	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier reports use of sodium glucoheptonate in biocidal products. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Boiler water additive	Consumer, commercial, industrial	FDA (2018); Dionisio et al. (2015); ECHA (2018c); Synapse Information Resources (n.d.) Sodium Glucoheptonate is listed as a boiler water additive on the U.S. FDA's Food Additive Status List. It is currently regulated by the FAA as a boiler compound with less than 1 ppm of cyanide. Additionally, the ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in the manufacture of food and in consumer and commercial water softeners. Expected users are based on identification under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Cosmetics, personal care products	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c); Synapse Information Resources (n.d.) Synapse Information Resources identifies use of sodium glucoheptonate as a chelating agent in cosmetics. The ECHA registration dossier reports use of sodium glucoheptonate as a chelating agent in cosmetics and other personal care products. No personal care products containing sodium glucoheptonate could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Food additive	Unknown	Synapse Information Resources (n.d.) Synapse Information Resources identifies use of sodium glucoheptonate as a sequestrant. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. The expected users are unknown, due to the limited availability of information.
Perfumes	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c) The ECHA registration dossier identifies use of sodium glucoheptonate as a chelating agent in perfumes. No relevant products containing sodium glucoheptonate could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Pharmaceuticals	Consumer, commercial, industrial	ECHA (2018a); ECHA (2018d); ECHA (2018c); Synapse Information Resources (n.d.) Synapse Information Resources identifies use of sodium glucoheptonate in intravenous pharmaceuticals, and the ECHA registration dossier reports use of sodium glucoheptonate in pharmaceuticals and health services. No further information could be found in DrugBank, and it is unknown whether this is an ongoing use in the United States. Expected users are consumer, commercial, and industrial based on reporting under ECHA's consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Sodium Glucoheptonate		
Use	**Expected Users**	**Description of Use and References**
Children's Products		
CDR and other databases did not specifically indicate uses in children's products; however, use in finger paints was identified in European countries (see above).		
Recycling and Disposal		
In the 2016 CDR, one facility, Milport Enterprises Inc., reported recycling (e.g., recycled, remanufactured, reprocessed, or reused) sodium glucoheptonate. Four facilities reported not recycling sodium glucoheptonate, and one facility withheld recycling information (EPA 2017b).		
Note(s): 1. Assumed to be a mix of TSCA and non-TSCA products. It is expected that more specifically-defined uses in the table are representative of the uses that fall into this category. 2. Potentially a non-TSCA use as category may contain both TSCA and non-TSCA uses, however, because information is insufficient to determine, it is assumed to be covered by TSCA.		

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Appendix B: Hazard Characterization

Table B.1: Human Health Hazard

ADME

Source (HERO ID)	Exposure Route	Species & Strain (if available)	Duration	Doses and Replicate Number	Effect	Study Details
4940231, 4940243	Oral (gavage)	Wistar rats	Single dose	**Dose:** 0 and 4000 mg/kg **Replicates:** 4-14 male rats	Enzyme levels of glucose-6-phosphate and 6-phosphogluconate were 163 and 27 µmol/kg 5 hours following treatment and were similar to levels in the control animals	• Test substance reported as CASRN 90-80-2 • Purity not reported • OECD Guideline 417 • GLP compliance not reported
4947912	Oral	Humans	Single dose, urine collected 7 hours post exposure	**Dose:** 84 or 167 mg/kg **Replicates:** 3 healthy males	The recovered GDL in urine was 0 and 7.7-15% of the original dose at 84 and 167 mg/kg, respectively	• Test substance reported as CASRN 90-80-2 • Purity not reported • Pre-dates GLP compliance
4940243	Oral (gavage)	Wistar rats	Single dose	**Dose:** 800 mg/kg mg/kg **Replicates:** 9-10 fasted male rats	The radioactivity of D-glucono-delta-lactone was reported to be 25.0 (whole body), 23.1 (intestines and feces), 29.5 (urine), and 7.0% (exhaled carbon dioxide)	• Test substance reported as CASRN 90-80-2 • Purity not reported • OECD Guideline 417 • GLP compliance not reported
4940231, 4940243	Oral (gavage)	Wistar rats	Single dose	**Dose:** 800 mg/kg mg/kg **Replicates:** 9-23 fasted male rats	After 5 hours, radioactivity was reported to be 12.1% (exhaled carbon dioxide) 19.7% (whole body), 44.9% (intestine and feces) and 5.0% (urine).	• Test substance reported as CASRN 527-07-1 • Purity not reported • OECD Guideline 417 • GLP compliance not reported
4941343	Oral (gavage)	Sprague-Dawley rats	Single dose	**Dose:** 30 mg/kg **Replicates:** 7 male rats	Total amount of radiolabeled calcium excreted in urine was 1.241 ± 0.473%. The highest concentration of radioactivity was found in bone as 98.7 ± 1.6%	• Test substance reported as CASRN 299-28-5 (radiolabeled) • Purity not reported • GLP compliance not reported

Table B.1: Human Health Hazard						
4946680	Nasogastric tube	Humans	Single dose	**Dose:** 20 mL of 10% calcium gluconate **Replicates:** 15 fasting males	Acid secretion post dosing was greater than levels prior to testing. Serum gastrin levels also increased 30min after dosing.	• Test substance reported as CASRN 299-28-5 • Purity not reported • Pre-dates GLP compliance
Acute Mammalian Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and Replicate Number**	**Effect**	**Study Details**
4851345, 4864278	Oral gavage	Wistar rat	Single exposure, observed for 14 day	**Doses and replicates:** 354 mg/kg (175 mg active/kg),1 female 1112 mg/kg (550 mg active/kg), 1 female 4042 mg/kg (2000 mg active/kg), 3 females	**LD_{50}** > 2000 mg/kg	**Methods:** • Test substance reported as CASRN 31138-65-5 • Purity: 49.5% • OECD Guideline 425 • GLP compliant
4864277	Dermal	Wistar rats	24-hour exposure, observed for 14 days	**Dose:** Single dose of 4041 mg/kg or 2000 mg active/kg **Replicates:** 5 per sex	**LD_{50}** > 2000 mg/kg	**Methods:** • Test substance reported as CASRN 31138-65-5 • Purity: 49.5% • OECD Guideline 402, EU method B.3. • GLP compliant
Repeated Dose Toxicity						
Source	**Exposure Route**	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4851346, 4864281, 4864283, 4864285	Oral (gavage)	Wistar rats	8 weeks	**Doses**: 0, 30, 300, and 1000 mg/kg-day	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 31138-65-5 • Purity: 50.5% • OECD Guideline 422

Table B.1: Human Health Hazard						
			• Dosing began 2 weeks prior to mating • Dosing continued, through gestation to lactation day 5 (for females)	**Replicates:** 12 per sex per group		• GLP compliant
Reproductive Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4864285	Oral (gavage)	Wistar rats	8 weeks • Dosing began 2 weeks prior to mating • Dosing continued, through gestation to lactation day 5 (for females)	**Doses:** 0, 30, 300, and 1000 mg/kg-day **Replicates**: 12 per sex per group	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 31138-65-5 • Purity: 50.5% • OECD Guideline 422 • GLP compliant
Developmental Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**

4947912, 4940251, 4947704	Oral (gavage)	Albino CD-1 mice	GD 6-15	**Doses:** 0, 6.95, 32.5, 150 and 695 mg/kg-day **Replicates:** 21-25 per dose	**NOAEL:** 695 mg/kg/-day	**Methods** • Test substance reported as CASRN 90-80-2 • Purity not reported • OECD Guideline 414 • Pre-dates GLP
4947912, 4940249, 4947704	Oral (gavage)	Golden outbred hamsters	GD 6-10	**Doses:** 0, 5.6, 26, 121, and 560 mg/kg/d **Replicates:** 20-25 per dose	**NOAEL:** 560 mg/kg-day	**Methods** • Test substance reported as CASRN 90-80-2 • Purity not reported • OECD Guideline 414 • Pre-dates GLP
4947912, 4940230, 4947704	Oral (gavage)	Dutch rabbits	GD 6-18	**Doses:** 0, 7.8, 32.2, 168 and 780 mg/kg-day **Replicates:** 10-13 per dose	**NOAEL:** 780 mg/kg-day	**Methods** • Test substance reported as CASRN 90-80-2 • Purity not reported • OECD Guideline 414 • Pre-dates GLP
4947912, 4940250, 4947704	Oral (gavage)	Wister rat	GD 6-15	**Doses:** 0, 5.94, 27.6, 128 and 594 mg/kg-day **Replicates:** 21-25 per dose	**NOAEL:** 594 mg/kg-day	**Methods** • Test substance reported as CASRN 90-80-2 • Purity not reported • GLP not reported

Cancer

Source	Effect	Study Details
OncoLogic v8.0	Structure could not be evaluated by Oncologic.	OncoLogic currently has no assessment criteria regarding sugar derivatives.
ISS v2.4[39]	Negative (Estimated) Monosodium D-glucoheptonate is a multi-hydroxy acid which does not contain any structural features indicative of electrophilic potential.	**Methods:** Carcinogenicity alerts (genotoxic and non-genotoxic) by ISS profiler as available within the OECD Toolbox v4.3 **Results:** No alerts were identified for the parent structure (an aldehyde alert was identified for the initial aldehyde metabolite that is formed in the first oxidation transformation that occurs during the metabolism of

[39] Carcinogenicity alerts by ISS profiler comprises 55 structural alerts for genotoxic and non-genotoxic carcinogenicity. The alerts have been compiled upon existing knowledge of mechanism of action of carcinogenic chemicals that have been published elsewhere (Benigni and Bossa (2011) *Chem Rev* 111: 2507-2536 and Benigni R et al. (2013) *Chem Rev.* 113: 2940-2957).

		Monosodium D-glucoheptonate). This aldehyde will be rapidly transformed to the corresponding carboxylic acid.
VEGA 1.1.4[40]	Monosodium D-glucoheptonate was processed through all 4 models. ISS 1.0.2and IRFMN/ISSCAN-GX 1.0.0 predicted it to be non-carcinogenic with moderate reliability[41] .	**Methods:** VEGA 1.1.4 contains 4 models for carcinogenicity – CAESAR 2.1.9, ISS 1.0.2, IRFMN/Antares 1.0.0, IRFMN/ISSCAN-GX 1.0.0 **Results:** • CAESAR 2.1.9: Low reliability (Monosodium D-glucoheptonate lies outside of the applicability domain (AD) of the model) • ISS 1.0.2: Moderate reliability (Monosodium D-glucoheptonate could lie outside of the AD) • IRFMN/Antares 1.0.0:Low reliability (Monosodium D-glucoheptonate lies outside of the AD) • IRFMN/ISSCAN-GX 1.0.0:Moderate reliability (Monosodium D-glucoheptonate could be outside of the AD)

Genotoxicity

Source	Test Type & Endpoint	Species & Strain (if available)	Metabolic Activation	Doses and Controls	Results	Study Details
4851347	*In vivo* (Mouse, IP exposure) DNA Damage and Repair	Albino CD-1 mice	Yes	**Doses:** 500, 1000, and 2000 mg/kg **Replicates:** 7 male per group	Negative	**Methods:** • Test substance reported as CASRN 31138-65-5 • Purity: 50.5% • OECD Guideline 474

[40] VEGA 1.1.4 contains 4 different models to facilitate an in silico assessment of carcinogenicity potential. The models are summarized in Golbamaki et al. (2016) J Environ Sci and Health Part C http://dx.doi.org/10.1080/10590501.2016.1166879 as well as in documentation that is downloadable from within the VEGA tool itself (https://www.vegahub.eu/).

- CAESAR 2.1.9 is a classification model for carcinogenicity based on a neural network.
- ISS 1.0.2 is a classification model based on the ISS ruleset (as described above for the OECD Toolbox).
- IRFMN/Antares 1.0.0 and IRFMN/ISSCAN-GX 1.0.0 are classification models based on a set of rules built with SARpy software (part of the same suite of VEGA tools https://www.vegahub.eu/) extracted from the Antares and ISSCAN-CGX datasets respectively.

[41] Each model is characterized by an applicability domain (AD) that depends on at least 5 various components:

- Similar substances with known experimental values within the underlying training set
- Accuracy of prediction for similar substances
- Concordance for similar substances
- Fragments similarity check on the basis of atom centered fragments
- Model descriptors range check.

A global AD index takes into account the other 5 components to provide an overall reliability score – low, moderate or high. EPA has not included low-reliability model results

						• GLP compliant
4940235	Gene mutation (*in vitro*)	Salmonella typhimurium TA1535, 1537, 98, 100, and 102	With and without	**Doses:** 50, 150, 500, 1500, and 5000 µg/plate	Negative	**Methods**: • Test substance reported as CASRN 526-95-4 • Purity: 52% • OECD Guideline 471 • GLP compliant
4940252	Chromosomal aberrations (*in vitro*)	Human lymphocytes	With and without	**Doses:** 0, 0.16, 0.31, 0.625, 1.25, 2.5, and 10 mM	Negative	**Methods**: • Test substance reported as CASRN 526-95-4 • Purity: 52% • OECD Guideline 473 • GLP compliant
4940247, 4940234	Gene mutation (*in vitro*)	Mouse lymphoma L5178Y cells	With and without	**Doses:** 1.25, 2.5, 5, and 10 mM	Negative	**Methods**: • Test substance reported as CASRN 526-95-4 • Purity: 52% • OECD Guideline 490 • GLP compliant
4940109	Gene mutation (*In vitro*)	Salmonella typhimurium TA97, 98, 100, and 1535	With and without	**Doses**: 0, 100, 333, 1000, 3333, and 10000 µg/plate	Negative	**Methods**: • Test substance reported as CASRN 90-80-2 • Purity not reported • NTP mutagenicity protocol for Ames test • GLP compliance not reported
4947757	Gene mutation (*In vitro*)	Salmonella typhimurium TA1535, 1537, 1538	With and without	**Doses:** 0.25% and 0.5% test substance	Negative	**Methods**: • Test substance reported as CASRN 90-80-2 • Purity not reported • GLP compliance not reported
4947757, 2072857	Gene mutation (*In vitro*)	Saccharomyces cerevisiae strain D4	With and without	**Doses:** 1.25% and 2.5% test substance	Negative	**Methods**: • Test substance reported as CASRN 90-80-2 • Purity not reported • GLP compliance not reported
2072857	Gene mutation (*In vitro*)	Salmonella typhimurium TA1535, 1537, 1538	With and without	**Doses:** 0.25% and 0.5% test substance	Negative	**Methods**: • Test substance reported as CASRN 90-80-2 • Purity not reported • OECD Guideline 471 • Not GLP compliant **Endpoints:** Cytotoxicity observed at 1%

2072857	Chromosomal aberrations (*In vivo*)	C57BL mice	With	Single dose study: **Doses:** 2000, 4000, and 8000 mg/kg **Replicates:** 3 per group Repeat dose study: **Doses:** 2000 and 4000 mg/kg-day **Replicates:** 2-3 per group	Negative	**Methods**: • Test substance reported as CASRN 90-80-2 • Purity not reported • GLP compliance not reported **Mortality Results:** 3/3 died in 8000 mg/kg
4947764, 2072857	Gene mutation (*in vitro)*	*Saccharomyces cerevisiae* strain D4	With and without	**Doses:** 0.75, 1.50, and 3.00% of substance	Negative	**Methods**: • Test substance reported as CASRN 299-28-5 • Purity not reported • OECD Guideline 471 • GLP not reported **Endpoints:** Cytotoxicity observed at 3%
4947764, 2072857	Gene mutation (*in vitro)*	*Salmonella typhimurium* strains TA1535, TA1537, and TA1538	With and without	**Doses:** 1.25, 2.5 and 5.0% of substance	Negative	**Methods**: • Test substance reported as CASRN 299-28-5 • Purity not reported • OECD Guideline 471 • GLP not reported
4947765, 2072857	Gene mutation (*in vitro)*	*Salmonella typhimurium* strains TA1535, TA1537, and TA1538	With and without	**Doses:** 0.0006, 0.0012, and 0.0024% substance	Negative	**Methods**: • Test substance reported as CASRN 527-07-1 • Purity not reported • OECD Guideline 472 • Non-GLP compliant **Results:** Cytotoxicity was observed at 0.0024%
4947765, 2072857	Gene mutation (*in vitro)*	*Saccharomyces cerevisiae* strain D4	With and without	**Doses:** 1.25%, 2.5%, and 5% substance	Negative	**Methods**: • Test substance reported as CASRN 527-07-1 • Purity not reported • OECD Guideline 472 • Non- GLP compliant **Results:** Cytotoxicity was observed at 5%.

2072857	Chromosomal aberrations (*In vivo*)	C57BL mice	With	**Doses:** 0, 2500, 5000, and 1000 mg/kg-day for 1 day, and 1250 and 2500 mg/kg-day for 4 consecutive days.	Negative	**Methods**: • Test substance reported as CASRN 527-07-1 • Purity not reported • GLP not reported **Results:** • In the single dose groups, all mice in the 5,000 and 10,000 mg/kg groups died. Only two mice in the 2,500 mg/kg dose could be evaluated due to technical issues. Sodium gluconate induced chromosomal aberrations at a rate of 0.5% which was comparable to controls. • In the 1250 mg/kg-day and 2500 mg/kg-day animals, one mouse in each treatment group died. Chromosomal aberrations in surviving animals were similar to the negative controls. • The test substance was considered non-genotoxic
Sensitization						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and Replicate Number**	**Effect**	**Study Details**
4864280	Dermal	CBA mice	3 day	**Doses**: 25 µL of 25%, 50%, and 100% substance **Replicates**: 4 per group	Not sensitizing	**Methods:** • Test substance reported as CASRN 31138-65-5 • Purity not reported • OECD Guideline 429 • GLP compliant **Results:** • Stimulation index was 0.93, 0.86, and 0.61 at 25%, 50%or 100% substance, respectively
Irritation						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses**	**Effect**	**Study Details**

4864279	*In vitro* skin	EPISKINTM tissues	15-minute exposure followed by 42 hour of post-exposure incubation	**Dose:** 10 µL	Non-irritating	**Methods:** • Test substance identified as CASRN 31138-65-5 • Purity: 99% • OECD Guideline 439 and EU method B.46 • GLP compliant
4940239	Dermal	New Zealand white rabbits	Exposures after 3 minutes, 1 hour, and 4 hours; observed for 72 hours	**Dose:** 0.5 mL undiluted test substance **Replicates:** 3 rabbits 2/3 rabbits were exposed for 4 hours (single dose) 1/3 rabbits were exposed after 3 minutes, 1 hour, and 4 hours (three doses)	Negative	**Methods**: • Test substance reported as CASRN 526-95-4 • Purity reported as 54.4% • Based on EU Method B.4 • GLP compliant
2072857	Dermal	Albino rabbits	4-hour exposure observed for 72 hours	**Dose:** 0.5 mL undiluted test substance **Replicates:** 12 rabbits	Negative	**Methods**: • Test substance reported as CASRN 526-95-4 • Purity not reported • Test method: 'Directive 79/831/EEC, B.4. • GLP compliance not reported **Endpoints:** • Erythema was observed in 3 / 6 animals 1-hour post exposure and in 1 / 6 animals through 48 hours post exposure
4940242	Ocular	New Zealand white rabbits	Single exposure observed for 72 hours	**Dose:** 0.1 mL test material **Replicates:** 3 rabbits	Positive	**Methods**: • Test substance reported as CASRN 526-95-4 • Purity: 54.4% • OECD Guideline 405 • GLP compliance not reported **Endpoints:** • At 1 hour, chemosis and conjunctival redness were mild-moderate or moderate to severe in all animals. 2 animals exhibited lacrimation, iris lesions, and 1 animal had corneal lesion • At 24 hours, one animal had severe chemosis, lacrimation and conjunctival redness with lesions of iris and cornea whereas the other 2 animals had slight to minimal effects

						• At 48 hours, 1 animal had chemosis, lacrimation, conjunctival redness, iris lesions, and corneal lesions • At 72 hours, slight chemosis and conjunctival redness persisted in one animal • All effects were fully reversible • D-gluconic acid was considered mildly irritating
2072857	Ocular	New Zealand white albino rabbits	Single exposure, observed for up to 7 days	**Dose:** 0.1 mL of 50% test substance **Replicates**: 9 rabbits	Negative	**Methods**: • Test substance reported as CASRN 526-95-4 • Purity not reported • Test method: Draize Test • GLP compliance not reported **Endpoints:** • Some redness and chemosis of the conjunctivae, irritation of the iris and discharge were observed 1-hour post exposure • Conjunctivae redness and chemosis were also observed at 24 and 48 hours post exposure • All effects were reversed by 72 hours • D-gluconic acid was considered non-irritating
2077994	Ocular	Bovine	4 hours	**Dose:** 0.75 mL of 20% suspension of test material **Replicates:** 6	Severely irritating	**Methods**: • Test substance reported as CASRN 90-80-2 • Purity not reported • According to bovine corneal opacity and permeability assay based on the method of Muir (1984) • GLP not reported **Endpoints:** • Corneal opacity scores were evaluated before and after treatment. Classification of this test material is a severe irritant
Neurotoxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses**	**Effect**	**Study Details**
4864283, 4864285	Oral (gavage)	Wistar rats	8 weeks • Dosing began 2 weeks	**Doses:** 0, 30, 300, and 1000 mg/kg-day **Replicates**: 5 per sex per group	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 31138-65-5 • Purity: 49.5% • OECD Guideline 422 • GLP compliant

			prior to mating • Dosing continued, through gestation to lactation day 5 (for females)			

Table B.2: Environmental Hazard

Aquatic Toxicity: Experimental

Source	Species & strain (if available)	Duration	Doses and Replicate Number	Effect	Study Details
4851242	*Oncorhynchus mykiss*	96 hours	**Dose**: 100 mg/L **Replicates:** 10	**LC_{50}** > 100 mg/L	**Methods:** • Test substance reported as CASRN 31138-65-5 • Purity: 39.94% • OECD Guideline 203 and U.S. EPA Draft Ecological Effects Test Guidelines OPPTS 850.1075 • GLP Compliant
4864288	*Oncorhynchus mykiss*	96 hours	**Doses:** 0, 100, 180, 320, 560, and 1000 mg/L	**LC_{50}** > 1000 mg/L	**Methods:** • Test substance identified as CASRN 31138-65-5 • Purity: 49.5% • OECD Guideline 203 • GLP compliant
4851344	*Daphnia magna*	48 hours	**Doses:** 0, 0.10, 1, 10, and 100 mg/L **Replicates:** 4 replicates per dose	**EC_{50}** > 100 mg/L	**Methods:** • Test substance reported as CASRN 31138-65-6 • Purity: 39.94% • OECD Guideline 202 and the U.S. EPA Draft Ecological Effects Test Guidelines OPPTS 850.1010 • GLP compliant

Table B.2: Environmental Hazard					
4864287	*Daphnia magna*	48 hours	**Doses:** 0, 100, 180, 320, 560, and 1000 mg/L **Replicates:** 4 replicates per dose	**EC_{50}** > 1000 mg/L	**Methods:** • Test substance reported as CASRN 31138-65-6 • Purity: 49.5% • OECD Guideline 202 • GLP compliance not reported
4851140, 4897790	*Pseudokirchneriella subcapitata*	96 hours	**Doses:** 0, 10, 32, 100, 320 and 1000 mg/L **Replicate**: 3 replicates per dose	**EC_{50}**: 790 mg/L (growth rate)	**Methods:** • Test substance reported as CASRN 31138-65-6 • Purity: 49.5% • OECD Guideline 201 • GLP compliant

Aquatic Toxicity: Estimated

Model	Species	Predicted Effect Level	Notes
ECOSAR v2.0 (Class: Neutral Organics)	Aquatic Vertebrates	ChV = 8.6E+5 mg/L	Estimated with the following inputs: SMILES [O-]C(=O)C(O)C(O)C(O)C(O)C(O)CO.[Na+]; MP = 146.5°C (est); WS = 1.0E6 mg/L (est); $LogK_{ow}$ = -2.32
ECOSAR v2.0 (Class: Neutral Organics)	Daphnia magna	ChV = 1.75E+5 mg/L	Estimated with the following inputs: SMILES [O-]C(=O)C(O)C(O)C(O)C(O)C(O)C(O)CO.[Na+]; MP = 146.5°C (est); WS = 1.0E6 mg/L (est); $LogK_{ow}$ = -2.32
ECOSAR v2.0 (Class: Neutral Organics)	Green algae	ChV = 8.3E+4 mg/L	Estimated with the following inputs: SMILES [O-]C(=O)C(O)C(O)C(O)C(O)C(O)C(O)C(O)CO.[Na+]; MP = 146.5°C (est); WS = 1.0E6 mg/L (est); $LogK_{ow}$ = -2.32

Table B.3: Fate					
Environmental Fate: Experimental					
Source	**Endpoint**	**Duration**	**Doses and number of replicates**	**Results**	**Study Details**
4864276	Biodegradation, O_2 consumption	28 day	**Dose:** 49.5 mg/L	Readily biodegradable, 10-day window met	**Methods:** • Test substance reported as CASRN 31138-65-5 • Purity: 49.5% • OECD Guideline 301F • GLP compliant
2072857	Anaerobic mineralization	35 days	**Dose:** 303 mg/L	100% degradation after 35 days (based on net-mass carbon)	**Methods**: • Test substance reported as CASRN 527-07-1 • Purity not reported • Test method: DIN EN ISO 11734 • GLP compliant **Results:**

					Degradation kinetics: 1 days (8%); 8 days (51%); 15 days (57%), 22 days (61%), 35 days (100%), when accounting for biogas production and dissolved inorganic carbon (DIC)
Experimental Fate: Modelled					
Model	**Data Type**	**Endpoint**	**Results**	**Notes**	
EPI Suite v4.11	Estimated	BCF	0.89		
EPI Suite v4.11	Estimated	BAF	3.16		

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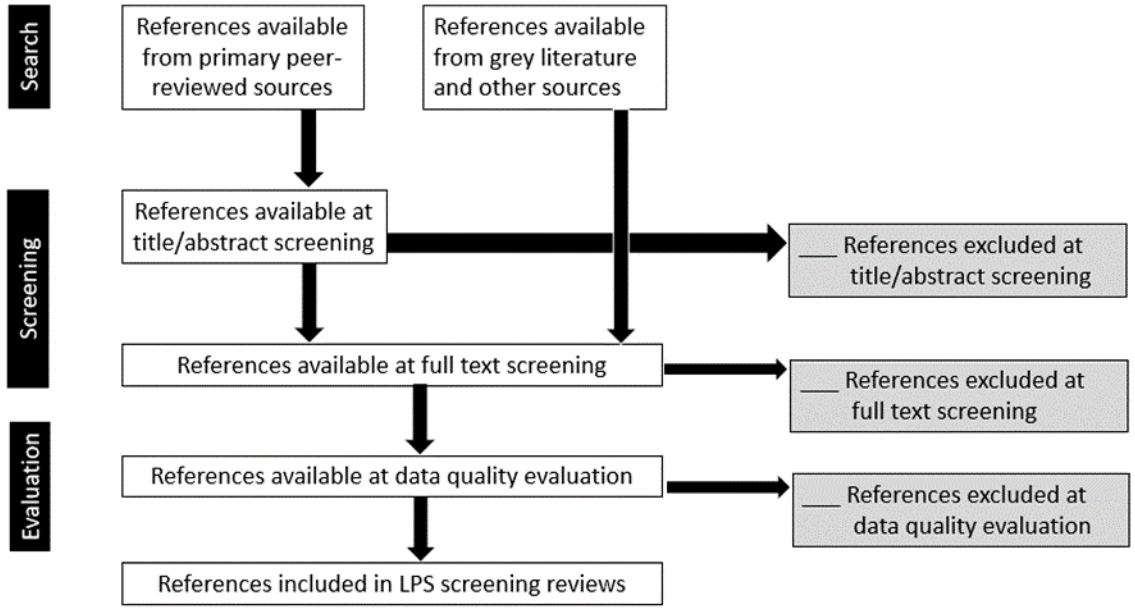
Appendix C: Literature Search Outcomes

C.1 Literature Search Review

This section briefly describes the literature search and review process, search terms, and search outcomes for the hazard and fate screening of sodium glucoheptonate. Search outcomes and reference details are provided on the candidate's HERO[42] project page.

EPA created a fit-for-purpose process to transparently document the literature search and review[43] of available hazard and fate information for low-priority substance (LPS) candidates. References from peer-reviewed primary sources, grey sources,[44] and other sources were identified, screened at the title/abstract and full-text level, and evaluated for data quality based on discipline-specific criteria. An overview of the literature search and review process is illustrated in Figure C1.

Figure C.1: Overview of the Literature Search and Review Process



C.1.1 Search for Analog Data

To supplement the information on the candidate chemical, sodium glucoheptonate, the following LPS candidates were used as analogs for read-across: D-gluconic acid (CASRN 526-95-4)), sodium gluconate (CASRN 527-07-1), calcium gluconate (CASRN 299-28-5), and glucono-delta-lactone (CASRN 90-80-

[42] The HERO low-priority substance candidate project pages are accessible to the public at https://hero.epa.gov/hero/.

[43] Discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA", also released at proposal.

[44] Grey literature and additional sources are the broad category of studies not found in standard, peer-reviewed literature database searches. This includes U.S. and international government agency websites, non-government organization (NGO) websites, and data sources that are difficult to find, or are not included, in the peer-reviewed databases, such as white papers, conference proceedings, technical reports, reference books, dissertations, and information on various stakeholder websites.

2). For more details and justification on analogs, see section 6.1.1. Analogs were used to fill data gaps on endpoints for which sodium glucoheptonate lacked quality data, such as developmental toxicity, or to add to the weight of the scientific evidence. Analog references were searched, screened, and evaluated using the same process as references on sodium glucoheptonate described above.[43]

C.1.2 Search terms and results

EPA began the literature review process for the hazard screening of sodium glucoheptonate by developing search terms. To gather publicly available information, specific search terms were applied for each discipline and across databases and grey literature sources. Table C.1 lists the search terms used in the database search of peer-reviewed literature for sodium glucoheptonate. For grey literature and other secondary sources, Table C.2 lists the search terms used for sodium glucoheptonate.

Table C.1: Search Terms Used in Peer-Reviewed Databases

Discipline	Database	Search terms[45]
Human Health	PubMed	31138-65-5[rn] OR "D-Gluco-heptonic acid, monosodium salt, (2.xi)-"[tw] OR "D-gluco-Heptonic acid, monosodium salt, (2.xi.)-"[tw] OR "D-gluco-Heptonic acid, monosodium salt, (2xi)-"[tw] OR "D-gluco-Heptonic acid, sodium salt (1:1), (2.xi.)-"[tw] OR "D-gluco-Heptonic acid, sodium salt (1:1), (2xi)-"[tw] OR "Monosodium D-glucoheptonate"[tw] OR "Sodium glucoheptonate"[tw] 29039-00-7[rn] OR 10094-62-9[rn] OR 100897-12-9[rn] OR "Calcihept"[tw] OR "Calcium bis 2xi -D-gluco-heptonate"[tw] OR "calcium bis 2ξ -D-GLUCO-heptonate"[tw] OR "Calcium gluceptate"[tw] OR "Calcium glucoheptonate"[tw] OR "Calcium heptagluconate"[tw] OR "D-gluco-Heptonic acid, calcium salt"[tw] OR "Glucoheptonic acid, calcium salt"[tw] OR "D-alpha-Glucoheptonic acid, sodium salt, dihydrate"[tw] OR "D-glycero-D-gulo-Heptonic acid, monosodium salt, dihydrate"[tw] OR "D-glycero-D-gulo-Heptonic acid, sodium salt, dihydrate"[tw] OR "Gluceptate sodium dihydrate"[tw] OR "Sodium D-alpha-glucoheptonate dihydrate"[tw] OR "Sodium D-glycero-D-gulo-heptonate dihydrate"[tw] OR "Ammonium gluceptate"[tw] OR "alpha-glucoheptonic acid "[nm]
	Toxline	(31138-65-5 [rn] OR "d-gluco-heptonic acid monosodium salt (2 xi) -" OR "d-gluco-heptonic acid monosodium salt (2 xi) -" OR "d-gluco-heptonic acid monosodium salt (2xi) -" OR "d-gluco-heptonic acid sodium salt (1 1) (2 xi) -" OR "d-gluco-heptonic acid sodium salt (1 1) (2xi) -" OR "monosodium d-glucoheptonate" OR "sodium glucoheptonate") AND (ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR FEDRIP [org] OR HEEP [org] OR HMTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org]) 29039-00-7 [rn] OR 10094-62-9 [rn] OR 100897-12-9 [rn] OR "calcihept" OR "calcium bis 2xi -d-gluco-heptonate" OR "calcium bis 2ξ -d-gluco-heptonate" OR "calcium gluceptate" OR "calcium glucoheptonate" OR "calcium heptagluconate" OR "d-gluco-heptonic acid calcium salt" OR "glucoheptonic acid calcium salt" OR "d-alpha-glucoheptonic acid sodium salt dihydrate" OR "d-glycero-d-gulo-heptonic acid monosodium salt dihydrate" OR "d-glycero-d-gulo-heptonic acid sodium salt dihydrate" OR "gluceptate sodium dihydrate" OR "sodium d-alpha-glucoheptonate dihydrate" OR "sodium d-glycero-d-gulo-heptonate dihydrate" OR "ammonium gluceptate") AND (ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR FEDRIP [org] OR HEEP [org] OR HMTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org]

[45] Additional language or syntax such as [tw], [rn], [org], and [nm] were added to search terms. These are unique to individual databases and must be applied to search terms so that the query can run properly.

Table C.1: Search Terms Used in Peer-Reviewed Databases		
Discipline	**Database**	**Search terms[45]**
		OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org]) AND NOT PubMed [org] AND NOT pubdart [org]
	TSCATS 1	31138-65-5 [rn] AND tscats[org] (29039-00-7 [rn] OR 10094-62-9 [rn]) AND tscats[org]
	WOS	TS=("31138-65-5" OR "D-Gluco-heptonic acid, monosodium salt, (2.xi)-" OR "D-gluco-Heptonic acid, monosodium salt, (2.xi.)-" OR "D-gluco-Heptonic acid, monosodium salt, (2xi)-" OR "D-gluco-Heptonic acid, sodium salt (1:1), (2.xi.)-" OR "D-gluco-Heptonic acid, sodium salt (1:1), (2xi)-" OR "Monosodium D-glucoheptonate" OR "Sodium glucoheptonate") Indexes=SCI-EXPANDED, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC Timespan=All years TS=("29039-00-7" OR "10094-62-9" OR "100897-12-9" OR "Calcihept" OR "Calcium bis 2xi -D-gluco-heptonate" OR "calcium bis 2ξ -D-GLUCO-heptonate" OR "Calcium gluceptate" OR "Calcium glucoheptonate" OR "Calcium heptagluconate" OR "D-gluco-Heptonic acid, calcium salt" OR "Glucoheptonic acid, calcium salt" OR "D-alpha-Glucoheptonic acid, sodium salt, dihydrate" OR "D-glycero-D-gulo-Heptonic acid, monosodium salt, dihydrate" OR "D-glycero-D-gulo-Heptonic acid, sodium salt, dihydrate" OR "Gluceptate sodium dihydrate" OR "Sodium D-alpha-glucoheptonate dihydrate" OR "Sodium D-glycero-D-gulo-heptonate dihydrate" OR "Ammonium gluceptate")
Environmental Hazard	WOS	Same as human health strategy synonyms only
	Toxline	Same as human health strategy synonyms only
	TSCATS 1	Same as human health strategy CASRN only
	Proquest	"31138-65-5" OR "D-Gluco-heptonic acid, monosodium salt, (2.xi)-" OR "D-gluco-Heptonic acid, monosodium salt, (2.xi.)-" OR "D-gluco-Heptonic acid, monosodium salt, (2xi)-" OR "D-gluco-Heptonic acid, sodium salt (1:1), (2.xi.)-" OR "D-gluco-Heptonic acid, sodium salt (1:1), (2xi)-" OR "Monosodium D-glucoheptonate" OR "Sodium glucoheptonate"
Fate	WOS	Same as human health strategy synonyms only

Table C.2: Search Terms Used in Grey Literature and Additional Sources	
Chemical	**Search terms**
Sodium Glucoheptonate	Searched as a string or individually depending on source: “31138-65-5” OR "D-Gluco-heptonic acid, monosodium salt, (2.xi)-" OR "D-gluco-Heptonic acid, monosodium salt, (2.xi.)-" OR "D-gluco-Heptonic acid, monosodium salt, (2xi)-" OR "D-gluco-Heptonic acid, sodium salt (1:1), (2.xi.)-" OR "D-gluco-Heptonic acid, sodium salt (1:1), (2xi)-" OR "Monosodium D-glucoheptonate" OR "Sodium glucoheptonate"

After the search terms were applied, more than 180 references were returned by all search efforts across peer-reviewed databases and grey literature sources. The total number of references include database results and additional strategies. All references from the search efforts were screened and evaluated through the LPS literature search and review process.[43] Of these, 19 references were included for data evaluation and used to support the designation of sodium glucoheptonate as LPS. The included hazard and fate references are listed in the bibliography of Appendix B.

C.2 Excluded Studies and Rationale

This section lists the excluded references, by HERO ID, found to be off-topic or unacceptable for use in the hazard screening of sodium glucoheptonate. The excluded references are organized by discipline (human health hazard, environmental hazard, and fate), presented along with a rationale based on exclusion criteria. The criteria[43] was used to determine off-topic references in the title/abstract or full-text screening and to determine unacceptable references in the data quality evaluation are provided in the form of questions.

C.2.1 Human Health Hazard Excluded References

For the screening review of sodium glucoheptonate, EPA excluded a total of 81 references when assessing human health hazard. Off-topic references (e.g., studies that did not contain information relevant to human health) were excluded at either title/abstract screening (see Table C.3), or full-text screening (see Table C.4). Unacceptable references (e.g., studies that did not meet data quality metrics) were excluded at full-text screening (see Tables C.5 and C.6). Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.3: Off-Topic References Excluded at Title/Abstract Screening for Human Health Hazard

Reference excluded (HERO ID) because the reference did NOT appear to contain information needs[46] relevant to human health hazard									
24923	4837160	4837180	4850272	4837145	4837170	4850041	4837155	4837176	4850265
2976788	4837162	4837182	4850278	4837146	4837172	4850100	4837156	4837177	4850268
2989178	4837163	4837183	4850279	4837147	4837173	4850116	4837158	4837178	4850269
3692509	4837164	4837184	4850280	4837150	4837174	4850175	4837159	4837179	4850270
4120475	4837165	4837185	4850281	4837152	4837175	4850185	4837168	4850039	4850283
4123163	4837167	4837203	4850282	4837169	4850040	4850285	4837124	4825460	
Reference excluded (HERO ID) because the reference primarily contained *in silico* data									
N/A									

Table C.4: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Human Health Hazard

Question	Off-topic if answer is:	References excluded (HERO ID)
Does the reference contain information pertaining to a low- priority substance candidate?	No	4850126
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A
What kind of evidence does this reference primarily contain?	*In silico* studies that DO NOT contain experimental verification	N/A

[46] The information needs for human health hazard includes a list of study characteristics pertaining to the study population/test organism, types of exposures and routes, use of controls, type and level of effects. A complete list of the information needs is provided in Table A1 of the "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA". These information needs helped guide the development of questions for title/abstract and full-text screening.

Table C.4: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
The following question apply to HUMAN evidence only		
Does the reference report an exposure route that is or is presumed to be by an inhalation, oral, or dermal route?	No	N/A
Does the reference report both test substance exposure(s) AND related health outcome(s)?	No	N/A
If the reference reports an exposure to a chemical mixture, are measures of the test substance or related metabolite(s) reported independently of other chemicals? Note: If the paper does not pertain to mixtures, choose "Not Applicable".	No	N/A
The following question apply to ANIMAL evidence only		
Does the reference report an exposure route that is by inhalation, oral, or dermal route?	No	4837125 4837151 4837154 4850267 4850273 4850277 4851347
Does the reference report both test substance-related exposure(s) AND related health outcome(s)?	No	4837154
Does the reference report the duration of exposure?	No	N/A
Does the reference report an exposure to the test substance only (i.e. no mixtures with the exception of aqueous solutions and reasonable impurities and byproducts)?	No	N/A
Does the paper report a negative control that is a vehicle control or no treatment control?	No[47]	N/A
The following questions apply to MECHANISTIC/ALTERNATIVE TEST METHODS evidence only		
Does the reference report a negative control that is a vehicle control or no treatment control?	No	N/A
Does the reference report an exposure to the test substance only (i.e. no mixtures with the exception of aqueous solutions and reasonable impurities and byproducts)?	No	N/A
For genotoxicity studies only: Does the study use a positive control?	No	N/A

[47] Except for acute mammalian toxicity and skin and eye irritation studies, where the use of a negative control may not be required (e.g., OECD 403 Acute Inhalation Toxicity Guidelines).

Table C.5: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance identity	The test substance identity cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	4864284 4864282
Metric 2: Negative and vehicle controls	A concurrent negative control group was not included or reported. **OR** The reported negative control group was not appropriate (e.g., age/weight of animals differed between control and treated groups).	N/A
Metric 3: Positive controls	When applicable, an appropriate concurrent positive control (i.e., inducing a positive response) was not used.	N/A
Metric 4: Reporting of doses/concentrations	Doses/concentrations were not reported and could not be calculated using default or reported estimates of body weight and diet/water intake (e.g., default intake values are not available for pregnant animals).	4864282
Metric 5: Exposure duration	The duration of exposure was not reported. **OR** The reported exposure duration was not suited to the study type and/or outcome(s) of interest (e.g., <28 days for repeat dose).	N/A
Metric 6: Test animal characteristics	The test animal species was not reported. **OR** The test animal (species, strain, sex, life-stage, source) was not appropriate for the evaluation of the specific outcome(s) of interest (e.g., genetically modified animals, strain was uniquely susceptible or resistant to one or more outcome of interest).	4851347
Metric 7: Number of animals per group	The number of animals per study group was not reported. **OR** The number of animals per study group was insufficient to characterize toxicological effects (e.g., 1-2 animals in each group).	N/A
Metric 8: Outcome assessment methodology	The outcome assessment methodology was not sensitive for the outcome(s) of interest (e.g., evaluation of endpoints outside the critical window of development, a systemic toxicity study that evaluated only grossly observable endpoints, such as clinical signs and mortality, etc.).	4851346
Metric 9: Reporting of data	Data presentation was inadequate (e.g., the report does not differentiate among findings in multiple exposure groups). **OR** Major inconsistencies were present in reporting of results.	N/A

Table C.6: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – In Vitro		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A
Metric 2: Negative controls	A concurrent negative control group was not included or reported. **OR** The reported negative control group was not appropriate (e.g., different cell lines used for controls and test substance exposure).	N/A
Metric 3: Positive controls	A concurrent positive control or proficiency group was not used.	N/A
Metric 4: Assay type	The assay type was not reported. **OR** The assay type was not appropriate for the study type or outcome of interest (e.g., *in vitro* skin corrosion protocol used for *in vitro* skin irritation assay).	N/A
Metric 5: Reporting of concentration	The exposure doses/concentrations or amounts of test substance were not reported.	N/A
Metric 6: Exposure duration	No information on exposure duration(s) was reported. **OR** The exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 24 hours exposure for bacterial reverse mutation test).	N/A
Metric 7: Metabolic activation	No information on the characterization and use of a metabolic activation system was reported. **OR** The exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 24 hours exposure for bacterial reverse mutation test).	N/A
Metric 8: Test model	The test model was not reported **OR** The test model was not routinely used for evaluation of the specific outcome of interest.	N/A
Metric 9: Outcome assessment methodology	The outcome assessment methodology was not reported. **OR** The assessment methodology was not appropriate for the outcome(s) of interest (e.g., cells were evaluated for chromosomal aberrations immediately after exposure to the test substance instead of after post-exposure incubation period).	N/A

C.2.2 Environmental Hazard

For the screening review of LPS candidate sodium glucoheptonate, EPA excluded a total of 117 references when assessing environmental hazard. Off-topic environmental hazard references excluded at title/abstract screening are listed in Table C.7, and those excluded at full-text screening are listed in Table C.8. References in Table C.9 represent unacceptable studies based on specific data quality metrics for environmental hazard. Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.7: Off-Topic References Excluded at Title/Abstract Screening for Environmental Hazard

Reference excluded (HERO ID) because the reference did NOT appear to contain information needs[48] relevant to environmental hazard									
229154	4850145	4850115	4850099	4850267	4837156	4850169	4850130	4850193	4850138
667743	4850146	4850116	4850100	4850268	4837202	4850174	4850131	4850194	4850139
3491604	4850147	4850117	4850101	4850269	4850085	4850175	4850132	4850199	4850140
3702885	4850148	4850118	4850102	4850270	4850086	4850176	4850133	4850201	4850141
3718142	4850150	4850119	4850104	4850272	4850087	4850177	4850134	4850202	4850142
4123163	4850151	4850121	4850105	4850273	4850088	4850183	4850135	4850203	4850143
4759430	4850152	4850122	4850106	4850277	4850090	4850185	4850136	4850265	4850144
4805432	4850153	4850123	4850107	4850278	4850091	4850189	4850137	4850097	4850283
4825459	4850154	4850124	4850108	4850279	4850092	4850168	4850129	4850098	4850285
4825460	4850159	4850125	4850109	4850280	4850093	4850167	4850128	4850095	4850112
4837125	4850164	4850126	4850110	4850281	4850094	4850111	4850282	4850096	4850114
4837146	4850166	4850127	4837151	4837150					
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental hazard data									
N/A									

Table C.8: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Environmental Hazard

Question	Off-topic if answer is:	References excluded (HERO ID)
Does the reference contain information pertaining to a low- priority substance candidate?	No	N/A
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A
Is quantitative environmental hazard data presented?	No	N/A
Is this primarily a modeling/simulation study? [Note: select "No" if experimental verification was included in the study]	Yes	N/A

[48] The information needs for environmental hazard includes a list of study characteristics pertaining to the test organism/species, type and level of effects, and use of controls. A complete list of the information needs is provided in Table A2 of the "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA". These information needs helped guide the development of questions for title/abstract and full-text screening.

Table C.8: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Environmental Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Is environmental hazard data presented for standard or non-standard aquatic or terrestrial species (fish, invertebrates, microorganisms, non-mammalian terrestrial species)?	No	N/A
Is exposure measured for the target substance or is the test substance a mixture (except for reasonable impurities, byproducts, and aqueous solutions) or formulated product?	Mixture	N/A
	Formulated Product	N/A
Does the reference report a duration of exposure?	No	N/A
Does the reference report a negative control that is a vehicle control or no treatment control?	No	N/A
Does the reference include endpoints in the information needs?	No	N/A

Table C.9: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Environmental Hazard		
Question	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear, CASRN or structure were not reported, substance name/ description does not match CASRN). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A
Metric 2: Negative controls	A concurrent negative control group was not included or reported.	N/A
Metric 3: Experimental system	The experimental system (e.g., static, semi-static, or flow-through regime) was not described.	N/A
Metric 4: Reporting of concentrations	Test concentrations were not reported.	N/A
Metric 5: Exposure duration	The duration of exposure was not reported. **OR** The reported exposure duration was not suited to the study type and/or outcome(s) of interest (e.g., study intended to assess effects on reproduction did not expose organisms for an acceptable period of time prior to mating).	N/A
Metric 6: Test organism characteristics	The test species was not reported. **OR** The test species, life stage, or age was not appropriate for the outcome(s) of interest.	N/A
Metric 7: Outcome assessment methodology	The outcome assessment methodology was not reported.	N/A
Metric 8: Reporting of data	Data presentation was inadequate. **OR** Major inconsistencies were present in reporting of results.	4851172 4851343

C.2.3 Fate

For the screening review of LPS candidate sodium glucoheptonate EPA excluded a total of 26 references when assessing environmental fate. Off-topic fate references excluded at title/abstract screening are listed in Table C.10, and those excluded at full-text screening are listed in Table C.11. References in Table C.12 represent unacceptable studies based on specific data quality metrics for fate. Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.10: Off-Topic References Excluded at Initial Screening for Fate

Reference excluded (HERO ID) because the reference did NOT appear to contain information needs[49] relevant to environmental fate								
4123163	4850265	4850281	4837156	4850277	4837146	4850270	4850175	4850280
4825459	4850267	4850282	4837202	4850278	4837150	4850272	4837125	4850269
4825460	4850268	4850283	4850273	4850279	4837151	4850137	4850285	
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental fate data								
N/A								

Table C.11: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Fate

Question	Off-topic if answer is:	References excluded (HERO ID)
Does the reference contain information pertaining to a low-priority substance candidate?	No	N/A
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A
Is quantitative fate data presented?	No	N/A
Is this primarily a modeling/simulation study? [Note: Select "Yes" only if there is no experimental verification]	Yes	N/A

Table C.12: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate

Data quality metric	Unacceptable if:	References excluded (HERO ID)
Metric 1: Test substance identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A
Metric 2:	The study did not include or report crucial control groups that consequently made the study unusable (e.g., no positive control for a biodegradation study reporting 0% removal).	N/A

[49] The information needs for fate includes a list of study characteristics pertaining to the associated media and exposure pathways, associated processes, and use of controls. A complete list of the information needs is provided in Table A3 of the "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA". These information needs helped guide the development of questions for title/abstract and full-text screening.

Table C.12: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Study controls	**OR** The vehicle used in the study was likely to unduly influence the study results.	
Metric 3: Test substance atability	There were problems with test substance stability, homogeneity, or preparation that had an impact on concentration or dose estimates and interfered with interpretation of study results.	N/A
Metric 4: Test method suitability	The test method was not reported or not suitable for the test substance. **OR** The test concentrations were not reported. **OR** The reported test concentrations were not measured and the nominal concentrations reported greatly exceeded the substances water solubility, which would greatly inhibit meaningful interpretation of the outcomes.	N/A
Metric 5: Testing conditions	Testing conditions were not reported and the omission would likely have a substantial impact on study results. **OR** Testing conditions were not appropriate for the method (e.g., a biodegradation study at temperatures that inhibit the microorganisms).	N/A
Metric 6: System type and design-partitioning	Equilibrium was not established or reported, preventing meaningful interpretation of study results. **OR** The system type and design (e.g. static, semi-static, and flow-through; sealed, open) were not capable of appropriately maintaining substance concentrations, preventing meaningful interpretation of study results.	N/A
Metric 7: Test organism-degradation	The test organism, species, or inoculum source were not reported, preventing meaningful interpretation of the study results.	N/A
Metric 8: Test organism-partitioning	The test organism information was not reported. **OR** The test organism is not routinely used and would likely prevent meaningful interpretation of the study results.	N/A
Metric 9: Outcome assessment methodology	The assessment methodology did not address or report the outcome(s) of interest.	N/A
Metric 10: Data reporting	Insufficient data were reported to evaluate the outcome of interest or to reasonably infer an outcome of interest. **OR** The analytical method used was not suitable for detection or quantification of the test substance. **OR** Data indicate that disappearance or transformation of the parent compound was likely due to some other process.	N/A
Metric 11: Confounding variables	There were sources of variability and uncertainty in the measurements and statistical techniques or between study groups.	N/A
Metric 12:	Reported value was completely inconsistent with reference substance data, related physical chemical properties, or otherwise implausible, indicating that a serious study deficiency exists (identified or not).	N/A

Table C.12: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Verification or plausibility of results		