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Assessment Plan for Ethanesulfonic Acid, 2-Hydroxy-, Monosodium Salt (Sodium Isethionate, CAS #1562-00-1) in Accordance with the USEPA High Production Volume Chemical Challenge Program

Prepared for:

The Sodium Ethyl Sulfonates Coalition

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EXECUTIVE SUMMARY

The Sodium Ethyl Sulfonates Coalition (SESC) is sponsoring ethanesulfonic acid, 2-hydroxy-, monosodium salt, commonly called sodium isethionate (SI), in the US High Production Volume (HPV) Challenge program. SI is primarily used in detergent bar soaps and body washes and as an intermediate in the production of sodium cocoyl isethionate (SCI). Most of the production of SI is used as an intermediate in the production of SCI, and as such is primarily for uses regulated by the US Food and Drug Association (FDA). The SESC assembled and reviewed the available public and private toxicological data, and developed an assessment plan for the sponsored chemical.

SI is highly soluble in water and has a very low affinity for bioaccumulation. SI is readily biodegradable, exhibiting 63-100% degradation in 10-28 days. SI was found to be non-toxic to aquatic organisms. No mortality or other significant effects were observed in several acute toxicity tests conducted on fish, *Daphnia*, and algal species. SI also exhibited no apparent toxicity in mammalian toxicity studies. It is not irritating to the skin or eyes of rabbits, and is not mutagenic to *Salmonella* or *E. coli* in genotoxicity studies. No data are available for the skin sensitization, repeated dose, reproductive and developmental toxicity endpoints. Human studies illustrate that SI is used in consumer products with no reported effects. When testing SI as a component of products containing both SCI and SI, no observable effects were also shown. Potential read across to the available repeated dose data for SCI (via oral and dermal routes) would indicate no significant mammalian toxicity is likely following repeated exposure to SI.

Manufacturing and processing of sodium isethionate takes place in controlled work environments that are designed to minimize worker and environmental exposure. Workers wear standard personal protective equipment and local exhaust ventilation to control vapor, mist or dust generation is recommended. In addition, engineering controls are in place at all manufacturing sites to minimize releases to the environment. Consumer exposure to diluted SI is primarily via the dermal route as an ingredient in moisturizing soap bars, other skin cleansers and personal wash products, at levels ranging from 0 to 15%. SI is much milder than soap to the skin, and is rinsed off immediately in the act of washing due to its high water solubility and low skin penetration potential. Therefore, consumer exposure to SI is not considered to be a significant concern.

Based on the availability of data and the lack of apparent toxicity, sodium isethionate is considered to be of low concern and no further testing is being proposed at this time.

INTRODUCTION

The High Production Volume (HPV) Challenge Program is a voluntary initiative of the US chemical industry to complete hazard data profiles for approximately 2800 HPV chemicals as identified on the US Environmental Protection Agency's (USEPA) 1990 Toxic Substances Control Act (TSCA) Inventory Update Rule (IUR). In the US, HPV chemicals are those that are manufactured or imported in quantities greater than 1 million pounds per year. The hazard data to be provided in the program are those that meet the requirements of the Screening Information Data Set (SIDS) Program (OECD 1997). SIDS, which has been internationally agreed to by member countries of the Organization for Economic Cooperation and Development (OECD), provides the basic screening data needed for an initial assessment of the physical-chemical properties, environmental fate, and adverse human and environmental effects of chemicals. The information for completing the SIDS can come from existing data or may be generated as part of the HPV Challenge Program. Once the available studies are identified or conducted, "robust summaries" are prepared.

The USEPA, industry, and non-governmental organizations (NGOs) are unified in their commitment to minimize the numbers of animals tested in the HPV Challenge Program whenever it is scientifically justifiable (USEPA 1999a, 2000). Therefore, this test plan evaluates all of the existing data for the sponsored chemical in an effort to adequately characterize the health and environmental hazard while reducing the number of animals required for testing.

The Sodium Ethyl Sulfonates Coalition (SESC) has agreed to assemble and review available public and private toxicological data, develop and provide an assessment plan for the sponsored chemical and conduct additional research, including testing when necessary, for ethanesulfonic acid, 2-hydroxy-, monosodium salt, which is more commonly and hereafter called in this report, sodium isethionate (SI). SI is a surfactant-cleansing agent used in synthetic soaps. The SESC is comprised of the following member companies:

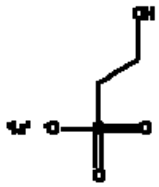
BASF Corporation
Clariant Corporation
Huntsman Petroleum Corporation
Unilever Home and Personal Care

This assessment plan is the result of the SESC's efforts and provides a summary and analysis of the available data, and identifies any data gaps in the SIDS data profile. The first section of this assessment plan provides an identification of the sponsored chemical, including its structure, production process, and use pattern. Following that are sections on the process used to collect the unpublished and published data and how those data were evaluated for quality and acceptability. This is followed by a discussion of the physical-chemical properties, environmental fate and transport, ecotoxicity and mammalian toxicity data as summarized in the accompanying robust summary document. Finally, conclusions regarding data availability and identification of data gaps in the SIDS profiles for the sponsored chemical are presented.

IDENTIFICATION OF SPONSORED CHEMICAL

A. Chemical Structure

The chemical being sponsored by the SESC is Sodium Isethionate (CAS #1562-00-1). Sodium isethionate (SI) is the sodium salt of isethionic acid and functions as a surfactant and lathering agent in synthetic cleansing bars and detergents. SI is also known by several synonyms, including: ethanesulfonic acid, 2-hydroxy-, monosodium salt; 2-hydroxyethanesulfonic acid, sodium salt; isethionic acid, sodium salt; and sodium hydroxyethylsulfonate. The basic chemical formula for SI is $C_2H_5NaO_4S$, and can be represented by:



B. Production Process

SI is prepared in a relatively simple two step process (Friedman 2004). The first step involves reacting sodium hydroxide (NaOH) with sulfur dioxide (SO_2) to form sodium bisulfite ($NaHSO_3$). The second step reacts the sodium bisulfite with ethylene oxide to form sodium isethionate ($HO - CH_2 - CH_2 - SO_3Na$). SI is normally provided with a nominal active content of 57.0% in water to manufacturers of sodium cocoyl isethionate, where it may be concentrated further.

C. Use Patterns and Exposure Potential

SI is primarily used in synthetic and combination detergent bar soaps and as an intermediate in the production of sodium cocoyl isethionate (SCI). Other uses of SI include skin cleansing and personal washing agents, cosmetics, intermediates, and ingredients in shampoo and bubble baths. SI and SCI are milder on the skin than soap and are non-drying. They offer a dense lather in addition to the lather made by the soap. SI works equally well in both hard and soft water (Friedman 2004). Most of the production of SI is used as an intermediate in the production of SCI for use directly in personal wash products and as such is primarily for uses regulated by the US Food and Drug Administration (FDA).

Manufacturing and processing of sodium isethionate takes place in controlled work environments that are designed to minimize worker and environmental exposure. Workers wear standard personal protective equipment, which may include chemical-type safety goggles or glasses, chemical-resistant safety shoes, impervious gloves, and protective clothing designed to minimize skin contact. Local exhaust ventilation to control vapor, mist or dust generation is recommended. If needed, mechanical ventilation and/or use of masks and respirators may be

used. Safety showers and eyewash stations are provided in all areas where the material is handled. In addition, extensive engineering controls are in place at all manufacturing sites to minimize releases to the environment.

Consumer exposure to SI is primarily dermal as a diluted material in personal wash products. SI is used as an ingredient in moisturizing soap bars, and other skin cleansers and skin detergents, at levels ranging from 0 to 15%. In these uses, SI is one component of a multi-component formulation that includes other surfactants (e.g., SCI), free fatty acids, fragrances, and water. SI is much milder than soap to the skin, and is rinsed off immediately in the act of washing. Therefore, consumer exposure to SI is not considered to be a significant concern.

Based on the use patterns described above, exposure to SI is expected to be adequately controlled and not of concern for workers, consumers, and the environment.

COLLECTION OF UNPUBLISHED AND PUBLISHED DATA

Coalition member companies contributed in-house studies of physical-chemical properties, environmental fate and transport, ecotoxicity, and mammalian toxicity for the chemicals and mixtures in the category. To supplement the industry data, literature searches were conducted of on-line databases (*e.g.*, Hazardous Substances Databank [HSDB], Registry of Toxic Effects of Chemical Substances [RTECS], and the USEPA's ECOTOX database), standard scientific data compendia (*e.g.*, *CRC Handbook of Chemistry and Physics* and *The Merck Index*), and other published sources (*e.g.*, International Uniform Chemical Information Database [IUCLID]). The sum total of the in-house studies, reference books, and literature searches of on-line databases was the identification of a substantial amount of available data for the sponsored chemical.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the USEPA and OECD SIDS guidance (USEPA 1999b; OECD 1997) and the systematic approach described by Klimisch et al. (1997). These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. The Klimisch et al. (1997) approach specifies four categories of reliability for describing data adequacy. These are:

1. **Reliable without Restriction:** Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.

2. **Reliable with Restrictions:** Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.

3. **Not Reliable:** Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.

4. **Not Assignable:** Includes studies or data in which insufficient detail is reported to assign a rating, *e.g.*, listed in abstracts or secondary literature.

Only those studies which are deemed reliable for the current HPV Challenge Program purposes are included in the data set for this assessment plan. Reliable studies include both categories rated 1 (Reliable without restriction) and 2 (Reliable with restrictions). Studies rated 3 (Not reliable) were not used. Studies rated 4 (Not assignable) were used when professional judgment deemed it appropriate as part of a weight-of-evidence approach.

Much of the available data were from study reports conducted by either outside contract laboratories or in-house industry laboratories. These study reports followed standard procedures for testing of physical-chemical properties, environmental fate and transport, aquatic toxicity, and mammalian toxicity. Some of the most recent studies were conducted under GLP provisions. In addition, some data were obtained from the published, peer-reviewed, scientific literature. Finally, some data were gleaned from the initial IUCLID data set prepared in 2000. Where the original study reports from the IUCLID data set could be obtained these were reviewed directly and summarized. Some of the reports cited in the IUCLID document could not be located; these data were included as appropriate and the IUCLID data set cited accordingly. Klimisch scores of 4 (not assignable) were given for data cited in IUCLID but not directly obtainable. Reliable data from all sources were incorporated into the data set as appropriate. Overall, a substantial amount of data are available for sodium isethionate.

Robust summaries were prepared according to the format recommended by the USEPA (1999c) and OECD (1997). These summaries present the salient information from each of the reliable studies. All of the summaries are collected into a dossier. The robust summary dossier for SI is attached as an appendix and should be used in conjunction with this assessment plan.

SUMMARY OF AVAILABLE DATA

The following discussion reviews the available data identified for each of the four major data areas: physical-chemical properties, environmental fate and transport, ecotoxicity, and mammalian toxicity.

Physical-Chemical Properties

Physical-chemical property data are available primarily from the IUCLID 2000 data set for sodium isethionate and from estimations made using the USEPA EPI Suite software. These data are summarized in Table 1:

Table 1. Physical-Chemical Properties

Endpoint	Value	Source	Reliability
Melting Point	193-196°C	IUCLID 2000	4
	214.41°C	EPI Suite	2
	191-194°C	Chemfinder.com	4
Boiling Point	>230°C	IUCLID 2000	4
	503.88°C	EPI Suite	2
Density	800-1000 kg/m^3	IUCLID 2000	4
Vapor Pressure	1.37 x 10^{-12} mm Hg at 25°C	EPI Suite	2
Partition Coefficient (Log K_{ow})	-5.50 at 25°C	EPI Suite	2
Water Solubility	1000 g/L at 25°C	EPI Suite	2
	650 g/L at 20°C	IUCLID 2000	4

Melting and boiling point data were presented in the IUCLID 2000 data set and were also estimated using EPI Suite. The data are consistent with a material that is a solid at room temperature. Vapor pressure data were estimated with EPI Suite and indicate that sodium isethionate would not be expected to volatilize significantly. The EPI Suite estimation of the log K_{ow} value indicates that sodium isethionate is unlikely to bioaccumulate. Finally, the IUCLID data set data and EPI Suite estimations confirm that sodium isethionate is very highly soluble in water.

Based on the availability of IUCLID data set data and EPI Suite estimations, no further testing for physical-chemical properties is being proposed at this time.

Environmental Fate and Transport

Environmental fate data are important for demonstrating the primary mechanism or mechanisms of degradation and how a material's properties affect its transport in the environment. For organic chemicals, fate is generally a function of the breakdown of compounds into smaller constituents by biological degradation. Other breakdown mechanisms that may be important are photolysis and hydrolysis. These breakdown mechanisms are necessarily dependent on what environmental compartment (air, water, soil, sediment) to which the chemicals are distributed. Fugacity modeling can be used to estimate the relative percentage of chemicals that will partition to various compartments at steady state. The results of the Level III fugacity modeling using EPI Suite using its standard estimated input parameters are shown in Table 2. EPI Suite utilizes input values for relevant physicochemical parameters from its resident database, which has undergone extensive peer review and is accessed by input of the CAS number.

Table 2. Environmental Distribution of Sodium Isethionate Based on EQC Modeling

Environmental Compartment	Sodium Isethionate
Air	0.173%
Water	34.7%
Soil	65.1%
Sediment	0.06%

Based on physical-chemical properties, the fugacity modeling predicts that most of the sponsored chemical will partition to the soil and water. Very little is expected to partition to the air or sediment. It should be noted that these results are estimates of theoretical distribution in the environment. Actual fate and distribution in the environment would be a function of both the physical-chemical properties and the use pattern of sodium isethionate.

The atmospheric oxidation potential of sodium isethionate was estimated using the EPI Suite software. This estimation suggests that photodegradation may be a significant mechanism for the breakdown of sodium isethionate in the atmosphere. Based on the model estimates, the hydroxyl radical reaction half-life was about 24 hours. With respect to stability in water, no hydrolysis information is available for sodium isethionate, however, hydrolysis is not a critical endpoint as SI is primarily eliminated via biodegradataion, as described below. The material can therefore be expected to be highly removed through wastewater treatment processes and in the environment. Data for hydrolysis or photolysis would not provide any significant additional information on the fate of the material.

Measured biodegradation data are available from five separate studies for sodium isethionate and are summarized in Table 3. These data indicate substantial microbial degradation under aerobic conditions. In the first study, conducted to GLP, sodium isethionate of 95.3% purity was tested in accordance with OECD Guideline 301A and EU Directive 92/69/EEC, C.4A. Results show that DOC elimination reached 98% and 101% in just 10 days for the two samples tested at 121 mg/L. In the second study, sodium isethionate as a 57% aqueous solution was tested using the Modified Sturm Test (OECD Guideline 301B). After 28 days the percent biodegradation was 66% and 76% (average 71%) for the two samples tested at 181.3 mg/L and 176.8 mg/L, respectively. Sodium benzoate was used as the positive control and resulted in 74% degradation, confirming the viability of the inoculum (activated sludge). Although this second study was not conducted according to GLP, it is a well conducted, reliable study that shows SI is readily biodegradable.

Table 3. Summary of Biodegradation Studies

Test Material	Value	Source	Reliability
Lutensit A-IS 95.3%	90-100% after 10 days	Taeger 2006	1
Hostapon SI 57%	71% after 28 days	Hirschen and Weber 2004	2
SI	>90% after 22 days	IUCLID 2000 (Hoechst 1986)	4
SI	63% after 15 days	IUCLID 2000 (Hoechst 1979)	4
SI	82% after 15 days	IUCLID 2000 (Hoechst 1980)	4

Three additional biodegradation studies were reported in the 2004 IUCLID data set. All three studies were conducted in accordance with OECD Guideline 302B, "Inherent Biodegradability: Modified Zahn-Wellens Test." Results showed biodegradation of >90% after 22 days, 63% after 15 days, and 82% after 15 days, respectively.

The IUCLID data set also reports BOD_5 values of 400 mg O_2/L and COD values of 570 and 600 mg/g substance. In addition, bioaccumulation was estimated using the EPI Suite software. The calculated BCF of sodium isethionate was 3.162 (log BCF = 0.500), which indicates that SI is not likely to bioaccumulate in body tissues.

Results of the environmental fate and transport studies demonstrate that sodium isethionate is readily biodegradable and has a very low affinity for bioaccumulation. Based on the availability of high quality biodegradation data and other estimated values, no further testing of environmental fate endpoints is being proposed at this time.

Ecotoxicity

Several studies are available to evaluate the aquatic toxicity of sodium isethionate (Table 4).

Well documented GLP studies are available to address the acute aquatic toxicity of sodium isethionate to the zebra fish (*Brachydanio rerio*). In the first study, zebra fish were exposed to static concentrations up to 10,000 mg/L for 96 hours in accordance with OECD Guideline 203. Sodium isethionate of 95.3% purity was used. After 96 hours, no mortality or other effects were observed at any test concentration (LC_{50} > 10,000 mg/L). In the second study, zebra fish were exposed to a limit test concentration of 100 mg/L, again according to OECD Guideline 203. Again, no mortality was observed during the 96 hour study. Some behavioral changes (hypoactivity, swimming posture, projecting opercula, irregular respiration) were observed in the first 3-6 hours of the study but disappeared after 24 hours. The 96 hour LC_{50} was greater than the limit concentration of 100 mg/L.

Table 4. Summary of Aquatic Toxicity Studies

Test Material	Value	Source	Reliability
Fish (*Brachydanio rerio*)			
Lutensit A-IS 95.3%	96-h LC_{50} >1.0 x 10^4 mg/L	Munk 1998	1
SI 97%	96-h LC_{50} >100 mg/L	Zok 1996	1
Invertebrate (*Daphnia magna*)			
Lutensit A-IS 95.3%	48-h EC_{50} >100 mg/L	Maisch 1997a	1
Hostapon SI 57%	48-h EC_{50} >1000 mg/L	Noack 2005	1
SI	48-h EC_{50} >1000 mg/L	IUCLID 2000 (Hoechst 1986)	4
Algae (*Scenedesmus subspicatus*)			
Lutensit A-IS 95.3%	72-h EC_{50} >100 mg/L	Maisch 1997b	1
Microorganisms (Bacteria)			
SI	24-h EC_{50} >2500 mg/L	IUCLID 2000 (Hoechst 1986)	4
SI	24-h SG = 1500 mg/L	IUCLID 2000 (Hoechst 1979)	4
SI	24-h SG = 800 mg/L	IUCLID 2000 (Hoechst 1980)	4

Well documented GLP studies are also available regarding the acute aquatic toxicity of sodium isethionate to *Daphnia magna*. In the first study, *Daphnia* were exposed to five concentrations ranging from 6.25 to 100 mg/L of 95.3% pure sodium isethionate for 48 hours. No immobilization or other effect was observed during the study, except for the mortality of two animals in the 25 mg/L concentration that appeared unrelated to the test material. The 48 hour EC_{50} is greater than the highest concentration tested, 100 mg/L. In the second study, *Daphnia* were exposed in a limit test to 1000 mg/L sodium isethionate in a 57% aqueous solution for 48 hours. Again, no mortality or other effects were observed during the study. The 48 hour EC_{50} is greater than the limit concentration of 1000 mg/L.

The aquatic toxicity to the green unicellular algae, *Scenedesmus subspicatus*, was evaluated in a well documented GLP study using 95.3% pure sodium isethionate. Algae were exposed to nine concentrations ranging from 0.29 to 100 mg/L for 72 hours. Cell counts were made with a Newbauer counting chamber and any inhibition on biomass and growth rate was noted. Results indicate no significant effects on either biomass or growth rate during the study. The resultant 72 hour EC_{50} was greater than the highest concentration tested of 100 mg/L.

Toxicity to aquatic anaerobic bacteria was also evaluated in three studies reported in the IUCLID 2000 data set. In the first study using the ETAD Fermentation tube method, the resultant EC_{50} value was >2500 mg/L. In the second two studies, again using the ETAD Fermentation tube method, results indicate an SG (equivalent to a lowest observable effect concentration) of 1500 and 800 mg/L, respectively.

Estimates of chronic aquatic toxicity data were made using the EPA's ECOSAR software. The calculated fish 30 day ChV (chronic value) was 4.74×10^7 mg/L. The calculated 16 day daphnid EC_{50} was 1.52×10^6 mg/L. Similarly, ECOSAR was used to estimate the 14 day LC_{50} of the terrestrial earthworm as 1.86×10^5 mg/L.

In summary, both high quality experimental studies and estimated data are available for the aquatic toxicity endpoints and demonstrate that sodium isethionate is not toxic to aquatic organisms. Based on the available information, which indicates low toxicity to aquatic organisms, high water solubility and ready biodegradation, plus the very low estimated log K_{ow}, no chronic aquatic toxicity would be expected. Furthermore, due to the low aquatic toxicity and likely low partitioning to soils and sediments, terrestrial toxicity is unlikely. Therefore, no further ecological toxicity studies are being proposed at this time.

Toxicity

The available data to assess the mammalian toxicity of sodium isethionate are shown in Table 5. Two well documented GLP studies are available to evaluate the acute oral toxicity of sodium isethionate to mammals. In the first study, male and female Wistar rats were given a single limit dose of 2000 mg/kg bw in an aqueous vehicle by gavage. Animals were observed for 14 days post-administration for signs of stress or toxicity and then necropsied to evaluate any internal signs. No mortality was observed during the study. No effects were observed in any of the female animals. Non-specific signs of toxicity were observed in the male animals within 1-3 hours after administration, including impaired general state, dyspnoea, staggering, and diarrhea. These animals all appeared normal within 2 days after application and remained that way. No effects on body weight gain and no abnormalities at necropsy were observed. In the second study, male and female Wistar rats were given a single oral dose of 5000 mg/kg bw in distilled water by gavage and observed for 14 days. No mortality was observed during the study with the exception of one female at the one week time period. Necropsy revealed no apparent signs of toxicity and its death did not appear to be treatment related. No other effects were observed in any of the remaining animals.

Table 5. Summary of Mammalian Toxicity Studies

Test Material	Value	Source	Reliability
Acute Oral			
Lutensit A-IS 95.3%	LD_{50} >2000 mg/kg	Kuehlem 1998a	1
SI 97%	LD_{50} >5000 mg/kg	Hofmann and Hollander 1986a	1
Skin Irritation			
Lutensit A-IS 95.3%	Not irritating	Kuehlem 1998b	1
SI 97%	Not irritating	Hofmann and Hollander 1986b	1
Eye Irritation			
Lutensit A-IS 95.3%	Not irritating	Kuehlem 1998c	1
SI 97%	Not irritating	Hofmann and Hollander 1986c	1
Genotoxicity – Ames Test			
SI 99.6%	Negative (with and without S-9) (*Salmonella typhimurium*)	Stammberger 1993	1
SI 99.6%	Negative (with and without S-9) (*Escherichia coli*)	Stammberger 1993	1

No specific data are available on acute inhalation or acute dermal toxicity. Inhalation is not expected to be a significant route of exposure. Furthermore, while no specific acute dermal toxicity data were located, data are available on dermal exposure in two GLP skin irritation studies. In the first study, the skin on the backs of healthy white rabbits was exposed to a single dose of 0.5 g sodium isethionate (95.3% purity) for four hours. The test sites were covered with a test patch held in place with a semi-occlusive dressing. After four hours the patches were removed and the areas rinsed. Barely perceptible erythema was observed in all three animals at the one hour observation time, but this had completely disappeared by 24 hours. In the second study, 0.1 mL of 500 mg sodium isethionate (≥97% purity) was applied to the intact skin on the backs of three rabbits and covered with a test patch and a semi-occlusive dressing. After four hours the patch was removed and the area rinsed. Results indicate no incidence of erythema/eschar or edema at any time during the study. Based on these two studies, sodium isethionate is not irritating to the skin.

Eye irritation was also examined in two GLP studies. In the first study, a single application of 0.1 mL (approximately 58 mg) of sodium isethionate (95.3% purity) was placed in the conjunctival sac of three rabbits. After 24 hours this was washed out and readings taken at 1, 24, 48 and 72 hours after application. No effects were observed for corneal opacity or iris. Minor chemosis was observed at the one hour period only and disappeared shortly thereafter. Minor conjunctival redness was observed at the one and 24 hour periods but not thereafter. Similarly, conjunctival discharge was observed at one hour but not thereafter. In the second study, a single application of 0.1 mL (100 mg) of sodium isethionate (≥97% purity) was placed in the conjunctival sac of one eye in each of three rabbits and washed out after 24 hours. Swelling of the lids and redness of the conjunctiva and iris were observed one hour after application. A clear

discharge was also observed. These symptoms were reduced at 24 hours and disappeared by 48 hours.

Data were not available for the sensitization, repeated dose, reproductive and developmental toxicity endpoints.

Well documented GLP data are available to evaluate genotoxicity. In a bacterial reverse mutation assay (Ames test), five strains of *Salmonella typhimurium* were exposed to sodium isethionate (99.6% purity) concentrations ranging from 4 to 5000 µ/plate. Tests were conducted both with and without S-9 metabolic activation. Results demonstrated no significant increases in revertant colonies in any of the tester strains either in the presence or absence of S-9 mix. In a second study conducted with *Escherichia coli* with the same test material at the same concentrations, no significant effects were observed. These studies confirm that sodium isethionate is not mutagenic in these test systems. DEREK and TIMES structure activity software both predict that SI will be non-mutagenic and has no structural alerts for this endpoint (Unilever personal communication).

In summary, well documented studies are available for many of the toxicity endpoints. These data demonstrate that sodium isethionate is not acutely toxic, not a skin or eye irritant, and not mutagenic. Data are not available for the sensitization, repeated dose, reproductive and developmental toxicity endpoints. However, structure activity software predictions indicate that no alerts were seen for SI for skin sensitization and skin penetration is predicted as low (Unilever personal communication). Given the fact that sodium isethionate does not show any significant toxicity characteristics in the available studies, it is unclear that conducting additional long-term exposure studies would provide any new information. Furthermore, mammalian toxicity data for sodium cocoyl isethionate from repeated dose studies conducted via both oral and dermal routes show no significant systemic toxicity. These repeated dose data are relevant for read across to SI as ADME studies indicate that SCI is metabolized to SI by hydrolysis of the ester bond in SCI (see Howes 1975 in robust summary document). Therefore, in the interest of responsible animal welfare management the SESC is proposing not to conduct additional animal testing at this time.

Evaluation of Data Completeness

Substantial data are available for sodium isethionate. These data are derived from a variety of sources, including GLP laboratory studies, IUCLID-reported studies, and estimations using the EPA models EPI Suite and ECOSAR. Data for physical-chemical properties are primarily based on EPI Suite estimations. EPI Suite was also used to estimate photodegradation and fugacity-based distribution in the environment. High quality GLP studies have been provided to address the biodegradation endpoint. Similarly, high quality GLP studies are provided to meet the requirements for acute aquatic toxicity. For mammalian toxicity, high quality GLP studies are available for acute oral toxicity, as well as skin and eye irritation and mutagenicity with *Salmonella typhimurium* and *E. coli*. Data are not available to address the skin sensitization, repeated dose, reproductive and developmental toxicity endpoints. However, read across from the SCI data set could help to address some of these endpoints for SI.

SUMMARY OF SODIUM ISETHIONATE PROPERTIES

Sodium isethionate is an intermediate in the production of SCI and also may be a component in syndet bars and other cleansers and cosmetics. SI is highly soluble in water and has a very low affinity for bioaccumulation. SI is readily biodegradable, generally exhibiting 63-100% degradation in as little as 10 days. SI was found to be non toxic to aquatic organisms. No mortality or other significant effects were observed in several acute toxicity tests conducted on fish, *Daphnia*, and algal species. SI also exhibited no apparent toxicity in mammalian toxicity studies. It is not irritating to the skin or eyes of rabbits, and is not mutagenic to *Salmonella* or *E. coli* in genotoxicity studies. No data are available for the skin sensitization, repeated dose, reproductive and developmental toxicity endpoints. However, based on the lack of observed toxicity demonstrated in all of the available studies, and in the interest of responsible animal welfare management, the SESC is not proposing to conduct additional animal testing at this time.

Table 6 summarizes the availability of data and assessment plan status for sodium isethionate.

It should be noted that separate robust summary and assessment plan documents, also prepared in support of the HPV Challenge program, are available for sodium cocoyl isethionate (SCI). SI is used as an intermediate in the synthesis of SCI, and some SI is also present in the final products that use SCI as the primary ingredient. As a consequence, several of the studies summarized in the SCI robust summary document were conducted on products that contain up to 15% SI in their composition. Furthermore, several Repeat Insult Patch Tests (RIPT) have been conducted for products containing both SCI and SI and are reported in the SCI documents. Therefore, the SCI documents should be consulted for additional information relevant to the evaluation of SI.

CONCLUSIONS

Substantial data are available for sodium isethionate. These data consistently demonstrate that sodium isethionate is not toxic to aquatic or mammalian organisms. Worker exposure is adequately controlled by engineering controls and the use of personal protective equipment. Dermal exposure occurs through use of moisturizing detergent bar soaps and body washes and cosmetic use of products containing SI. However, studies confirm that SI is not irritating to the skin, and in fact is much milder to the skin than conventional soap products.

Based on the availability of data and the lack of toxicity, sodium isethionate is considered to be of low concern and no further animal testing is being proposed at this time.

Table 6. Data Availability and Status for Sodium Isethionate

	Data Available	Data Acceptable	Testing Required
Physical-Chemical Properties			
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Octanol/Water Partition Coefficient	Y	Y	N
Water Solubility	Y	Y	N
Environmental Fate and Pathways			
Photodegradation	Y	Y	N
Stability in Water	N	-	N
Biodegradation	Y	Y	N
Bioaccumulation	Y	Y	N
Ecotoxicity			
Acute/Prolonged Toxicity to Fish	Y	Y	N
Acute Toxicity to *Daphnia*	Y	Y	N
Toxicity to Aquatic Plants (algae)	Y	Y	N
Chronic Toxicity to Fish	Y	Y	N
Chronic Toxicity to Aquatic Invertebrates	Y	Y	N
Toxicity			
Acute Oral Toxicity	Y	Y	N
Acute Inhalation Toxicity	N	-	N
Acute Dermal Toxicity	N	-	N
Skin Irritation	Y	Y	N
Eye Irritation	Y	Y	N
Skin Sensitization	N	-	N
Repeated Dose Toxicity	N	-	N
Genetic Toxicity in vitro (Bacterial test)	Y	Y	N
Genetic Toxicity in vitro (Non-bacterial test)	N	-	N
Genetic Toxicity in vivo	N	-	N
Carcinogenicity	N	-	N
Toxicity to Reproduction	N	-	N
Developmental Toxicity	N	-	N

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