Assessment Plan for Fatty acids, coco, 2-sulfoethyl esters, sodium salts (Sodium Cocoyl Isethionate; CAS #61789-32-0) in Accordance with the USEPA High Production Volume Chemical Challenge Program

Prepared for:

The Sodium Ethyl Sulfonates Coalition

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Keller and Heckman LLP

1001 G Street, NW
Washington, DC 20001
www.khlaw.com

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EXECUTIVE SUMMARY

The Sodium Ethyl Sulfonates Coalition (SESC) is sponsoring Fatty acids, coco, 2-sulfoethyl esters, sodium salts, commonly called Sodium Cocoyl Isethionate (SCI) in the US High Production Volume (HPV) Challenge program. SCI is primarily used as an anionic surfactant-cleansing agent in synthetic soaps. These soap preparations are used by consumers as personal care products. The SESC assembled and reviewed available public and private toxicological data, and developed an assessment plan for the sponsored chemical.

SCI has a low vapor pressure and would not be expected to volatilize significantly. SCI is somewhat soluble in water (0.01%). SCI is readily biodegradable and has a very low affinity for bioaccumulation. It is only slightly toxic to aquatic organisms. Mammalian toxicity data demonstrate that SCI is not acutely toxic, is not capable of skin sensitization, does not produce significant systemic toxicity in repeated dose studies via dermal or oral routes of exposure, and is not mutagenic. SCI is mildly to moderately irritating to the skin and eyes. While no reproductive or developmental toxicity data are available, data from repeated dose studies give some reassurance of the lack of effects on fertility. There is also a considerable history of safe use of consumer products containing SCI.

The potential for worker exposure to SCI during the manufacturing, processing, and distribution is limited by process design and standard operational controls. Engineering controls are also in place to minimize releases to the environment. Consumer exposure occurs through the use of SCI in consumer products, including syndet bars, skin cleansers, and grooming products. Primarily this exposure will be dermal due to application of the product to skin, though some uses may result in occasional accidental eye exposure. However, SCI has been shown to be of generally low toxicity, and combined with overall low dermal absorption, the only likely effects that may occur are slight skin irritation in some individuals that have sensitive skin. Since the success of SCI in consumer products is largely due to its mildness to the skin relative to soaps and other surfactants, no significant effects are expected from normal and foreseeable use.

Based on the data available and the limited systemic exposure potential in consumer end uses, SCI is considered to be of low concern and the SESC proposes that further testing is not warranted 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 Fatty acids, coco, 2-sulfoethyl esters, sodium salts, which is more commonly and hereafter called in this report, sodium cocoyl isethionate (SCI). SCI is a surfactant-cleansing agent used in synthetic soaps. The SESC is comprised of the following member companies:

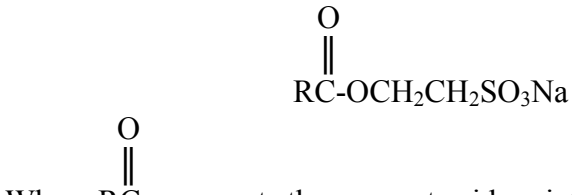
BASF Corporation
Clariant Corporation
Huntsman Petroleum Corporation
Unilever Home and Personal Care

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. The process used to collect the unpublished and published data and how those data were evaluated for quality and acceptability is described. 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 Cocoyl Isethionate (CAS #61789-32-0). Sodium Cocoyl Isethionate (SCI) the sodium salt of the coconut fatty acid ester of isethionic acid and functions as an anionic surfactant-cleansing agent (Zondlo 1993). SCI is also known by several synonyms, including: coconut fatty acid, 2-sulfoethyl ester, sodium salt; Jordapon CI; and DEFI. The basic chemical formula for SCI is:

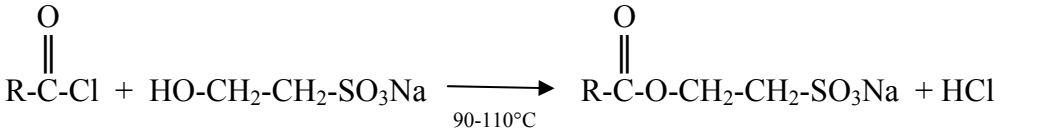


Where RC represents the coconut acid moiety.

B. Production Process

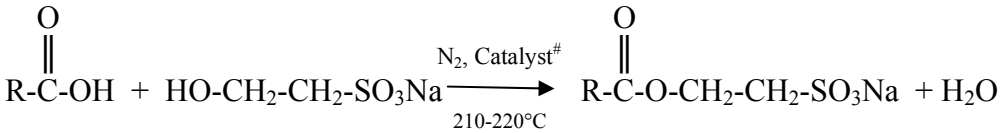
SCI is prepared by reacting sodium isethionate (SI) with either the fatty acid mixture from coconut oil or the corresponding chlorides. The two primary methods of synthesis are shown below as described in Friedman (2004):

Method 1: Fatty Acid Chloride Route (Liquid-Solid Reaction)



Fatty Acid Chloride | Sodium Isethionate | Sodium Cocoyl Isethionate | Hydrochloric Acid

Method 2: Direct Condensation (Esterification)



Coconut Fatty Acid* where R=$C_{11}H_{23}$ | Sodium Isethionate | Sodium Cocoyl Isethionate | Water

* Excess of fatty acids in final product: 15-25% Stearic Acid; 3-5% Coconut Acid
# Catalyst could be: H_2PO_4, H_2SO_4, PtO_2, Boric Acid, ZnO, $ZnSO_4$, ZnO/Org. Sulfonic Acid, Al, Zr, St, Ti, Cd, Hg Sulfates, Zr/Zr soaps, Zn soaps, MgO, Mg soaps

The above methods use fatty acid excess to shift the reaction equilibrium to sodium cocoyl isethionate synthesis (Friedman 2004). The acid chloride route has been largely supplanted by the direct esterification route because the latter is extremely efficient, i.e., it produces virtually no waste and even the excess fatty acid to drive the reaction forward is incorporated into the final product.

In the direct esterification route, the sodium isethionate starting material is concentrated to approximately 75%. It is then added to a batch reactor along with the coconut fatty acid and zinc oxide powder. Coconut fatty acid is added at an approximate excess of 1.3 to help dirve the reaction. The mixture is stirred, inerted with nitrogen and gradually heated to 238°C. During this process the water initially in the system, the water of reaction, and some fatty acid are condensed and separated. The fatty acid is returned to the reactor. After approximately 1 hour, molten stearic acid is added to the reactor. The vessel is then placed under vacuum and volatile fatty acids are driven off, condensed and retained for future use. The standard reactor time cycle is approximately 2.5 hours. The final conversion efficiency of sodium isethionate is approximately 95%.

The finished sodium cocoyl isethionate has an approximate formula composition of:

75 %	SCI
12 %	Stearic Acid
8 %	Coconut Fatty Acid
3 %	Sodium Isethionate
2 %	Miscellaneous

Other processing systems may result in slightly different percentages, but the constituents and relative compositions remain similar. In the above example, the finished reaction product is referred to as DEFI, Directly Esterified Fatty Isethionate. Most DEFI is used for production of synthetic soap bars.

C. Use Patterns and Exposure Potential

SCI is as a mild foaming and cleansing agent, primarily for use in synthetic detergent (syndet) bars (Zondlo 1993) that are used as consumer personal care products. It is an anionic surfactant designed to rectify the two main disadvantages of conventional soaps, that is, the tendency of soaps to hydrolyze in water and release caustic alkali, and the tendency for soaps to form insoluble and inactive salts when used with hard or salt water. The synthetic surfactants, including SCI, do not have these disadvantages. In fact, the mildness of SCI to the skin relative to soaps has allowed SCI to become a product of choice for cosmetic and baby cleansing bars (Friedman 2004).

In practice, SCI is mixed with several other soap ingredients, including additional SI for stability, to form the bars. The final maximum concentration of SCI in syndet bars is approximately 50%, though the exact composition varies by manufacturer (Unilever, personal communication).

The Cosmetic Ingredient Review (Zondlo 1993) indicates that SCI has been used in the preparation of bath soaps and detergents (about 60% of formulations); non-coloring shampoos (13%); tonics, dressings, and other hair grooming aids (13%); and skin cleansing preparations (15%). Reporting of concentrations of SCI in cosmetic products has not been required since 1992, but data from 1984 indicate that SCI was used at a concentration of ≤50% in bath soaps and detergents and at 10-25% in non-coloring shampoo formulations (Zondlo 1993).

The potential for worker exposure during the manufacturing, processing, and distribution is limited by standard operational controls. Manufacture is in a closed reactor and normal engineering controls are in place to minimize worker exposure during formulation into the finished preparation. Local exhaust ventilation is used to control dust. Workers also wear standard personal protective equipment including safety goggles, chemical resistant protective gloves, protective clothing as necessary to minimize contact, and respiratory masks to minimize inhalation of dust.

Engineering controls are also in place to minimize releases to the environment. Waste disposal is to licensed facilities and controls are in place to avoid discharging into the sewer system. Spills are easily contained in placed in appropriate containers for disposal.

Consumer exposure occurs through the use of SCI in various consumer products, including syndet bars, skin cleansers, and grooming products. Primarily this exposure will be dermal during application of the product to skin, though some uses may result in occasional accidental eye exposure. However, SCI has been shown to be of generally low toxicity via both dermal and oral routes of exposure (see Appendix A). This fact, combined with overall low dermal absorption (Howes 1975, Howes and Cordell 1974), and extensive metabolism, suggests that the only effect that may occur is slight skin irritation in some individuals with sensitive skin. In fact, the success of SCI in consumer products is largely due to its mildness to the skin relative to soaps and other surfactants.

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 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 general 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.

The majority 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 biodegradation, aquatic toxicity, and mammalian toxicity. Many of the studies were conducted under GLP provisions. Reliable data from these sources were incorporated into the data set as appropriate. Overall, a substantial amount of data of high quality was available for SCI.

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 SCI is attached as an appendix and should be used in conjunction with this assessment plan.

SUMMARY OF AVAILABLE DATA

Physical-Chemical Properties

Physical-chemical property data are available primarily as estimates using the USEPA's EPI Suite software (v.3.12) for sodium cocoyl isethionate. These data are summarized in Table 1:

Table 1. Physical-Chemical Properties

Endpoint	Value	Source	Reliability
Melting Point	293.07°C	EPI Suite	2
Boiling Point	672.26°C	EPI Suite	2
Vapor Pressure	9.58×10^{-16} mm Hg at 25°C	EPI Suite	2
Partition Coefficient (Log K_{ow})	2.38 at 25°C	EPI Suite	2
Water Solubility	0.01% (100 ppm) at 25°C	Sun et al. 2003	2
Bioaccumulation Factor (BCF)	70.79 (log BCF = 1.850)	EPI Suite	2

Melting and boiling point data were estimated using EPI Suite and are consistent with a material that is a solid at room temperature. Vapor pressure data were also estimated with EPI Suite and indicate that SCI would not be expected to volatilize significantly. The EPI Suite estimation of the log K_{ow} value suggests that SCI has a low to moderate affinity for partitioning to organic systems. The calculated BCF indicates a low affinity for bioaccumulation in aquatic organisms. Finally, in a published journal article focusing on the understanding of the enthalpy and equilibrium of SCI solubilization, Sun et al. (2003) found that SCI is somewhat soluble in water (0.01%).

Based on the availability of the EPI Suite estimations and other data, the Coalition believes that the physical-chemical properties are adequately characterized for HPV Challenge purposes. Therefore, no further testing for these 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. Although data for hydrolysis or photolysis are not available, SCI is shown to be readily biodegradable (Table 3) and therefore data on these two endpoints would not provide significant additional information on the fate of SCI.

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 physical-chemical 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 Cocoyl Isethionate Based on EQC Modeling

Environmental Compartment	Sodium Cocoyl Isethionate
Air	0.632%
Water	24.3%
Soil	74.9%
Sediment	0.141%

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 cocoyl isethionate.

The atmospheric oxidation potential of sodium cocoyl isethionate was estimated using the EPI Suite software. This estimation suggests that photodegradation may be a significant mechanism for the breakdown of sodium cocoyl isethionate in the atmosphere. Based on the model estimates, the hydroxyl radical reaction half-life was about 6 hours. With respect to stability in water, no hydrolysis information is available for sodium cocoyl isethionate.

Measured biodegradation data are available from four separate studies for sodium cocoyl isethionate and are summarized in Table 3. These data indicate substantial microbial degradation under aerobic conditions. In the first study, conducted to GLP standards (Watson 1983), sodium cocoyl isethionate of 66% purity[1] was tested using the Modified Sturm test procedure. Results show that biodegradation reached approximately 78% after 28 days for the two samples tested at 10 and 20 mg/L, respectively. Sodium acetate was used a positive control and resulted in 81.5% biodegradation. This study shows that SCI is readily biodegradable. In a second study with the same test material (Birch 1983), primary biodegradation reached 99.6% after only 14 days using the Modified OECD Screening Test. Furthermore, two variations of SCI (Hostapon SCI and Hostapon SCID)[2] were tested to determine the aerobic ready biodegradation using the Modified OECD Screening Test (Bücking et al. 1994a,b). Results of the two tests showed biodegradation of 94.1% and 93.5% after 28 days for the Hostapon SCI and SCID, respectively. From these results, therefore, it can be expected that SCI would be highly removed through waste water treatment plant processes and in the environment.

[1] DEFI Base consists of sodium acyl coconut isethionate (66% by weight), free stearic/palmitic acids (16%), coconut fatty acids (4%), sodium isethionate (7%) and water (2%).

[2] Hostapon SCI consists of sodium coconut isethionate (85-89% by weight), coco fatty acids (≤2.5%), sodium isethionate (10.5%), and sodium sulfate (≤1%). Hostapon SCID consists of sodium coconut isethionate (66% by weight), stearic acid (19±2%), coco fatty acids (7±2%), and sodium isethionate (max 4%).

Table 3. Summary of Biodegradation Studies

Test Material	Value	Source	Reliability
DEFI Base 66%	78% after 28 days (20 mg/L) 77.8% after 28 days (10 mg/L)	Watson 1983	2
DEFI Base 66%	99.6% after 14 days	Birch 1983	2
Hostapon SCI 85-89%	94.1% after 28 days	Bucking and Pleschke 1994a	2
Hostapon SCID 66%	93.5% after 28 days	Bucking and Pleschke 1994b	2

In addition, bioaccumulation was estimated using the EPI Suite software. The calculated bioconcentration factor (BCF) of sodium cocoyl isethionate was 70.79 (log BCF = 1.850), indicating a low affinity for uptake by aquatic organisms.

Results of the environmental fate and transport studies demonstrate that sodium cocoyl 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 cocoyl isethionate (Table 4).

Well documented GLP studies are available to address the acute aquatic toxicity of sodium cocoyl isethionate to rainbow trout (*Oncorhynchus mykiss*) and the zebra fish (*Brachydanio rerio*). In the first study (Marshall 1984), rainbow trout were were exposed to semi-static concentrations up to 100 mg/L nominal for 96 hours. DEFI Base, which is sodium cocoyl isethionate of 66% purity, was used. After 96 hours, no mortality was observed at any test concentration, except in one of the two chambers of the 100 mg/L nominal where two fish died (10% mortality for the concentration). Therefore, the LC_{50} is greater than the highest concentration tested of 100 mg/L nominal (>25 mg/L measured). In the second study (Zonk and Jung 1994), zebra fish were exposed to three static concentrations (10, 22, and 50 mg/L) and a control for 96 hours. Results indicate an LC_{50} of 33 mg/L.

Table 4. Summary of Aquatic Toxicity Studies

Test Material	Value	Source	Reliability
Fish			
DEFI Base 66%	96-h LC_{50} >25 mg/L[a]	Marshall 1984	2
Hostapon SCID 66%	96-h LC_{50} = 33 mg/L[b]	Zok and Jung 1994	2
SCI	ChV = 10.903 mg/L	ECOSAR	2
Invertebrate (*Daphnia magna*)			
SCI	48-h EC_{50} >32 mg/L	Jardine and Roberts 2005	2
DEFI Base 66%	48-h EC_{50} >73 mg/L	Turner 1984	2
Hostapon SCI 85-89%	48-h EC_{50} >30 mg/L	Bucking and Ivanovic 1994	2
Algae (*Chlorella vulgaris*)			
DEFI Base 66%	96-h EC_{50} (growth) = 9.6 mg/L 96-h EC_{50} (biomass) = 10.2 mg/L	Turner 1985	2
Microorganisms (Bacteria)			
SCI 68.7%	3-h EC_{50} >1000 mg/L	Reinhardt 1994	2

[a] *Oncorhynchus mykiss* (rainbow trout); formerly called *Salmo gairdneri*

[b] *Brachydanio rerio* (zebra fish)

Three well documented GLP studies are also available regarding the acute aquatic toxicity of sodium cocoyl isethionate to *Daphnia magna*. In the first study (Jardine and Roberts 2005), *Daphnia* were exposed to five concentrations ranging from 5.6 to 32 mg/L of SCI for 48 hours. Solutions were renewed after 24 hours. No immobilization or other effect was observed and all of the test organisms appeared healthy throughout the study. The 48 hour EC_{50} is greater than the highest nominal concentration tested, 32 mg/L. A small amount of precipitation was observed at 18 and 32 mg/L but did not appear to interfere with the *Daphnia*. In the second study (Turner 1984), *Daphnia* were exposed to seven static concentrations ranging from 1.0 to 100 mg/L DEFI Base (66% SCI) for 48 hours. Some mortality was observed but appeared to be random and not dose related. Results indicate that the 48 hour EC_{50} was greater than the highest nominal concentration tested (100 mg/L, corresponding to >73 mg/L measured concentration), measured as isethionate. In the third study (Bücking and Ivanovic 1994), *Daphnia* were exposed for 48 hours to nominal concentrations of Hostapon SCI ranging from 1 to 100 mg/L. The percent immobilized at 48 hours were 0, 0, 10, 25, 35, and 90% for the 1, 5, 10, 20, 50 and 100 mg/L concentrations, respectively.

The aquatic toxicity to the green unicellular algae, *Chlorella vulgaris*, was evaluated in a well documented GLP study (Turner 1985) using DEFI Base (66% SCI). Algae were exposed to five concentrations ranging from 4.2 to 32 mg/L nominal for 72 hours. During the test period, the DEFI Base precipitated out in all test concentrations causing an increase in absorbance which was taken into account by subtracting the absorbance of the test substance blanks from the absorbance of test flasks containing *C. vulgaris*. The resultant 72 hour EC_{50} values were 9.6 and 10.2 mg/L for the growth and biomass endpoints, respectively.

Toxicity to aquatic anaerobic bacteria was evaluated in a study conducted on SCI of 68.7% purity. The inoculum was activated sludge from a wastewater treatment plant in Frankfurt, Germany. Results show that SCI does not inhibit microorganism activity at the highest concentration tested (1000 mg/L).

Estimates of chronic aquatic toxicity data were made using the EPA's ECOSAR software using an estimated log K_{ow} value of 2.38. The calculated fish ChV (chronic value) was 10.903 mg/L.

In summary, high quality data are available for the aquatic toxicity endpoints and demonstrate that sodium cocoyl isethionate is slightly toxic to aquatic organisms (fish, aquatic invertebrates and algae). Based on the available information, 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 Tables 5 and 6.

Acute Toxicity

Three well documented studies are available to evaluate the acute oral toxicity of sodium cocoyl isethionate to mammals. In the first study, male and female Sprague-Dawley albino rats were given a single limit dose of 5000 mg/kg bw in distilled water by gavage. The test material consisted of 47.5% SCI in a syndet bar and was a white, waxy solid administered as a uniform suspension at a concentration of 0.25 g/mL. Animals were observed at 1, 2.5 and 4 hours and then daily for 14 days post-administration for signs of stress or toxicity. No mortality was observed during the study. One male animal exhibited diarrhea and another exhibited red-stained face and possible respiratory congestion at 1, 2.5 and 4 hours, but these symptoms disappeared by day 1 and were not observed for the remainder of the study. Similarly, all female rats experienced one or more symptoms including red-stained face, diarrhea or hypoactivity, but again these symptoms largely disappeared by day 1 and completely disappeared by day 2. All male and female animals appeared normal for the remainder of the study. These sub-lethal symptoms are common and rats adapted quickly and showed no signs of long-term adverse effects. In the second study, a 15% solution of SCI in a gel cleanser was administered to male and female Sprague-Dawley albino rats in a single oral dose of 5000 mg/kg bw. The dose was administered directly as a white cream by oral intubation without the use of a vehicle and the animals observed for 14 days. No mortality was observed in either sex over the duration of the 14 day observation period. All animals exhibited normal weight gains. One female rat exhibited signs of diarrhea on day 3, but appeared normal both before and after that date. All other animals exhibited no clinical signs during the study. Finally, in a third study, male only rats were exposed to five dose levels (3.3, 4.1, 5.1, 6.4 and 8.0 g/kg) of a 20% solution of DEFI (SCI). The test material was administered on day 1 and the animals observed for mortality and other overt signs of stress on days 1, 2, 3, 4, 7 and 14. Mortality occurred in two of 5 animals in the 8.0 g/kg dose and 1 of 5 animals in the 6.4 g/kg dose. No mortality was observed in the other doses. Slight diarrhea was observed in two animals in the 4.1 g/kg dose within 1-2 hours of dosing. Moderate diarrhea was observed in 2, 4 and 5 animals after 1 hour in the 5.1, 6.4 and 8.0

g/kg doses, respectively. Gross pathology at necropsy revealed no significant findings, however, moderate inflammation of the gastric mucosa was observed in the animals that died on days 1 and 2 in the 8.0 g/kg dose. Results of these three studies indicates that SCI is not significantly toxic to rats at doses exceeding 5000 mg/kg bw.

Table 5. Summary of Mammalian Acute and Irritation Toxicity Studies

Test Material	Value	Source	Reliability
Acute Oral (rat)			
SCI 47.5% in a Syndet Bar	LD_{50} >5000 mg/kg	Glaza 1986a	2
SCI 15% in a Gel Cleanser	LD_{50} >5000 mg/kg	Blaszcak 1985a	2
DEFI 20%	LD50 = 8400 mg/kg	Stern 1982	2
Skin Irritation (rabbit)			
Jordapon CI 5%	Moderately irritating (PDII 2.24)	Wo and Shapiro 1984a	2
SCI	Moderately irritating (PDII 4.5)	Lodestedt 1986	2
DEFI 93.7%	Moderately irritating (PDII 2.4)	van Baaren 1982	2
SCI 47.5% in a Syndet Bar	Mildly irritating (PDII 0.4-0.5)	Baszcak 1987	1
SCI 5% solution	Mildly irritating (PDII 1.38)	Nitka and Palanker 1984	2
Eye Irritation (rabbit)			
DEFI	Irritating	van Baaren 1983	2
SCI 15% in a Gel Cleanser	Moderately irritating	Blaszcak 1985b	2
SCI 15% in a Gel Cleanser (Low Volume Exposure)	Mildly irritating	Blaszcak 1985c	2
SCI 2% solution	Mildly irritating	Nitka and Palanker 1982	2
SCI 47.5% solution	Moderately irritating	Glaza 1986b	2
Jordapon CI 5%	Mildly irritating (unwashed) Minimally irritating (washed)	Wo and Shapiro 1984b	2
Sensitization (guinea pig)			
SCI 47.5% in a Syndet Bar	Not sensitizing	Buehler 1986	1
SCI 15% in a Gel Cleanser	Not sensitizing	Hiles and Liao 1985	2
Hostapon SCID	Not sensitizing	Bury 1994	1
Fenopon AC78	Not sensitizing	SSM83.078	1
Hostapon KA	Not sensitizing	SSM78.397	1

No specific data are available on acute inhalation toxicity. Inhalation is not expected to be a significant route of exposure for consumers using preparations containing SCI as products either

in solid bars or in liquid products that are used with water or rinsed off. Typical consumer use of such products (e.g., lathering in shower) has been found to give rise to inhalable airborne concentrations of product up to 20 $\mu g/m^3$ (Unilever personal communication). Assuming arbitrary formulation values of 50% SCI and 2% SI (and using 20 $\mu g/m^3$ as a worst-case exposure), this relates to a daily inhaled dose of 0.6 µg SCI and 0.024 µg SI. If using the assumption that 100% becomes systemically available (which is highly unlikely considering the partition coefficient of either material), this in turn relates to a systemic dose for SCI and SI of 10.4 and 0.4 ng/kg bw/day respectively, each several orders of magnitude lower than the systemic NOEL derived from the feeding studies. The lack of repeated dose inhalation toxicology data does present a knowledge gap in terms of lung-specific toxicity, however, considering the system dose concentrations induced by feeding studies that represent the NOEL, it is unlikely that any toxicology would be observed at consumer exposure levels.

Inhalation is also not a significant route of occupational exposure because of the manufacturing process design and associated engineering controls for SCI. Factory dust levels are controlled due to a potential explosivity hazard as well as for a standard occupational hygiene purposes (Unilever personal communication). Therefore, no acute inhalation study is proposed, based on lack of potential exposure and no structural alerts for this compound.

While no specific acute dermal toxicity studies were located, data are available on dermal exposure in a series of high quality and GLP skin irritation studies in rabbits (Table 5) and from two repeated dose dermal toxicity studies in rats (Section 5.4 and Table 6). From the dermal 14 and 28 day studies it is apparent that no systemic toxicity occurred when dosing up to 36% SCI, equivalent to 2.07 g/kg bw/day for 28 days (>2000 mg/kg). The weight of evidence of these rat data and that from rabbit skin irritation studies in Table 5 (at doses of 5%), plus supporting human experience, is sufficient so that no acute dermal study is proposed. It should also be noted that skin penetration appears to be low to medium, thus further reducing the likelihood of acute toxicity via the dermal route (Howes 1975, Howes and Cordell 1974).

Skin and Eye Irritation

In the first of the skin irritation studies, the skin on the back of six healthy white rabbits was exposed to a single dose (0.5 mL) of 5% SCI for 24 hours. The test sites (both intact and abraded) were covered with a test patch held in place with a semi-occlusive dressing. After 24 hours the patches were removed and the areas wiped with a cloth to prevent further exposure. The resultant primary irritation (PDII) score was 2.24 (moderately irritating). In the second study, 0.5 g of SCI was applied to intact and abraded skin on the backs of 6 rabbits. Results show SCI to be moderately irritating to the skin (PDII = 4.5), with no significant difference between intact and abraded skin. Three similarly conducted skin irritation studies using DEFI (93.7%), SCI (47.5% in a syndet bar), and SCI (5% solution) resulted in moderate, mild, and mild irritation and PDII scores of 2.4, 0.4-0.5, and 1.38 for the three studies, respectively. The sum total of these five studies demonstrate that SCI is mildly to moderately irritating to the skin.

Six separate studies are reported that evaluate the potential for eye irritation in rabbits exposed to various solutions of SCI (Table 5). In the first study, a single application of 55 mg of SCI (DEFI) was placed in the conjunctival sac of three rabbits. Corneal opacity and transient iritis

was observed in one animal during the first 72 hours after treatment, and was still present at day 7 but healed completely by day 14. The other two animals exhibited only slight iridal and conjunctival irritation, which completely healed by day 7. Based on the effects seen in the one animal, the test substance was classified as an irritant. In a second study, 0.1 mL of a 15% solution of SCI in a gel cleanser was placed in the conjunctival sac of six rabbits. Most animals experienced moderate conjunctival irritation and other effects and SCI was classified as moderately irritating. Another study conducted by the same authors and using the same test material but as a "low volume procedure" (10 µL instead of 0.1 mL) resulted in a "mildly irritating" classification. In other studies, a 47.5% solution of SCI was considered to be moderately irritating, a 2.5% solution of SCI was mildly irritating, and a 5% solution of SCI was considered to be mildly (unwashed) or minimally (washed) irritating.

Skin Sensitization

Five separate dermal sensitization studies using guinea pigs have been conducted (Table 5). All five were conducted according to GLP procedures. In the first study, four guinea pigs were exposed to 2.0, 1.5, 1.0 and 0.5% w/v solutions of SCI (47.5% in a syndet bar) during the primary irritation phase. The solutions were placed on the backs of each animal, from which the hair had been clipped, and covered with 25 mm Hill Top chambers and occluded. After 24 hours the clipped areas were depilated and the sites scored for severity of response at 24 and 48 hours. The induction phase of this study was conducted with a 2.0% solution of the test material, which was placed on the test sites for six hours, after which the patches were removed. This was repeated weekly for a total of three applications and scored each time. In the final, primary challenge, phase of this first study, a 2.0% solution of the test material was placed on a fresh application site of each animal for six hours, after which the patches were removed. After another 24 hours the sites were depilated and scored. Results indicate that SCI does not induce skin sensitization.

In the second and third studies, 10 Guinea pigs were used in a Guinea Pig Maximization Test (GPMT) for skin sensitization, performed as per the Magnusson and Kligman method. Study SSM83.078 was carried out in accordance with test guidelines, with 10 test and 7 control Guinea pigs used. The intradermal induction injections were at a concentration of 0.2%. Topical induction was at 2.5% and subsequent topical challenge was at 1.0%. There were some reactions at each challenge to the test material but these were invariably of only faint or very faint erythema. The increased intensity of reaction at the 48 hour reading versus the 24 hour reading that typifies a genuine allergic response was absent in all cases. There was no clear reproducibility in the appearance of reactions in individual animals between challenges. Based on the above, this study does not provide convincing evidence that any of the animals have been sensitized in the GPMT study. All seven controls responded appropriately.

Study SSM78.397 was also carried out in accordance with test guidelines, with 10 test and 8 control animals used. The intradermal induction injections were at a concentration of 0.15%. Topical induction was at 20% and subsequent topical challenge was at 5.0%. There were a number of faint/very faint erythema reactions observed following each challenge. There is some evidence of reactions in one or two of the animals. However, the level of background irritation in control and treated animals causes this study to be classified as inconclusive.

Two additional studies conducted with SCI (15% in a gel cleanser) and SCID (66%) showed that SCI is not a skin sensitizer. Taking all five studies into consideration, the weight of evidence on SCI indicates that it is not a skin sensitizer.

Repeated Dose Toxicity – Dermal Exposure

Several generally well-documented GLP repeated dose studies are available for SCI (Table 6). In the first dermal study, male and female rats were given dermal doses of 10, 20, 40 and 60% SCI (72.4% purity) for 10 days as part of a study to define dose levels for a 28 day dermal application study. Aqueous concentrations were administered daily at a constant volume of 10 mL/kg to the shaved dorsal surface of the test animals. The sites were covered with gauze held in place with an adhesive bandage for six hours, after which the gauze was removed and the sites rinsed clean of any excess test material. The animals were observed twice daily for any signs of toxicity or irritation. On day 4 after application, mild dermal irritation was observed in one animal in the 60% dose. This irritation increased in severity through day 7 before reaching a plateau. Mild irritation was observed on day 6 in the 20% and 40% doses, but these quickly disappeared. No adverse findings were seen in the gross necropsy conducted at study completion. Due to the transient mild irritation seen in the 20% dose and above, the NOAEL was reported as 20%. As a follow up to the 10 day study, the full 28 day dermal study (based on OECD Guideline 410) was conducted in a similar manner at doses of 1, 14, and 36%, which correspond to 0.08, 0.91 and 2.07 g/kg bw d. Body weight and food consumption were recorded weekly. On each day of treatment, signs of local irritation were recorded using the Draize method. Bleeds for haematology and blood chemistry were performed after 28 days of treatment and the animals were subjected to a full necropsy with subsequent histological examination. In this study, there were no clear adverse effects and gross observation of the test animals did not reveal any signs of systemic toxicity attributable to the test material. One male in the mid dose group (14%) SCI died on day 19 of treatment; this death was attributed to mechanical trauma caused by struggling during the wrapping procedure. There were no other deaths. No significant irritancy was observed in the male animals. Slight local irritancy (grade 1 erythema) was observed in the high dose males during the 3rd and 4th weeks of the study. Local irritancy (slight erythema) was observed for females in all treated dose groups during the first week of the study only, after which incidence and severity decreased for the remainder of the study. Inconsistent effects were seen in some of the other parameters measured, but these either did not appear to be related to dose response or were within historical control ranges for this strain of rat. Food consumption and body weight were unaffected by treatment. There were no toxicologically significant changes in haematology parameters. Fasting glucose levels were slightly lower in the high dose compared with the control. Clinical chemistry parameters were otherwise unaffected. There were no toxicologically significant changes noted in organ weights, macropathology or histopathology. The NOAEL was 2.07 g/kg bw/day. The results of this 28 day dermal study are considered important in indicating a lack of potential human systemic toxicity via this route as consumer exposure to SCI-containing products is primarily by the dermal route.

Table 6. **Summary of Mammalian Repeated Dose Toxicity and Genotoxicity Studies**

Test Material	Value	Source	Reliability
Repeated Dose Toxicity (Dermal and Oral Feeding Studies)			
SCI	14d Dermal NOAEL: 20% 14d Dermal LOAEL: 40%	Mitchell 1991	2
SCI 72.4%	28d Dermal NOAEL: 36% (2.07 g/kg bw/d 28d Dermal LOAEL: >36% (>2.07 g/kg bw/d)	Grieco 1991	1
Jordapon CI	14d Oral NOAEL: 1.0% 14d Oral LOAEL: >1.0%	Lea 1994	1
Jordapon CI	28d Oral NOAEL: 1.0% (1000 mg/kg bw/day) 28d Oral LOAEL: >1.0%	Lea 1995	1
Genotoxicity – Ames Test and *In Vitro* Cytogenetics Study			
Hostapon SCID (66%)	Negative (with and without S-9) (*Salmonella typhimurium*)	Muller 1994	1
SCI 72.45%	Negative (with and without S-9) (*Salmonella typhimurium*)	Hillgardner and Fung 1991a	1
SCI 72.45%	Negative (with and without S-9) (IVC in Chinese Hamster Ovary cells)	Hillgardner and Fung 1991b	1

Repeated Dose Toxicity – Oral (Feeding) Exposure

Two additional repeated dose studies are reported in which rats were exposed to SCI in the diet (Table 6). In the first study, groups of four male and four female Sprague-Dawley rats were given 1, 3 or 5% w/w Jordapon SCI in the diet for 14 days as a preliminary test to define doses. These dietary inclusion levels resulted in approximate exposures of 1000, 3000, or 5000 mg/kg bw/day. No mortality was observed during the study and no treatment-related clinical signs were evident. Slight reductions in food intake in the 5% dose group and reduced body weight gains in the 3% and 5% groups were observed, but these appeared to be as a result of palatability issues rather than actual toxicity. Following up this preliminary test, the full 28 day oral feeding study was conducted at doses of 0.1, 0.3 and 1.0% Jordapon SCI in the diet (approximately 100, 300 and 1000 mg/kg bw/day). This study was performed according to the pre-1995 OECD 407 guideline, but differences between this study and the subsequent current guideline updated in 1995 are not expected to have significantly compromised the predictive ability of this study. Diets were prepared weekly and given *ad libitum* for 28 days to groups of 10 male and 10 female animals per dose. Results show that treated male animals exhibited increased body weight gain during the first week of the study. Body weight gains of the treated females decreased during the second week of the study only. No further changes were observed. Plasma creatinine was decreased slightly in male rats fed 0.3% and 1.0%. Relative kidney weight was increased slightly in female rats fed 1.0%. No macroscopic or histological effects were observed. The results indicate that that daily dietary administration of SCI had no significant toxicological

effect related to treatment. The top dose in this feeding study was equivalent to approximately 1000 mg/kg/day, which is identified as the NOAEL.

Specific studies addressing the reproductive and developmental toxicity endpoints were not available, however, from the 28 day repeated dose feeding study above (Lea 1995), data are available to give some reassurance of the lack of effects on fertility at up to 1000 mg/kg bw/day. In this study, the sex organs from both sexes were weighed, retained and examined histologically. There were no significant changes in the weight or macroscopic or microscopic appearance of these sex organs from either sex. Furthermore, the testes were fixed initially in Bouin's solution, which results in higher quality sections of this tissue then if formalin was used.

Genotoxicity

Well documented GLP data are available to evaluate genotoxicity. In a bacterial reverse mutation assay (Ames test), four strains of *Salmonella typhimurium* were exposed to Hostapon SCID (66% SCI) concentrations ranging from 4 to 5000 µg/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. The test material was toxic to most of the bacterial strains at 500 or 2500 µg/plate and above. In a second Ames study conducted with five strains of *Salmonella typhimurium* using another SCI (72.45% purity) at concentrations ranging from 1 to 1000 µg/plate, significant effects also were not observed, confirming a lack of potential point mutations. This test material was also tested in an *in vitro* cytogenetics assay using Chinese hamster ovary (CHO) cells to test for chromosome damage. Doses of 19, 38, 75, 150 and 300 µg/mL were tested both in the presence and absence of S-9 activation. Results were negative. These three studies confirm that SCI is not mutagenic or clastogenic, causing neither gene mutations nor chromosomal abberations under the conditions of these studies. In addition, a SAR/QSAR review for SCI produced no alerts for either genotoxicity or carcinogenicity (Unilever personal communication).

Summary of Mammalian Toxicity

In summary, well documented studies are available for most of the mammalian toxicity endpoints. These data demonstrate that SCI is not acutely toxic, is mildly to moderately irritating to the skin and eyes, does not produce significant systemic toxicity in repeated dose studies via the dermal or oral routes, and is not mutagenic. Separate studies are not available for the reproductive and developmental toxicity endpoints but information from repeated dose toxicity studies gives some reassurance of lack of potential effects on fertility. Given that SCI does not appear to cause any significant toxicity in the available studies, it is unclear that conducting additional long-term exposure studies would provide any significant new information. Therefore, in the interest of responsible animal welfare management the SESC believes that further animal testing is not warranted at this time.

Human Exposure

In addition to the ecological and mammalian toxicity testing described above, many studies have been conducted in which SCI and SCI-containing products were applied to the skin of volunteers

to determine whether any skin irritation or sensitization would occur. These studies are in addition to a well established long history of safe use in consumer products and a lack of occupational toxicity due to SCI manufacture and formulation.

Six studies are reported that utilized the modified soap chamber test procedure. In these studies, occlusive patches consisting of aluminum chambers (Webril discs) are charged with the test material and affixed to several locations on the arms of healthy volunteer panelists. Chambers are generally applied for 24 hours, removed, the area scored, and new chambers applied daily for up to 5 days. At each scoring event, trained observers rate the presence and severity of erythema, edema and/or vesicles. A solution of 8% SCI was used in all six of the studies, the results of which are shown in Table 7. Results indicate that SCI is in most cases minimally irritating to the skin of volunteers.

Table 7. Summary of Modified Soap Chamber Tests

Number of Panelists	Duration of Exposure	Mean Total Score	Min/Max	Comments	Source
15	5	1.9733	0.0/4.4	Erythema only	CTFA 1985
14	5	0.529-1.014	0.0/4.0	Erythema; Range of 4 tests	CTFA 1986a
15	5	1.6267	0.2/3.6	Total of erythema, edema, vesicles	CTFA 1986b
19	5	2.269	-	TEWL 9.6 and 8.9 $g/m^2/hr$[a]	CTFA 1988a
21	2	2.5	-	Terminated early	CTFA 1988b
17	2	1.529	-	Total of erythema, edema, vesicles	CTFA 1990

[a] Transepidermal water loss (TEWL) on days 2 and 5, respectively

A series of patch application tests were also conducted with healthy volunteers. One study was conducted with a 4% aqueous solution in a gel cleanser containing 15% SCI for 48 hours. An occlusive patch (Webril pad) containing the test material was applied to the skin on the backs of 12 panelists, with the degree of dermal response graded at 6, 24, and 48 hours. No visible erythema or other effects was observed and the test material was classified as not irritating. Two additional studies used repeat applications of treated patches that were replaced daily for either 21 or 3 days. The first study exposed the skin of 35 panelists to a 0.10% aqueous solution of SCI for 21 days. Results are shown in Table 8 and demonstrate only very mild irritation. The second study included 10 panelists exposed to 0.2%, 0.4% or 1.0% SCI as aqueous solutions for 3 applications of 24 hours each. Again, the panelists exhibited only very mild skin irritation.

Table 8. Summary of Human Exposure Patch Testing

Study Type	Test Solution	Number of Panelists	Duration of Exposure	Result	Source
Single patch	4% aqueous in gel cleanser	12	48 hours	No erythema	CTFA 1989
Repeat patch	0.10% aqueous	35	21 days	Very mild	Hill Top Research 1985
Repeat patch	0.2%, 0.4%, 1.0% aqueous	10	3 days	Very mild	CTFA 1984
HRIPT[a]	49.85% in personal washing bars	191-199 (4 studies)	-	Not sensitizing	CTFA 1990
HRIPT	17% in skin cleanser	106	9 x 24 hours	Not sensitizing	Essex Testing 1989
HRIPT	2% aqueous	203	9 x 48 hours	Not sensitizing	Hill Top Research 1987
HRIPT	-	148	9 x 48 hours	Not sensitizing	CTFA 1985

[a] HRIPT = Human Repeat Insult Patch Test

Table 8 also shows the results of a series of human repeat insult patch tests (HRIPT). In these studies the skin of human volunteers are exposed to the test substance under a patch for 24 or 48 hours (the induction period) and scored for incidence and severity of erythema and other effects. After scoring a new patch treated with the test substance is applied and the process continued for a total of 9 applications. After the ninth application there is a rest period for up to 14 days without treatment. Following the rest period a challenge patch is applied to a previously unpatched site for 48 hours and then graded as before. Scores are generally based on the incidence and severity of erythema, induration, vesicles, and bullae. The results of all of the HRIPT studies indicate that the SCI materials tested are not sensitizing to the skin.

In summary, many studies have been conducted in which SCI and SCI-containing products were applied to the skin of human volunteers. Results demonstrate that SCI is generally only minimally irritating to the skin and is not a skin sensitizer.

Evaluation of Data Completeness

Substantial data are available to cover most of the recommended SIDS endpoints for SCI, as well as for non-SIDS endpoints such as irritancy and skin sensitization. Physical-chemical property and some environmental fate data are available primarily as estimates using the USEPA's EPI Suite software (v.3.12). In addition, measured biodegradation data are available, as are high quality data for the aquatic toxicity endpoints. Well documented studies are also available for most of the mammalian toxicity endpoints, including repeated dose toxicity and genotoxicity studies. No reproductive or developmental toxicity data are available, but data from repeated dose studies show that SCI has very low mammalian toxic potential. Furthermore, these tests show that at very high doses (1000 mg/kg bw/day) SCI does not affect the histology of the sex or accessory organs, giving some reassurance that SCI is unlikely to exert any adverse effects on

fertility. There is also a considerable history of safe use in consumer products containing SCI. These factors combine to indicate that there is a low priority for reproductive or developmental toxicity testing of SCI.

SUMMARY OF SODIUM COCOYL ISETHIONATE PROPERTIES

The sponsored chemical is an anionic surfactant commonly used in syndet bars and other skin cleansers. SCI has a low vapor pressure and would not be expected to volatilize significantly. SCI is somewhat soluble in water (0.01%). SCI is readily biodegradable and has a very low affinity for bioaccumulation. It is only slightly toxic to aquatic organisms. Well documented studies are available for most of the mammalian toxicity endpoints. These data demonstrate that SCI is not acutely toxic, is mildly to moderately irritating to the skin and eyes, does not produce significant systemic toxicity in repeated dose studies, and is not mutagenic. Substantial human exposure data collected over the years show that SCI exposure may result in minimal to mild dermal irritation and is not sensitizing to the skin.

Table 9 shows the availability of data and assessment plan status for sodium cocoyl isethionate (SCI).

CONCLUSIONS

Given that SCI does not appear to cause any significant toxicity in the available studies, it is unlikely that conducting additional toxicity studies would provide any significant new information. SESC has considered the low toxicological concern of SCI, the limited informational value of new studies, and in balance with animal welfare concerns, believes that further animal testing is not warranted at this time.

Table 9. Data Availability and Status for Sodium Cocoyl 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
pH Value, pK_a Value	N	-	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	N	-	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	Y	Y	N
Repeated Dose Toxicity	Y	Y	N
Genetic Toxicity in vitro (Bacterial test)	Y	Y	N
Genetic Toxicity in vitro (Non-bacterial test)	Y	Y	N
Genetic Toxicity in vivo	N	-	N
Carcinogenicity	N	-	N
Toxicity to Reproduction	N	-	N
Developmental Toxicity	N	-	N

* Estimated using EPI Suite v.3.12
** Estimated using ECOSAR v.0.99g

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