SCREENING-LEVEL HAZARD CHARACTERIZATION

SPONSORED CHEMICAL Sodium 2-(2-Dodecyloxyethoxy)ethyl sulfate CASRN 3088-31-1

SUPPORTING CHEMICAL

Sodium lauryl ether sulfate Alcohol ethoxysulfates CASRN 9004-82-4 No CASRN

Chemical Abstract Service	Spansored Chamical			
Registry Number	3088-31-1			
(CASRN)				
	Supporting Chemical			
	9004-82-4			
	No CASRN			
Chemical Abstract Index	Sponsored Chemical			
Name	Ethanol, 2-[2-(dodecyloxy)ethoxy]-, 1-(hydrogen sulfate),			
	sodium salt (1:1)			
	Supporting Chemical			
	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(dodecyloxy)-,			
	sodium salt (1:1)			
	Alcohol ethoxysulfates			
Structural Formula	Sponsored Chemical			
StructurarFormula	<u>Sponsoreu Chennear</u>			
	\land \land \land \land \land \land \land \land \land $S-0^{-}Na^{+}$			
	$H_3C^2 \rightarrow a a a a a a a a a a a a a a a a a a $			
	SMILES: S(=O)(=O)([O-])OCCOCCOCCCCCCCCCC.[Na+]			
<u>S</u>				

Summary

Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is a solid at room temperature with negligible vapor pressure that is dispersible in water. Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is expected to possess moderate mobility in soil. Volatilization is considered low since this substance is an ionic compound which will not volatilize. The rate of hydrolysis is expected to be negligible. The rate of atmospheric photooxidation is moderate; however, this is not a relevant environmental degradation pathway since this substance is not expected to exist in the vapor phase in the atmosphere. Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is expected to have low persistence (P1) and low bioaccumulation potential (B1).

The acute oral toxicity of sodium 2-(2-dodecyloxyethoxy) ethyl sulphate in rats is low. In 90-day oral (dietary and gavage) repeated-dose toxicity studies with the supporting chemicals, rats exposed to NaC12–15E3S or Synthetic NaC12 – 15E3S and NaC12AE3S (natural) via the diet

showed liver and kidney effects at 250 mg/kg-bw/day; the NOAEL is 50 mg/kg-bw/day. Lesions in the forestomach were observed in the stratified epithelium in rats exposed to NaC12–14AE2S via gavage at 225 mg/kg-bw/day; the NOAEL for systemic toxicity is 75mg/kg-day. In a two-generation drinking water reproductive toxicity study, the supporting chemical NaC12 – 14AE2S reduced straight-line sperm velocity in parental male rats and delayed sexual development in rat female offspring at 300 mg/kg-bw/day; the NOAEL for maternal toxicity in this study is 300 mg/kg-bw/day (highest dose tested). The NOAEL for maternal toxicity in this study is 300 mg/kg-bw/day (highest dose tested). The supporting chemicals NaC12 – 15E3S and NaC12 – 14AE2S were not mutagenic in bacteria and mammalian cells *in vitro*, respectively. The supporting chemical NaC12 – 15E3S did not induce chromosomal aberrations *in vitro*; and C12 – 15AES did not induce chromosomal aberrations *in vivo*. The supporting chemical C12AE3S did not increase the incidence of tumors in rats. Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate is irritating to rabbit skin and eyes. The supporting chemical, NaC12 – 15E3S, is a skin sensitizer in guinea pigs but NaC12 – 14AE2S is not.

For sodium 2-(2-dodecyloxyethoxy) ethyl sulphate, the 96-h LC₅₀ to fish is 25 mg/L. For the supporting chemical, sodium laurel ether sulfate, the 48-h EC₅₀ to aquatic invertebrates is 3.12 mg/L. No adequate data are available for the toxicity endpoint to aquatic plants.

A data gap for the aquatic plants toxicity endpoint was identified under the HPV Challenge Program.

The sponsor, Stepan Company, submitted a test plan and robust summaries to EPA for 2-(2-dodecyloxyethoxy) ethyl sulfate {CASRN 3088-31-1; CA Index Name: ethanol, 2-[2-(dodecyloxy)ethoxy]-, 1-hydrogen sulfate), sodium salt (1:1)} on July 18, 2006. EPA posted the submission on the ChemRTK HPV Challenge website on October 20, 2006 (http://www.epa.gov/chemrtk/pubs/summaries/sodium22/c16316tc.htm). The sponsor submitted updated/revised documents on September 21, 2006, which were posted to the ChemRTK website on March 8, 2007. EPA comments on the original and revised submissions were posted to the website. The sponsor submitted updated/revised documents on November 19, 2009, which were posted to the ChemRTK website on April 12, 2010.

Justification for Supporting Chemicals

The submitter proposed the use of sodium lauryl ether sulfate (CASRN 9004-82-4) and other alcohol ethoxysulfates (AESs) as supporting chemicals on the basis of structural similarity. The AES category comprises commercial grades of linear-type primary AESs, with the basic structure, $C_nH_{2n+1}O(C_2H_4O)_mSO_3X$, where n = 10 - 18, m = 0 - 8 and X = sodium, ammonium, triethanolammonium or magnesium ion. Toxicity studies summarized in this document use standard abbreviations for AESs, where the alkyl chain (C) and average number of ethoxy units (AE) are described after their respective descriptors.

EPA accepts the use of AESs as supporting chemicals for the aquatic toxicity endpoints. For human health endpoints, EPA accepts the use of AESs with sodium as counter-ions as appropriate to characterize the toxicity of 2-(2-dodecyloxyethoxy) ethyl sulfate. The limited data available for 2-(2-dodecyloxyethoxy) ethyl sulfate suggest that AESs with sodium as counter-ions will provide a conservative estimate of toxicity. AESs with counter-ions other than sodium are not accepted as supporting chemicals for human health endpoints because they may have intrinsic chemical properties that add a level of complexity not representative of 2-(2-dodecyloxyethoxy) ethyl sulfate. EPA also does not accept the use of mixtures comprised of more than one CAS-numbered substance. Therefore, human health data submitted from studies on chemicals with counter-ions other than sodium or mixtures comprised of more than one CAS-numbered substance.

1. <u>Chemical Identity</u>

1.1 Identification and Purity

Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is a solid at room temperature with negligible vapor pressure that is dispersible in water.

1.2 <u>Physical-Chemical Properties</u>

The physical-chemical properties of sodium 2-(2-dodecyloxyethoxy)ethyl sulfate are summarized in Table 1.

Table 1. Physical-Chemical Properties of Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate1			
CASRN	3088-31-1		
Molecular Weight	376.49		
Physical State	Solid or semi-viscous liquid		
Melting Point	No adequate data (measured) ²		
Boiling Point	>300°C at 760 mm Hg (estimated) ³		
Vapor Pressure	$<1.0\times10^{-10}$ mm Hg at 25°C (estimated) ³		
Dissociation Constant (pKa)	Not applicable		
Henry's Law Constant	$<1.0\times10^{-10}$ atm-m ³ /mole at 25°C (estimated) ³		
Water Solubility	Dispersible ^{4,5}		
Log K _{ow}	Not applicable ^{4,6}		

¹Stepan Company. 2009. Test Revised Plan and Robust Summary for 2-(2-Dodecyloxyethoxy)ethyl sulfate. Available online at <u>http://www.epa.gov/chemrtk/pubs/summaries/sodium22/c16316tc.htm</u> as of May18, 2012.

²A melting point/freezing point range of 7.5 - 10.4 C was reported for a substance STEOL® CS-270 containing 70% CASRN 3088-31-1; however, the pure substance is described as a solid so this melting point is probably not accurate for the pure substance.

³U.S. EPA. 2012. Estimation Programs Interface SuiteTM for Microsoft® Windows, v4.10. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at

http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm as of May 18, 2012

⁴Tolls J; Sijm, D. 2000. Estimating properties of surface active chemical. In: Handbook of Property Estimation for Chemicals. Boethling RS; Mackay D. (eds.). Lewis Publishers, Boca Raton, FL. pp 419–446.

⁵A water solubility of 9.8×10^3 mg/L at 25°C was estimated for CASRN 3088-31-1; however, this substance is a surfactant that will form micelles in solution and the term dispersible is more appropriate than reporting a water solubility. Reaxys reports a *critical micelle concentration* of 979 mg/L for this substance (**Minero, Claudio; Pramauro, Edmondo; Pelizzetti, Ezio; Degiorgio, Vittorio; Corti, Mario** Journal of Physical Chemistry, **1986**, vol. 90, # 8 p. 1620 – 1625).

⁶An estimated log K_{ow} value of 1.1 was calculated for CASRN 3088-31-1; however, this substance is a surfactant and the determination of the log Kow could yield erroneous results due to the emulsifying actions of the surfactants in octanol-water systems.

2. <u>General Information on Exposure</u>

2.1 <u>Production Volume and Use Pattern</u>

Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate was not reported in the 2006 IUR.

2.2 Environmental Exposure and Fate

Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is expected to possess moderate mobility in soil. It degraded 65% using a seawater inoculum and the biodegradability in seawater test (OECD TG 306) over the course of a 28-day incubation period. Structural analog, poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-(dodecyloxy)-, sodium salt (1:1) degraded 81% after 28 days as measured by CO_2 evolution and the modified Sturm test (OECD TG 301B). Based on these data, this substance was determined to be readily biodegradable. The rate of hydrolysis is negligible. Volatilization is considered low since this substance is an ionic compound. The rate of

atmospheric photooxidation is moderate; however, this is not a relevant environmental degradation pathway since this substance is not expected to exist in the vapor phase in the atmosphere. Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is expected to possess low persistence (P1) and low bioaccumulation potential (B1).

The environmental fate of sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is summarized in Table 2.

Table 2. Environmental Fate Properties of Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate				
CASRN	3088-31-1			
Photodegradation Half-life	2.8 hours (estimated) ²			
Hydrolysis Half-life	Stable; 10% decomposition at 100°C after 30 days (measured)			
Biodegradation	65% after 28 days (seawater biodegradation test) ; 81% after 26 days (readily biodegradable) ^{1,3}			
Bioaccumulation Factor	$BAF = 5.0 \text{ (estimated)}^2$			
Log K _{oc}	Not applicable			
Fugacity (Level III Model) ²				
Air (%)	0.2			
Water (%)	15.9			
Soil (%)	82.0			
Sediment (%)	1.9			
Persistence ⁴	P1 (low)			
Bioaccumulation ⁴	B1 (low)			

¹Stepan Company. 2009. Test Revised Plan and Robust Summary for 2-(2-Dodecyloxyethoxy)ethyl Sulfate. Available online at http://www.epa.gov/chemrtk/pubs/summaries/sodium22/c16316tc.htm as of May18, 2012.

² U.S. EPA. 2012. Estimation Programs Interface Suite[™] for Microsoft® Windows, v4.10. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at

http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm as of May 18, 2012

³Data for structural analog poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-(dodecyloxy)-, sodium salt (1:1) (CASRN 9004-82-4).

⁴Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. Federal Register 64, Number 213 (November 4, 1999) pp. 60194–60204.

Conclusion: Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is a solid at room temperature with negligible vapor pressure that is dispersible in water. Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is expected to possess moderate mobility in soil. Volatilization is considered low since this substance is an ionic compound which will not volatilize. The rate of hydrolysis is expected to be negligible. The rate of atmospheric photooxidation is moderate; however, this is not a relevant environmental degradation pathway since this substance is not expected to exist in the vapor phase in the atmosphere. Sodium 2-(2-dodecyloxyethoxy)ethyl sulfate is expected to have low persistence (P1) and low bioaccumulation potential (B1).

3. <u>Human Health Hazard</u>

A summary of health effects data for SIDS endpoints is provided in Table 3. The table also indicates where data for the supporting chemical is read-across (RA) to the sponsored chemical.

Acute Oral Toxicity

Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate (CASRN 3088-31-1)

Sprague-Dawley rats (5/sex) were administered 2-(2-dodecyloxyethoxy)ethyl sodium sulfate via gavage at 5000 mg/kg and observed for 14 days. No mortalities were observed. $LD_{50} > 5000 \text{ mg/kg}$

Repeated-Dose Toxicity

Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate (CASRN 3088-31-1) No Data

Synthetic NaC12 – 15AE3S and NaC12AE3S (natural) (no CASRN provided, supporting chemicals)

Rats (unspecified strain, sex and number/dose) were administered synthetic NaC12 – 15AE3S or natural NaC12AE3S at concentrations of 0, 40, 200, 1000 or 5000 ppm in feed (approximately 0, 2, 10, 50 or 250 mg/kg-bw/day) for 90 days. There were no treatment-related effects on clinical signs, behavior, body weight, food intake, hematology or urinary parameters. At 5000 ppm, total serum protein was elevated in males and significant increases in liver weights (in both sexes) and kidney weights (in males) were observed.

LOAEL ~ 250 mg/kg-bw/day (based on increases in total serum protein and kidney weights in males and liver weights in both sexes)

NOAEL ~ 50 mg/kg-bw/day

NaC12 – 15E3S (no CASRN provided, supporting chemical)

Rats (unspecified strain, sex and number/dose) were administered NaC12 – 15E3S at concentrations of 0, 40, 200, 500, 1000 or 5000 ppm in feed (approximately 0, 2, 10, 50 or 250 mg/kg-bw/day) for 90 days. There were no treatment-related effects on clinical signs, behavior, food intake, hematology, clinical chemistry, urinary parameters or histopathology. An increase in body weight was observed in males at 200 and 500 ppm, but not at higher doses, with no clear toxicological significance. A significant increase in liver weights and an increase (not significant) in testes weights were observed at 5000 ppm.

LOAEL ~ 250 mg/kg-bw/day (based on changes in liver weight)

NOAEL ~ 50 mg/kg-bw/day

NaC12 – 14AE2S (no CASRN provided, supporting chemical)

Rats (10/sex/dose, strain not specified) were administered NaC12 – 14AE2S via gavage at 0, 25, 75 or 225 mg/kg-day for 90 days. No treatment-related effects were observed on mortality, food and water consumption or body weight gain. Lesions were observed in the forestomachs of

animals receiving 225 mg/kg-day, including hyperplasia, submucosal edema and chronic ulceration. At 25 and 75 mg/kg-day, small eosinophilic foci were observed in the stratified epithelium of the forestomach that were considered to be local treatment-related irritations. LOAEL = 225 mg/kg-day (based on lesions in forestomach) NOAEL = 75 mg/kg-day

Reproductive Toxicity

Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate (CASRN 3088-31-1) No Data

NaC12 – 15E3S (no CASRN provided, supporting chemical)

In the repeated-dose study described previously, rats (unspecified strain, sex and number/dose) were administered NaC12 - 15E3S at concentrations of 0, 40, 200, 500, 1000 or 5000 ppm in feed (approximately 0, 2, 10, 50 or 250 mg/kg-bw/day) for 90 days. Increases in testes weights were observed at 5000 ppm.

NaC12 – 14AE2S (no CASRN provided, supporting chemical)

In a two-generation toxicity study, Sprague-Dawley Crl:CD(SD)BR rats (30/sex/dose) were administered NaC12 – 14AE2S in drinking water at 0, 0.03, 0.1 or 0.3% (approximately 0, 30, 100 or 300 mg/kg-bw/day for F0). At 300 mg/kg-bw/day, reduced straight-line velocity of sperm was observed among F0 males when compared to controls. A decrease in liver weight was observed in F0 and F1 males (doses not specified), but not in F2 males. In the absence of any evidence of hepatotoxicity in histopathological or clinical chemistry observations, the liver weight reduction was concluded to have no toxicological relevance. Female offspring exhibited delayed sexual development at ~ 300 mg/kg-bw/day.

LOAEL (reproductive toxicity) ~ 300 mg/kg-bw/day (based on reduced sperm velocity in F0 generation and delayed sexual development in female F1 offspring)

NOAEL (reproductive toxicity) ~ 100 mg/kg-bw/day

Developmental Toxicity

Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate (CASRN 3088-31-1) No Data

NaC12 – 14AE2S (no CASRN provided, supporting chemical)

(1) In the two-generation oral toxicity study described previously, exposure to NaC12 - 14AE2S resulted in delayed sexual development in rat female offspring at 300 mg/kg-bw/day. Dams exhibited no treatment-related effects.

NOAEL (maternal toxicity) ~ 300 mg/kg-bw/day (based on no effects at the highest dose tested)

LOAEL (developmental toxicity F1) ~ 300 mg/kg-bw/day) (based on delayed sexual development in female F1 offspring)

NOAEL (developmental toxicity) ~ 100 mg/kg-bw/day

(2) In a prenatal developmental toxicity study, pregnant CD rats ($\geq 24/dose$) were administered NaC12 – 14AE2S via gavage at 0, 100, 300 or 1000 mg/kg-day on gestation days 6 to 15. No maternal toxicity was observed since there were no clinical signs, body weight changes or abnormalities at necropsy after repeated exposure to pregnant rats. No treatment-related effects were observed on pre- or post-implementation loss, mean number of resorptions, embryonic deaths, total number of fetuses, mean fetal placental or uterine weights, fetal sex ratio or visceral or skeletal abnormalities.

NOAEL (maternal and developmental toxicity) = 1000 mg/kg-day (based on no treatmentrelated effects at the highest dose tested)

NaC12 – 15AE3S (no CASRN provided, supporting chemical)

In a prenatal developmental toxicity study, pregnant Colworth-Wistar rats (15/dose) were administered NaC12 – 15AE3S via gavage at 0, 375 or 750 mg/kg-day on gestation days 6 to 15. Females were monitored for signs of toxicity (details not specified). At 750 mg/kg-day, reduced body weight and other clinical and behavioral changes (unspecified) were observed in pregnant rats. Ten females per dose were sacrificed after exposure and were examined for pre- and post-implantation loss. Fetuses were weighed and examined for visceral and skeletal malformations. Five females per dose were allowed to give birth and wean their pups. Pup survival, weight and incidence of external and gross visceral and skeletal defects were monitored until weaning. No treatment-related developmental toxicity or teratogenic responses were observed.

LOAEL (maternal toxicity) = 750 mg/kg-day (based on reduced body weights and unspecified clinical signs and behavioral changes).

NOAEL (maternal toxicity) = 375 mg/kg-day

NOAEL (developmental toxicity) = 750 mg/kg-day (based on no treatment-related effects at the highest dose tested)

NaC16 – 18AE4S (no CASRN provided, supporting chemical)

In a prenatal developmental toxicity study, pregnant Colworth-Wistar rats (20/dose) were administered NaC16 – 18AE4S daily via gavage at 0, 63, 125 or 500 mg/kg-day on gestation days 6 to 15. Ten females per dose were sacrificed after exposure and were examined for preand post-implantation loss. Fetuses were weighed and examined for visceral and skeletal malformations. Five females per dose were allowed to give birth and wean their pups. Pup survival, weight and incidence of external and gross visceral and skeletal defects were monitored until weaning. There was no evidence of developmental toxicity.

NOAEL (maternal and developmental toxicity) = 500 mg/kg-day (based on no treatment-related effects at the highest dose tested)

Genetic Toxicity – Gene Mutation

In vitro

Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate (CASRN 3088-31-1) No Data

NaC12 – 15E3S (no CASRN provided, supporting chemical)

Salmonella typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 and Escherichia coli strains WP2 and WP2uvrA were exposed to NaC12 – 15E3S at unspecified concentrations with and without metabolic activation. The use of controls was not specified. NaC12 – 15E3S was not mutagenic in this assay.

NaC12 – 14AE2S (no CASRN provided, supporting chemical)

In a gene mutation study, L5178Y TK+/- mouse lymphoma cells were treated with NaC12 - 14AE2S with and without S9 metabolic activation. NaC12 - 14AE2S was assayed for the induction of trifluorothymidine-resistant mutants.

NaC12 – 14AE2S was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro

Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate (CASRN 3088-31-1) No Data

NaC12 – 15E3S (no CASRN provided, supporting chemical)

Rat liver cells were exposed to NaC12 – 15E3S at 25, 50 or 100 μ g/mL. The use of controls was not specified. It is unknown whether metabolic activation was used. Exposure to NaC12 – 15E3S did not result in an increase in the frequency of chromatid and chromosome aberrations. NaC12 – 15E3S did not induce chromosomal aberrations in this assay

In vivo

C12 – 15AES (no CASRN provided, supporting chemical)

Rats (unknown strain) were exposed to a maximum tolerated dose of C12 - 15AES in the diet for 90 days. There was no effect on the chromosomes of rat bone marrow cells. No additional details on the study were provided.

C12 – 15AES did not induce chromosomal aberrations in this assay.

Additional Information

Skin Irritation

Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate (CASRN 3088-31-1)

Rabbits (6/dose, unspecified strain and sex were treated with applications of 0.5 mL of 2-(2-dodecyloxyethoxy)ethyl sulfate to intact and abraded skin for 24 hours and observed for 72 hours. The primary irritation index (PII) was 4.0. Tissue damage characterized as coriaceousness was reported in two animals. Atonia, blanching, discoloration and spreading of irritative effects were also reported.

2-(2-Dodecyloxyethoxy)ethyl sulfate was irritating to rabbit skin in this study.

Eye Irritation

Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate (CASRN 3088-31-1)

Rabbits (6/dose, unspecified strain and sex) were administered 0.1 mL of undiluted 2-(2-dodecyloxyethoxy)ethyl sulfate in the right eye and observed for 7 days. Corneal, iris and conjunctival changes were noted in all treated animals. Mean irritation scores ranged from 34.8 at 24 hours to 10.2 after 7 days, on a scale from 0 (no effect) to 110 (most severe effects).
2-(2-Dodecyloxyethoxy)ethyl sulfate was moderately irritating to rabbit eyes in this study.

Sensitization

NaC12 – 14AE2S (28% active material) (no CASRN, supporting chemical)

Female guinea pigs (unspecified strain, sex and number/dose) were administered NaC12 – 14AE2S (28% active material) via injection in the shoulder region. Injection 1 was 0.1 mL of a 1:1 mixture of Freund's complete adjuvant (FCA) and water. Injection 2 was 0.1 mL of a 0.1% solution of NaC12 – 14AE2S in water, whereas injection 3 was 0.1 mL of a 1:1 solution of 0.1% test substance mixed with FCA. After 7 days, a patch containing 30% solution of the test substance was placed over the injection area for 48 hours. Two weeks later, an occlusive challenge patch containing a 10% solution of NaC12 – 14AE2S was applied to one flank of each animal for 24 hours. No treatment-related skin reaction was observed after 48 – 72 hours. NaC12 – 14AE2S (28% active material) was not sensitizing to guinea pig skin in this study.

NaC12 – 15E3S (no CASRN, supporting chemical)

Guinea pigs (20/dose, unspecified strain and sex) were administered NaC12 – 15E3S via injection as a 0.25% solution in FCA. After 7 days, an occlusive patch containing a 50% solution of the NaC12 – 15E3S was placed over the injection area for 48 hours. Two weeks later, an occlusive challenge patch containing a 20% solution of the test substance was applied. After 1 – 2 days, slight dermal reactions (score = 1) were observed in 7/20 animals. The challenge was repeated 7 days later using a 10% solution on the opposite flank. Weak dermal reactions were observed in 2/20 animals.

NaC12 – 15E3S was slightly sensitizing to guinea pig skin in this study.

Carcinogenicity

C12AE3S (no CASRN, supporting chemical)

Rats (unspecified quantity, strain and sex) were administered C12AE3S via diet at concentrations of 0, 0.1 or 0.5% for 2 years. Incidences of various types of tumor were not considered treatment related.

C12AE3S did not increase the incidence of tumors in rats in this study.

Conclusion: The acute oral toxicity of sodium 2-(2-dodecyloxyethoxy) ethyl sulphate in rats is low. In 90-day oral (dietary and gavage) repeated-dose toxicity studies with the supporting chemicals, rats exposed to NaC12–15E3S or Synthetic NaC12 – 15E3S and NaC12AE3S (natural) via the diet showed liver and kidney effects at 250 mg/kg-bw/day; the NOAEL is 50 mg/kg-bw/day. Lesions in the forestomach were observed in the stratified epithelium in rats

exposed to NaC12–14AE2S via gavage at 225 mg/kg-bw/day; the NOAEL for systemic toxicity is 75mg/kg-day. In a two-generation drinking water reproductive toxicity study, the supporting chemical NaC12 – 14AE2S reduced straight-line sperm velocity in parental male rats and delayed sexual development in rat female offspring at 300 mg/kg-bw/day; the NOAELs for reproductive and developmental toxicity are both 100 mg/kg-bw/day. The NOAEL for maternal toxicity in this study is 300 mg/kg-bw/day (highest dose tested). The supporting chemicals NaC12 – 15E3S and NaC12 – 14AE2S were not mutagenic in bacteria and mammalian cells *in vitro*, respectively. The supporting chemical NaC12 – 15E3S did not induce chromosomal aberrations *in vitro*; and C12 – 15AES did not induce chromosomal aberrations *in vivo*. The supporting chemical C12AE3S did not increase the incidence of tumors in rats. Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate is irritating to rabbit skin and eyes. The supporting chemical, NaC12 – 15E3S, is a skin sensitizer in guinea pigs but NaC12 – 14AE2S is not.

Table 3. Summary Table of the Screening Information Data Set under the U.S. HPV Challenge Program – Human Health Data				ie		
Endpoint	SPONSORED CHEMICAL Sodium 2-(2- dodecyloxyethoxy) ethyl sulphate (3088-31-1)	CHEMICAL C12AE3S	SUPPORTING CHEMICAL Synthetic NaC12 – 15E3S & NaC12AE3S (natural) (No CASRN)	SUPPORTING CHEMICAL NaC12 - 15E3S (No CASRN)	SUPPORTING CHEMICAL C12 – 15AES (No CASRN)	SUPPORTING CHEMICAL NaC12 - 14AE2S (No CASRN)
Acute Oral Toxicity LD50 (mg/L)	>5000	_	_	_	_	-
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg- bw/day)	No Data NOAEL = 75 LOAEL = 225 (RA)	_	(rat; 90-d) NOAEL ~ 50 LOAEL ~ 250	(rat; 90-d) NOAEL ~ 50 LOAEL ~ 250	_	(rat; 90-d) NOAEL = 75 LOAEL = 225
Reproductive Toxicity - NOAEL/LOAEL Oral (mg/kg- bw/day) Reproductive Toxicity	No Data NOAEL ~ 100 LOAEL ~ 300 (RA)	_	_	Increases in testes weights were observed in 90-day study in rats at 250 mg/kg	_	(rat; 2-gen) NOAEL ~ 100 LOAEL ~ 300
Developmental Toxicity NOAEL/LOAEL Diet (mg/kg- bw/day) Maternal Toxicity		_	_	_	NOAEL = 375 LOAEL = 750	(rat; 2-gen) NOAEL ~ 300 (Highest dose tested)
Developmental Toxicity					NOAEL = 750 (Highest dose tested)	NOAEL ~ 100 LOAEL ~ 300

Ta	Table 3. Summary Table of the Screening Information Data Set under theU.S. HPV Challenge Program – Human Health Data					
Endpoint		e				SUPPORTING CHEMICAL NaC12 - 14AE2S (No CASRN)
Genetic Toxicity – Gene mutation <i>In vitro</i>	No Data Negative (RA)	_	_	Negative	_	Negative
Genetic Toxicity – Chromosomal aberrations <i>In vitro</i> <i>In vivo</i>	No Data Negative Negative (RA)			Negative _	_ Negative	
Additional Information Skin Irritation Eye Irritation Skin	Moderately irritating			– – Slightly		_ _ Not sensitizing
Sensitization Carcinogenicity	-	Negative (rat)	-	sensitizing –	_	-

Measured data in BOLD; (RA) = read-across; - indicates endpoint not addressed for this chemical

4. <u>Hazard to the Environment</u>

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 4. The table also indicates where data for the supporting chemical is read-across (RA) to the sponsored chemical.

Acute Toxicity to Fish

Sodium 2-(2-dodecyloxyethoxy) ethyl sulphate (CASRN 3088-31-1)

Zebra fish (*Danio rerio*) (8/dose) were exposed to nominal test concentrations of sodium 2-(2-dodecyloxyethoxy) ethyl sulphate at 12.5mg/L, 25 mg/L, 50 mg/L, 75 mg/L or 100 mg/L under static conditions for 96 hours. See data at ECHA:

http://apps.echa.europa.eu/registered/data/dossiers/DISS-dffb4072-e290-47ae-e044-00144f67d031/AGGR-4d7e983a-9957-4b02-8a18-c598b63bb37b_DISS-dffb4072-e290-47aee044-00144f67d031.html#AGGR-4d7e983a-9957-4b02-8a18-c598b63bb37b 96-h LC50 = 25 mg/L

Acute Toxicity to Aquatic Invertebrates

Sodium laurel ether sulfate (CASRN 9004-82-4, supporting chemical)

Water fleas (*Ceriodaphnia dubia*) were exposed to sodium laurel ether sulfate at unspecified concentrations under unspecified conditions for 48 hours. The water was at a mean temperature of 23 °C and mean conductivity of 500 mmhos/cm. The dissolved oxygen concentration was unknown.

 $48-h EC_{50} = 3.12 mg/L$

Toxicity to Aquatic Plants

No adequate data are available for this endpoint.

Conclusion: For sodium 2-(2-dodecyloxyethoxy) ethyl sulphate, the 96-h LC₅₀ to fish is 25 mg/L. For the supporting chemical, sodium laurel ether sulfate, the 48-h EC₅₀ to aquatic invertebrates is 3.12 mg/L. No adequate data are available for the toxicity endpoint to aquatic plants.

Table 4. Summary of the Screening Information Data Set as Submitted under theU.S. HPV Challenge Program - Aquatic Toxicity Data				
Endpoint	SPONSORED CHEMICAL Sodium 2-(2- Dodecyloxyethoxy)ethyl sulfate	SUPPORTING CHEMICAL Sodium laurel ether sulfate		
	(3088-31-1)	(9004-82-4)		
Fish				
96-h LC50	25	-		
(mg/L)				
Aquatic Invertebrates	No Data			
48-h EC50 (mg/L)	3.12	3.12		
	(RA)			
Aquatic Plants				
96-h EC ₅₀ (mg/L)	No adequate data	-		

Bold = experimental data (i.e. derived from testing); (RA) = read-across; - indicates endpoint not addressed for this chemical