Robust Summaries

for

Nonanoic acid, sulfophenyl ester, Sodium salt
CAS #: 91125-43-8

Prepared for the HPV Challenge Program by:
The Procter & Gamble Company

December 21, 2001
Revised: January 21, 2003

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APPENDIX A: HPV Robust Summaries
PHYSICAL-CHEMICAL DATA

[1.1] Melting Point

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	Metal block method according to EEC Directive 67/548, Annex V, A1, as published in 84/449/EEC. The melting point is defined as the temperature at which the phase transition from solid to liquid state, at normal atmospheric pressure, takes place. A small amount of the dried, powdered test substance was packed tightly into a capillary tube. The capillary tube was then placed in the block and the heating rate was adjusted to 4 °C/min until a temperature of 360°C was reached. The physical state of the substance was noted during temperature increase.
GLP:	Yes
Year:	1988
Remarks:	

Results

Melting point:	Did not melt at temperature up to 360°C
Decomposition:	Slowly decomposed over the range 191-350°C
Sublimation:	Not determined
Remarks:	-

Conclusions

Remarks:	As stated in the report: The substance decomposed over the range 191 - 350°C

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000

Order number for sorting:	
Remarks:	-

[1.2] Boiling Point:

Test Substance

Identity:	-
Purity:	-
Remarks:	-

Method

Method/guideline followed:	-
GLP:	-
Year:	-
Remarks	

Results

Boiling point:	-
Decomposition:	-
Sublimation:	-
Remarks:	-

Conclusions

Remarks:	-

Data Quality

Reliability (Klimisch Rating):	-
Remarks:	-

References -

Other

Last changed:	September 5, 2000
Order number for sorting:	
Remarks:	The boiling point was not assessed as the ingredient slowly decomposed over the range 191-350°C before boiling.

[1.3] Density (Relative Density)

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	Pycnometer method as described in ISO Recommendation R1183 used in accordance with EEC Directive 67/548, Annex V, A3, as published in 84/449/EEC. The relative density (D^{20}_4) is defined as the ratio of the mass of a volume of substance to be examined, determined at 20°C, and the mass of the same volume of water at 4°C.
GLP:	Yes
Year:	1988
Remarks:	

Results $D^{20}_4 = 1.236$

Conclusions

Remarks:	As stated in the report: The relative density of the substance was determined as 1.236

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000
Order number for sorting:	
Remarks:	-

[1.4] Vapour Pressure

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	Vapour pressure according to EEC Directive 67/548, Annex V, A4, as published in 84/449/EEC. The vapour pressure is defined as the saturation pressure above a solid or liquid substance. At the thermodynamic equilibrium, the vapour pressure of a pure substance is a function of temperature only.
GLP:	Yes
Year:	1988
Remarks:	-

Results

Vapor Pressure value:	1.71×10^{-7} Pa
Temperature °C:	25°C
Decomposition:	No

Conclusions

Remarks:	As stated in the report: The result was considered reliable in absolute terms to two orders of magnitude.

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000
Order number for sorting:	-
Remarks:	-

[1.5] Partition Coefficient (n-Octanol/water)

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	The partition coefficient (n-octanol/water) was determined according to EEC Directive 67/548, Annex V, A8, as published in 84/449/EEC. The partition coefficient pressure is defined as the ratio of its equilibrium concentrations in a two phase system consisting of two largely immiscible solvents, in this study n-octanol and water.
GLP:	Yes
Year:	1988
Remarks:	-

Results

Log Pow:	- 0.572
Temperature °C:	24.5°C
Remarks:	The substance is not surface active, dissociative, or insoluble in water

Conclusions

Remarks:	As stated in the report: The partition coefficient (n-octanol/water) was determined as Log Pow = - 0.572 at 24.5°C

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000
Order number for sorting:	-
Remarks:	-

[1.6.] Water Solubility

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	Flask stirring method as described in EEC Directive 67/548, Annex V, A6, as published in 84/449/EEC. Solubility in water is specified by the saturation mass concentration of the substance in water at a given temperature. The solubility in water is specified in units of mass per volume of solution.
GLP:	Yes
Year:	1988
Remarks:	-

Results

Solubility in water:	245 ± 8 g/L at 20 ± 0.5 °C
Description of solubility:	Soluble
pH value, concentration, temperature:	7.02 (pH), 253 g/L at 30°C
pKa value at 25 °C	Not applicable

Conclusions

Remarks:	Solubility in water was determined as 245 ± 8 g/L (average and standard deviation of the results of three tests) at 20 ± 0.5 °C

Data Quality

Reliability (Klimisch Rating):	1
Remarks:	Reliable without restriction, guideline study, GLP

References Report # : P&G 1414/881420

Other

Last changed:	September 5, 2000
Order number for sorting:	-
Remarks:	-

[1.7] Particle size distribution:

Test Substance

Identity: Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)

Purity: 77.5%

Remarks: white pellets

Method

Method/guideline followed: CIPAC, Analysis of Technical and Formulated Pesticides, MT 170: "Dry Sieve Analysis of Water Dispersible Granules", CIPAC Handbook Volume F, 1995

GLP: Yes

Year: 1999

Remarks: The interval of the mesh size in which at least 80% of the test substance is collected was determined.
Analytical balance sensitive to 0.01g. (type PE 3600; Mettler-Toledo B.V., Tiel, The Netherlands)

Results

Particle size distribution:

Sieve (microm.)	% substance collected
Receiver pan	0.17
500	49.49
850	48.50
1000	1.79
2000	0.05

Remarks: -

Conclusions

Remarks: The interval of the mesh size in which at least 80% (>97%) of the test substance was collected, was 500 – 1000 μm.

Data Quality

Reliability (Klimisch Rating): 1

Remarks: Reliable without restriction, guideline study, GLP

References	NOTOX B.V., ‘s-Hertogenbosch, The Netherlands. Report # : NOTOX Project 270844, NOTOX Susbstance 94113

Other

Last changed:	September 3, 2001
Remarks:	-

2. ENVIRONMENTAL FATE AND PATHWAYS

[2.1] Photodegradation

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	100%
Remarks:	SMILES entered in QSAR computer program

Method

Method/guideline followed:	AOPWIN v1.90, US EPA
GLP:	No
Year:	2002
Remarks	Photodegradation half-life calculated by QSAR.

Results

Overall OH Rate Constant:	$9.1674.10^{-12}$ cm^3/molecule.sec
Half-life:	14 hours
Potential for ozone reaction:	NO
Remarks:	-

Conclusions

Remarks:	Although photodegradation is not relevant for NOBS (see below), AOPWIN calculation shows that it is not persistent in the atmosphere.

Data Quality

Reliability (Klimisch Rating):	2. Accepted method of estimation
Remarks:	-

References -

Other

Last changed:	December 9, 2002
Order number for sorting:	-
Remarks:	Since NOBS has low volatility (Calculated Fugacity Level III Type : Air: 2.5 x 10^{-18} %), is degraded in the wash; residual is rapidly and completely biodegraded and highly removed during wastewater treatment, NOBS photodegradation was not experimentally assessed. However, a photodegradation rate was calculated by QSAR.

[2.2] Stability in Water (Hydrolysis)

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	77.5%
Remarks:	-

Method

Method/guideline followed:	Solutions of 10mg/L, 100mg/L and 8g /L were prepared in deionised water (pH were respectively 6.4, 5.3 & 4.2) and were kept at 20°C on a bench. Aliquots were collected at various time intervals up to 192 hours and stored at -15°C till analysis. Residual concentration was determined by FI/MS/MS (Flow Injection/Mass Spectrometry/ Mass Spectrometry) for the solutions of 10 & 100mg /L and estimated by direct single $CatSO_3$ (total anionic content by a two-phase titration) for the 8g /L solution.
GLP:	No
Year:	1999
Remarks:	Duration: 192 hours Positive Controls: The calibration standards were dissolved in water/acetonitrile 50/50 v/v to obtain solutions in the µg/L range. Negative Controls: water/acetonitrile 50/50 v/v Analytical procedures: FI/MS/MS and direct single $CatSO_3$ (total anionic content by a two-phase titration) Presence of an undissolved material.

Results

Nominal value:	10 mg/L
Measured value:	7.3 mg/L after 192 hours
Degradation %:	27 % at pH 6.4 at 20°C after 192 hours
Nominal value:	100 mg/L
Measured value:	89 mg/L after 192 hours
Degradation %:	11 % at pH 5.3 at 20°C after 192 hours
Nominal value:	8 g/L
Measured value:	7.7 g/L after 168 hours
Degradation %:	4 % at pH 4.2 at 20°C after 168 hours
Breakdown products:	no
Remarks:	The undissolved material was further extracted in hexane and analysed by FI/MS for qualitative analysis. The main identified compounds were nonanoic and hexadecanoïc acid. Minor other

	fatty acids (C10, 12, 14 & 18) were also detected. Cloudiness observed in toxicity tests was probably due to the presence of these fatty acids as impurities in the raw material rather that precipitation of the test substance.
Conclusions	
Remarks:	Submitter comment: The substance is stable in water at pH<7 for a few days
Data Quality	
Reliability (Klimisch Rating):	1, Reliable without restriction, comparable to guideline study
Remarks:	-
References	S. Peeters, lab notebook ETS 775 pages 81 to 88 & 91-92, The Procter & Gamble Company, European Technical Center, Belgium
Other	
Last changed:	September 7, 2000
Order number for sorting:	-
Remarks:	-

[2.3] Biodegradation

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	98.3%
Remarks:	-

Method

Method/guideline followed:	OECD 301B. CO_2 production measured as the percentage of theoretical CO_2 ($ThCO_2$), calculated from the organic carbon content of the test substance
Test type:	Aerobic conditions
GLP:	Yes
Year:	2000
Contact time:	28 days
Inoculum:	The inoculum (10^8 cells/L) was not pre-adapted to the test substance.
Remarks:	The inoculum was activated sludge from an aeration tank of the waste water treatment plant of Zonhoven (Belgium). The test substance concentration was 10 mg C L^{-1} tested in duplicate. Temperature varied between 18 and 22°C. Direct addition of the test substance. Samples were collected before, then 2, 3, 4, 6, 8, 10, 15, and 28 days after addition of the test substance. Sodium benzoate was used as a positive control. Sodium benzoate + the test substance was used as a toxicity control. Deionized water with low carbon content was used for blank measurements. The two biodegradation values of the replicates were not averaged.

Results:

Degradation, test substance:	Theoretical CO_2: 84 and 89% (replicates 1 and 2, respectively) after 28 days. DOC removal: 96% and 96% (replicates 1 and 2, respectively) after 28 days.
Degradation, positive control:	Theoretical CO_2: 87% after 28 days. DOC removal: 96% after 28 days.
Degradation, toxicity control:	Theoretical CO_2: 83% and 84% (replicates 1 and 2, respectively) after 28 days. DOC removal: 97% and 97% (replicates 1 and 2, respectively) after 28 days.
Breakdown products:	No
Remarks:	No lag time, no inhibition, no excessive standard deviation, half-life: 4 to 5 days, time required for

	10% degradation: 3 days, total degradation at the end of the test: see above. Test substance would be classified as Readily Biodegradable in the EU.
Conclusions	
Remarks:	86% CO2 was produced within 28 days. 10% CO_2 production was achieved by day 3. By day 13, CO_2 production was over 70%. Test substance would be classified as Readily Biodegradable in the EU.
Data Quality	
Reliability (Klimisch Rating):	1, Reliable without restriction, guideline study, GLP
Remarks:	-
References	LISEC Report # : WB-04-124, Craenevenne 140, 3600 Genk, Belgium, Study Director: Dr M. Indeherberg
Other	
Last changed:	September 13, 2000
Order number for sorting:	-
Remarks:	-

[2.4] Ultimate removability

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	94.7%
Remarks:	-

Method

Method/guideline followed:	OECD 302A. Objective of the test is to determine the removability of the test material in the Semi-Continuous Activated Sludge (SCAS) test system, as measured by soluble organic carbon. The % carbon remaining = 100 x ((C concentration in test unit-average C concentration in blank)/(Test material C concentration added to test unit)).
Test type:	SCAS
GLP:	Yes
Year:	1984
Inoculum:	Avondale Sewage Treatment plant, Avondale PA
Test period:	7 days
Test concentration:	20 mg C/l
TOC stock solution:	0.534 mg C/mg active (0.533 at end of test)
Test temperature:	22-24°C
Remarks:	

Results:

Average % removal, DOC:	99.7%
95% confidence interval:	2.0%
Remarks:	

Conclusions

Remarks:	Author comment: The endpoint has been adequately characterized.

Data Quality

Reliability (Klimisch Rating):	1, Reliable without restriction, guideline study, GLP
Remarks:	-

References WESTON Report # : 84-007, West Chester, PA, USA, Study Director: Dr JD Curry

Other

Last changed:	October 17, 2000
Order number for sorting:	-
Remarks:	Ultimate removability is not a typical SIDS endpoint but was included in the list of robust summaries since this test provides additional information to predict NOBS environmental concentration.

[2.5] Transport between Environmental Compartments (Fugacity)

Test Substance

Identity: Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt; NOBS)

Method

Method/guideline followed:

Test type: Level III Fugacity Model, v1.01, MacKay, 1996. Emissions (1000 kg/hr) to water using standard defaults and physical/chemical properties documented in this report (summary below).

Half-life in water & soil	5 days or 120 hours
Half-life in sediment	20 days or 480 hours
Half-life in air	14 hours
Melting Point	> 360°C
Boiling Point	> 360°C
MW	336 g/mol
Relative Density	D^{20}_4 = 1.236
Vapor Pressure	1.71 x 10^{-7} Pa at 25° C
Partition Coefficient	Log P_{ow} = - 0.572
Water Solubility	245 ± 8 g/l at 20 °C
Particle size	500 - 1000μm

Year 2003

Results:

Distribution:
Air 2.9 x 10^{-18} %
Water: 99.9%
Sediment: 0.13%
Soil: 3 x 10^{-10} %

Remarks: Accepted model for theoretical estimation.

Conclusions

Remarks: This material is predicted to be distributed to surface waters.

Data Quality

Reliability (Klimisch Rating): 2. Accepted method of estimation

Remarks:

References

Other

Last changed: January 10, 2003

Order number for sorting:

3. ECOTOXICITY

[3.1] Acute Toxicity to Fish

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	96.8%
Remarks:	-

Method

Method/guideline followed:	Acute toxicity to fish, EPA-660/3-75-009
Test type:	96h Static
GLP:	No
Year (study performed):	1982
Species/Strain/Supplier:	*Lepomis macrochirus* (bluegill), Bionomics lot # 82A12. Commercial fish supplier in Connecticut
Analytical monitoring:	Nominal
Exposure period:	96h
Statistical methods:	LC50 values estimated using moving average angle analysis (Stephan 1978).
Remarks:	Test fish (Age/length/weight, loading, pretreatment): Age not provided, 30 mm, 0.27 g, 10 fish per test jar, held in a 500 L fiberglass tank under a photoperiod of 16 hours light and 8 hours darkness. Fed a dry pelleted food, ad libitum, daily, except during the 48 hours prior to testing. Details of test: Static Dilution water source: Soft water reconstituted from deionized water according to US EPA (1975) Dilution water chemistry: hardness: 42 mg $CaCO_3$/L, alkalinity: 30 mg $CaCO_3$/L, pH: 7.7, TOC, TSS, and salinity not reported (freshwater) Stock and test solution: Clear colorless working stock solution of 15 mg active ingredient/mL was prepared. Appropriate volume of stock solution was then added to each test jar and mixed by stirring with a glass rod. Vehicle/solvent: Not used. Stability of the test chemical solutions: Test substance stable in water for > 96 h (see 3.1.2. above). Exposure vessel type: photoperiod of 16 hours light and 8 hours darkness, no aeration, 15 L Number of replicates, fish per replicate: 1 test jar per concentration, 10 fish per jar.

Water chemistry in the control: D.O: 4.5 to 8.6 mg/L; pH: 7.0 to 7.7
Water chemistry where effects were observed: D.O: 1.2 to 8.3 mg/L; pH: 6.8 to 7.7. D.O. dropped below 20% saturation after 48 h. It is at that time that mortality occurred.
Test temperature: 22 °C

Results:

Nominal concentrations: control; 17; 28; 46; 78; 130 $mg.L^{-1}$
Measured concentrations: Not measured
Unit: $mg.L^{-1}$
Element value: LC50, 96 hours, based on nominal concentrations
Statistical results: described below
Remarks: Biological observations: All exposed fish were respiring rapidly
Table showing cumulative mortality; data between brackets are D.O. levels expressed as % saturation:

Conc. (mg/L)	0h (%)	24h (%)	48h (%)	72h (%)	96h (%)
130	0 (97)	0 (76)	60 (32)	100 (23)	100 (-)
78	0 (99)	0 (74)	70 (27)	90 (22)	90 (23)
46	0 (97)	10 (69)	40 (16)	40 (10)	50 (15)
28	0 (94)	0 (64)	30 (17)	50 (14)	60 (16)
17	0 (100)	0 (76)	0 (40)	10 (26)	20 (33)
Control	0 (98)	0 (75)	0 (60)	10 (51)	10 (58)

Lowest concentration 100% mortality: 130 mg/L
Mortality of controls: up to 10%
Abnormal responses: -
Reference substance: Na lauryl sulfate, 96h-LC50 = 4.9 mg/L
Observations: All test solutions were cloudy after 48hrs. During a subsequent study on stability in water (see 3.1.2. above), the undissolved material was further extracted in hexane and analysed by FI/MS for qualitative analysis. The main identified compounds were nonanoïc and hexadecanoïc acid. Minor other fatty acids (C10, 12, 14 & 18) were also detected. The fatty acids level in the tested raw material was < 2.4%. Cloudiness observed in toxicity tests was probably due to the presence of these fatty acids as impurities in the raw material rather that precipitation of the test substance.
Endpoint value: LC50 = 32 $mg.L^{-1}$

Conclusions

Remarks: The reported fish mortality was mainly the result of stress due to low oxygen level. Author

	comment: The endpoint has been conservatively characterized.
Data Quality	
Reliability (Klimisch Rating):	2, Comparable to guideline study with acceptable restrictions. Not GLP
Remarks:	-
References	EG&G Bionomics, 790 Main street, Wareham, Massachusetts, Report # : BW-82-7-1222; Stephan C (1978) US EPA, Environmental Research Laboratory, Duluth, Minnesota, Personal communication. US EPA (1975) Ecological research series (EPA-660/3-75-009), 61 p.
Other	
Last changed:	September 13, 2000
Order number for sorting:	-
Remarks:	-

[3.2] Acute Toxicity to Aquatic Invertebrates (Daphnia)

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	96.8%
Remarks:	-

Method

Method/guideline followed:	Acute toxicity to invertebrates, EPA-660/3-75-009
Test type:	48h Static
GLP:	No
Year (study performed):	1982
Analytical procedures:	Nominal concentrations
Species/Strain:	*Daphnia magna*
Test details:	Static, Single initial dosing
Statistical methods:	LC50 values estimated using moving average angle analysis (Stephan 1978).
Remarks:	Test organisms: were obtained from laboratory stocks cultured at EG&G, Bionomics. Age of the test organisms at study initiation was ⌠ 24h. Test conditions: For each test concentration, the appropriate amount of the test substance was added directly to 1L dilution water and the solution was vigorously mixed on a magnetic stirrer for 30 seconds. The set of control beakers contained the same dilution water and was maintained under the same conditions as the beakers for exposure, but were not dosed with the test substance. Test solutions were not aerated. Based on a subsequent study on stability in water (see 3.1.2. above), the test substance is expected to have been stable during the test. Test temperature range was 22 ± 1°C. Exposure vessel type: The toxicity test was conducted in 250 mL beakers each of which contained 200 mL of test solution. The dilution water used was fortified well water and had the same quality as the culture water. Dilution water source: The culture water was prepared by fortifying well water according to the formula for hard water presented by US EPA (1975) and filtering it through an Amberlite XAD-7 resin column to remove any potential organic contaminants.

Dilution water chemistry: This water had a total hardness and alkalinity as calcium carbonate ($CaCO_3$) of 160 ± 20 mg/L and 110 ± 10 mg/L, respectively; a pH range of 7.9-8.3; a dissolved oxygen concentration > 5.3 mg/L (i.e., 60% saturation).
Lighting: The test area was illuminated with Durotest (Optima) fluorescent lights at an intensity of 100-150 footcandles (as stated in the report).
Water chemistry in the control: D.O. 8.3 mg/L, pH 8.4; at test substance concentration of 1 g/L: D.O. 7.8-8.6 mg/L, pH 7.5-8.2.
Element basis (i.e., immobilization): EC50 (mg/L)
Test design: 3 replicates were used for each test concentration. 15 daphnia were randomly distributed to each concentration (5 fleas per replicate). Nominal concentrations: control; 50; 80; 120; 220; 360; 600; 1000 $mg.L^{-1}$. Exposure period: 48h.

Results:

Nominal concentrations:	control; 50; 80; 120; 220; 360; 600; 1000 $mg.L^{-1}$
Measured concentrations:	Not measured
Unit:	$mg.L^{-1}$
EC50, at 24 and 48 hours:	> 1000 $mg.L^{-1}$, > 1000 $mg.L^{-1}$
Statistical results:	The EC50 was empirically estimated to be > 1000 $mg.L^{-1}$, the highest concentration tested.
Remarks:	Biological observations: Several daphnia had undissolved test material attached to their carapace. During a subsequent study on stability in water (see 3.1.2. above), the undissolved material was further extracted in hexane and analyzed by FI/MS for qualitative analysis. The main identified compounds were nonanoïc and hexadecanoïc acid. Minor other fatty acids (C10, 12, 14 & 18) were also detected. Cloudiness observed in toxicity tests was probably due to the presence of these fatty acids as impurities in the raw material rather that precipitation of the test substance.

Immobilized/exposed daphnids: 8/105
Concentration response: EC50 > 1000 $mg.L^{-1}$, confidence interval not stated.
Cumulative immobilization: 40% were immobilized at 1000 $mg.L^{-1}$, 7% were immobilized at 600 $mg.L^{-1}$, none were immobilized at lower concentrations.

	Control response satisfactory: Yes
Conclusions	
Remarks:	Author comment: The endpoint has been adequately characterized.
Data Quality	
Reliability (Klimisch Rating):	2, Reliable with restriction due to the static renewal protocol. Actual exposure concentrations might have been < nominal values, though during a subsequent study on stability in water (see 2.2. above), the test substance was shown to be stable in water. Not GLP
Remarks:	-
References	EG&G Bionomics, 790 Main street, Wareham, Massachusetts, Report # : BW-82-7-1221; US EPA (1975) Ecological research series (EPA-660/3-75-009), 61 p.
Other	
Last changed:	September 13, 2000
Order number for sorting:	-
Remarks:	-

[3.3] Toxicity to Aquatic plants: Algae

Test Substance

Identity:	Nonanoyloxybenzene sulfonate, Na salt (CAS # 91125-43-8; Nonanoic acid, sulfophenyl ester, sodium salt)
Purity:	98.3%
Remarks:	-

Method

Method/guideline followed:	Toxicity to algae; OECD Guideline 201
Test type:	72h static
GLP:	Yes
Year (study performed):	1999
Species/strain # and source:	*Selenastrum capricornutum*, LISEC laboratory culture (ex. CCAP 278/4)
Element basis:	The concentration of the test substance that resulted in a 50% reduction in either growth (EbC50) or growth rate (ErC50) relative to the control.
Exposure period:	72h
Analytical monitoring:	Analytical confirmation of exposures with Flow Injection - Mass Spectrometry (FI/MS/MS). Sampling times: at the start and after 24, 48, 72h. 3 mL samples for all test concentrations. Formaldehyde (1%) added and acidification with HCl (pH 4).
Test details:	Static, Single initial dosing
Statistical methods:	EC50 and NOEC values were calculated incorporating measured exposure concentrations (geometric means, Probit method). For ECx value calculations, the statistical model was fitted to data using the SAS procedure NLIN. For NOEC value calculations, the statistical model was fitted to data using the SAS procedure GLM.
Remarks:	Microscopic observation revealed no deformed or abnormal algae cells in the pre-culture. The algal medium (recommended in OECD Guideline 201) was buffered to pH 7 by blowing 0.5% CO_2 in air into the medium solution. The test included 3 controls containing only algae and medium, 3 replicates at each concentration, containing algae, medium and test substance, and 1 reference test vessel for each test concentration containing the algal medium and the test substance. Temperature was recorded daily during the test in 1 replicate of each test concentration. Growth/test medium included $NaHCO_3$: 50 mg/L, pH7.1,

$Na_2EDTA.2H_2O$. Deionized water was used as dilution water source. Test containers were 250 mL glass flasks covered with a plastic stop. 100 mL of test solution were used in each flask. Solutions were shaken once a day before the spectrophotometrical measurement.
pH in test

Nominal conc.	pH at time (h)	
	0	72
Control	7.1	7.1
2 mg/L	7.1	7.1
4.5 mg/L	7.1	7.0
10 mg/L	7.1	7.0
23 mg/L	7.1	7.0
50 mg/L	7.0	6.9

Mean measured concentrations are expressed as geometric means.

Results:

Nominal concentrations:	control, 2, 4.5, 10, 23, 50 mg/L
Mean measured concentrations:	0.05, 0.19, 0.38, 0.91, 4.6, 35.5 mg/L
Unit:	$mg.L^{-1}$
Element value:	ErC50 = 26.3 $mg.L^{-1}$ at 72 hours; EbC50 = 9.3 $mg.L^{-1}$ at 72 hours.
NOEC:	biomass: 0.38 mg/L, rate: 0.91 mg/L
Control response satisfactory?	Yes
Statistical results:	ErC50 95% confidence interval: 18.2 - 38.0 at 72 hours; EbC50 95% confidence interval: 7.2 - 11.8 at 72 hours.
Remarks:	Inhibition: at 2 mg/L: biomass: 0.9%, growth rate: -3.8%, at 4.5 mg/L: biomass: 6.9%, growth rate: -2.4%, at 10 mg/L: biomass: 14%, growth rate: 3.7%, at 23 mg/L: biomass: 39%, growth rate: 29%, at 50 mg/L: biomass: 70%, growth rate: -50%.

Conclusions

Remarks:	The concentrations of the test substance that caused 50% reduction in biomass (EbC50, 0-72h) and inhibition of growth rate (ErC50, 0-72h) of *S. capricornutum* with respect to a control culture were 9.3 mg/L (95% confidence interval: 7.2 - 11.8), and 26.3 mg/L (95% confidence interval: 18.2 - 38.0), respectively. The No-Observed-Effect-Concentration for biomass and growth rate after 72h were 0.38 mg/L and 0.91 mg/L, respectively. Author comment: The endpoints have been adequately characterized.

Data Quality

Reliability (Klimisch Rating):	1, Reliable without restriction, guideline study, GLP
Remarks:	-
References	LISEC Report # : WE-06-248, Craenevenne 140, 3600 Genk, Belgium, Study Director: Dr M. Indeherberg; Analytico Report # : 4499060006, Berschot 69-71, 4817 PR Breda, P.O. Box 9910, The Netherlands.

Other

Last changed:	September 15 2000
Order number for sorting:	-

[4] HUMAN HEALTH TOXICITY STUDIES

SIDS ENDPOINTS

[4.1] Acute Oral Toxicity

Study Title	Acute Oral Toxicity(LD_{50}) Study
Date	October 22, 1982
Test Facility	Miami Valley Laboratories, Procter & Gamble Cincinnati, OH USA
GLP Compliance	Yes; EPA
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS, administered as a 40% w/v aqueous suspension)
Animal Species	Rat, Sprague-Dawley CD Prefasted body weights 190-300 grams
Number of Animals	10 rats /group (5 males, 5 females); 4 groups
Dosing	Oral gavage; 40% w/v (in distilled water) suspension used for each dose level, 5.10, 5.78, 6.46, and 7.14 g test material/kg body weight. Animals were fasted for 18-20 hours prior to dosing.
Observations	All animals were observed for mortality and clinical signs of toxicity at 0.5, 1, 2, 3 and 4 hours after dosing and daily thereafter for 14 days.
Results and Discussion	The oral LD_{50} for male and female rats (combined Probit method) was calculated to be 6.03 g/kg body weight (95% confidence limits: 5.62 - 6.44 g/kg). All mortality occurred within two days following administration of the test material (see table below). Clinical signs observed included diarrhea, abdominal gripping, hypoactivity and decreased respiratory rate. Generally, the signs and number of animals involved appeared to be dose related. All rats that died during the study had irritation or hemorrhaging of the stomach and intestines, consistent with irritation observed with other related surfactants .
Conclusion	The acute oral LD_{50} in rats is 6.03 g/kg.
Klimisch criterium	1

Mortality Summary (Number of Deaths)

Dosage Level	Days Post Administration															
	1		2		3		4		5		6		7-14		Total	
g/kg	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
5.10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5.78	1	5	0	0	0	0	0	0	0	0	0	0	0	0	1	5
6.46	2	4	0	0	0	0	0	0	0	0	0	0	0	0	2	4
7.14	1	2	3	3	0	0	0	0	0	0	0	0	0	0	4	5

[4.2] Acute Percutaneous Toxicity

Study Title	Acute Percutaneous Toxicity (Rabbits) APCT
Date	September 21, 1982
Test Facility	Miami Valley Laboratories, Procter & Gamble Cincinnati, OH USA
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS, administered as a 40% w/v aqueous suspension)
Animal Species	New Zealand White Rabbits; body weights 2.0 - 3.5 kg
Number of Animals	6 rabbits/group (3 males, 3 females) in 2 groups of 3 animals each
Dosing Route/ Regimen	A 40% w/v aqueous solution of the test material (2 ml/kg body weight) was applied dermally to the back. Prior to treatment, hair was clipped from shoulder to rump exposing an area approximately 15 cm wide. The skin of 3 animals was left intact and the skin of the other 3 animals was abraded (exposure of the horny layer of epidermis without causing bleeding). Test material was spread evenly over the prepared skin and immediately covered with 8-ply gauze held in place by a impermeable dressing covering the entire trunk. At the end of the 24 hour exposure period, dressings were removed and the treated area of the skin gently wiped to remove residual material.
Observations	All animals were observed for mortality and clinical signs at 24 hours after dosing and daily thereafter for 14 days. Dermal effects were assessed daily according to a defined grading scale for erythema, edema and eschar. All animals were necropsied either upon death or at the end of the 14 day observation period for gross morphologic alterations. Tissues representing gross lesions (other than treatment area skin) were collected for histological examination if the alteration was of possible treatment origin.

Results and Discussion	One animal from the abraded group died on Day 7 of non-treatment related causes (gastro-enteritis of unknown etiology). During the first 6 days following test material administration, dermal irritation range from moderate (1 of 6 sites) to severe (5 of 6 sites) erythema, moderate edema (6 of 6 sites) and slight atonia. Only slight erythema was observed beyond Day 7. All animals gained weight. Except for the local skin effects observed at the site of application, no treatment related gross or histopathological effects were observed at necropsy.
Conclusions	The dermal LD_{50} in rabbits is greater than 2.0 ml/kg (0.8 g/kg)
Klimisch criterium	1

[4.3] Escherichia coli WP2 and WP2 uvrA Reverse Mutation Assay and Salmonella/ Mammalian - Microsome Mutagenesis Assay (Ames Test)

Study Title	Escherichia coli WP2 and WP2 uvrA Reverse Mutation Assay and Salmonella/ Mammalian - Microsome Mutagenesis Assay (Ames Test)
Date	October 13, 1983
Test Facility	Microbiological Associates Bethesda, MD, USA
GLP Compliance	Yes; EPA
Test Material	Sodium Nonanoyloxybenzene Sulfonate
Animal Species	E. coli and Salmonella (TA1535, TA100, TA1537, TA1538 TA98)
Number of Animals	Not applicable
Dosing	Test material concentrations ranged from 50 to 20,000 µl per plate in the preliminary toxicity dose range finding studies and typically 50 to 7,000 µl per plate in the definitive studies. Appropriate positive, solvent and sterility controls were used. Tester strain titers were determined. All dose levels of test material, solvent and positive controls were plated in triplicate.
Observations	Following an approximate 48 hour incubation at 37 C, revertant colonies per plate were counted; for all replicate plating, mean revertant colonies per plate were calculated.
Results and Discussion	The results of the E. coli and Salmonella/mammalian microsome reverse mutation assays (Plate Incorporation Method) indicate that under the conditions of these studies, the test material did not cause a positive response on any of the tester strains in the presence or absence of Arochlor-induced rat liver microsomes.
Conclusion	The test material is not mutagenic.
Klimisch criterium	1

[4.4] *In vivo* Cytogenetics Study

Study Title	*In vivo* Cytogenetics Study in Rats: Compound E1235.01
Date	February 23, 1983
Test Facility	EG&G/ Mason Research Institute Worcester, MA USA
GLP Compliance	Yes; EPA
Test Material	Sodium Octanoyloxybenzene Sulfonate (C8 AOBS) -50% Sodium Decanoyloxybenzene Sulfonate (C10 AOBS) -50% Test material 87% active
Animal Species	Charles River Sprague Dawley Rats
Number of Animals	120 total 3 animals/sex/dose group/sacrifice time point 5 dose groups (negative control, positive control, high dose, mid dose, and low dose)
Dosing Route/ Regimen	Negative control - distilled water Positive control - methylmethane sulfonate Acute dosing regimen - doses 3.2, 1.1, or 0.32 g/kg C8/10 AOBS sacrifice times 6, 24, or 48 hours post dose Chronic dosing regimen - doses 1.6, 0.5, or 0.16 g/kg C8/10 AOBS for 5 days An i.p. injection of colchicine was given to inhibit mitosis ~ 2 hours prior to sacrifice. Bone marrow was collected, fixed, stained, and analyzed.
Observations	Many animals dosed acutely with mid and high dose levels showed some signs of toxicity such as diarrhea or exudate. In the subchronic group, few animals showed symptoms such as dyspnea and inactivity (including positive control group).
Results and Discussion	The appropriate positive and negative controls indicate a valid test. The results of this study indicate that C8/10 AOBS, administered orally over the dose range of 0.32 - 3.2 g/kg for the acute study and 0.16 - 1.6 g/kg for the subchronic study, did not induce a statistical increase in the number of chromosomal aberrations.
Conclusion	The test compound has no clastogenic potential under the conditions of this test.
Klimisch criterium	1

[4.5] Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells *In vivo*

Study Title	Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells *In vivo*
Date	October 3, 2000
Test Facility	BioReliance Rockville, MD
GLP Compliance	Yes
Test Material	Nonanoyloxybenzene sulfonate (NOBS extrudate: 78% C9 AOBS)
Animal Species	Sprague Dawley rats
Number of Animals	50 male rats total 10 animals dose group 5 dose groups (negative control, positive control, high dose, mid dose, and low dose)
Dosing Route/ Regimen	Negative control - sterile distilled water Positive control - Dimethylnitrosamine (DMN), 35 mg/kg bw NOBS 2,000 mg/kg bw NOBS 1,000 mg/kg bw NOBS 500 mg/kg bw The test article-vehicle mixture, negative control and positive control were administered via gavage at a constant volume of 10 mL/kg bw. All rats in the experimental and control groups were weighed immediately prior to dose administration and the dose volume was based on individual body weights.
Observations/ Procedures	Animals were observed after dose administration for clinical signs of toxicity. Hepatocytes were harvested at either 2-4 post dose or 12-16 hours post dose. In preparation of hepatocyte cultures, rats were anesthetized and livers were perfused. A minimum of 6 cultures were set up for reach rat. Ninety to 180 minutes after plating, hepatocytes were washed and refed with medium containing 10 μCi radiolabeled thymidine. Seventeen to 20 hours after exposure to thymidine, coverslips bearing cultures were washed, fixed, and scored. All coded slides were read without knowledge of treatment group. Fifty nuclei were scored from each of three replicate cultures for a total of 150 nuclei from each rat.

Results and Discussion	All animals appeared normal following dose administration prior to harvest. For each treatment slide, the net nuclear counts were averaged and the mean ± standard deviation reported. 2-4 hour post dose harvest: The mean net nuclear grain count for the negative control group was -0.1. The means of the net nuclear grain counts for the 0.5, 1.0, and 2.0 g/kg bw treatment were -2.3, -2.4, and -2.9, respectively. The mean net nuclear grain count for he positive control group was 9.0. None of the test article doses caused a significant increase in the mean net nuclear counts compared to the negative control group. 12-16 hour post dose harvest: The mean net nuclear grain count for the negative control group was -3.5. The means of the net nuclear grain counts for the 0.5, 1.0, and 2.0 g/kg bw treatment were -2.4, -3.3, and -2.4, respectively. The mean net nuclear grain count for he positive control group was 8.7. None of the test article doses caused a significant increase in the mean net nuclear counts compared to the negative control group.
Conclusion	All criteria for a valid study were met. The results of the unscheduled DNA synthesis test with mammalian liver cells *in vivo* indicate that, under the test conditions, the test article did not induce a significant increase in the mean number of net nuclear grain counts (i.e., an increase of at least 5 counts over the negative control).
Klimisch criterium	1

[4.6] Oral Teratology Study

Study Title	Oral Teratology Study in Rats
Date	October 17, 1984
Test Facility	International Research and Development Corporation Mattawan, MI USA
GLP Compliance	Yes
Test Material	Sodium Octanoyloxybenzene Sulfonate (C8 AOBS), 98.5% active
Animal Species	Sprague-Dawley Rats. Females were 80 to 120 days of age, nulliparous, sexually mature and a minimum of 220 grams at study initiation. Males were sexually mature, healthy, gross normal in appearance.
Number of Animals	25 female rats /group ; 4 groups
Dosing	Doses of 0 (water vehicle control), 500, 1000, or 1500 mg/kg/day administered by oral gavage on gestation days 6 through 15. Dosing volume was 10 ml/kg.
Observations	Dams were checked daily for mortality and clinical signs of toxicity. Body weights and food consumption were recorded on gestation days 0, 6, 9, 12, 16 and 20. On gestation day 20, rats were sacrificed and examined macroscopically. Ovaries and uterine horns were examined for number of copora lutea, number and distribution of live young, number and distribution of fetal deaths or resorptions. Litter weights were recorded. Fetuses were individually weighed, sexed, and examined for external malformations and variations. One half of the fetuses were placed in Bouin's solution for soft tissue examination using Wilson's sectioning technique. The remaining one half of fetuses were prepared and stained with Alizarin Red for skeletal examination.
Results and Discussion (continued)	No mortality was present in the 0, 500, or 1000 mg/kg day groups. Three dams dosed with 1500 mg/kg/day died on gestation 13 or 15. Necropsy observations of animals that died on study included reddened stomach mucosa and distended intestines. Clinical observations in the mid and surviving high dose groups included respiratory rales and wet matted haircoat or material in the facial, ventral and/or anogenital areas. There were no differences in gross necropsy findings of the treated and control dams.

Results and Discussion (continued)	Oral administration of C8/10 AOBS from gestation day 6 through 15 resulted in a depression in maternal body weight change at all dosage levels during the first two measured intervals of treatment (days 6 to 9 and 9 to 12) and only in the high dose group during the last treatment interval (days 12 to 16). Similarly, mean food consumption was slightly decreased in the mid and high dose groups only during the treatment period. There were no indications of a treatment related effect on fetal or embryonic growth or survival. Ovulation, implantation, intrauterine development, and embryogenesis were uniform in all study groups. Similarly, the occurrence of malformations and developmental variations was not different in the treated groups relative to the control group. One nonviable fetus was observed in the 1000 mg/kg goup and one litter each in the control, 1000, and 1500 mg/kg groups had a single late resorption. Anomalies including vertebral anomalies with or without rib anomalies, microphthalmia, anophthalmia, sternoschisis, gastroschisis diaphragmatic hernia were noted occasionally in the control and mid dose groups. No malformed fetuses were present at the low and high dose levels.
Conclusion	When administered orally to pregnant Charles River CD rats on gestation days 6 through 15, C8/10 AOBS did not induce a teratogenic effect at dosage levels of 500, 1000, or 1500 mg/kg/day. The fetal NOEL was 1500 mg/kg/day and maternal NOAEL was 500 mg/kg/day.
Klimisch criterium	1

[4.7] Fertility Study

Study Title	Fertility Study in Rats
Date	March 28, 1986
Test Facility	International Research and Development Corporation Mattawan, MI USA
GLP Compliance	Yes
Test Material	Nonanoyloxybenzene Sulfonate (C9 AOBS), 98.5% active
Animal Species	Sprague-Dawley Rats
Number of Animals	38 rats /sex/group ; 4 dose groups; termination at gestation day 13 (for uterine examination group) or lactation day 21.
Dosing	Doses of 0, 100, 500, or 1000 mg/kg/day in deionized water (dosing volume of 5ml/kg) administered by oral gavage for 70 days prior to initiation of mating until termination, on either gestation day 13 or lactation day 21. F1 offspring were potentially exposed in utero and/or as neonates during lactation but did not directly receive the test article.
Observations	Estrous cycle determined in females 10 days prior to mating until the end of the mating period. Body weights and food consumption were recorded weekly until copulation, gestation days (GD) 0, 7, 13, and 20 and lactation days 0, 7, 14, and 21 for appropriate groups. Animals observed daily for clinical signs of toxicity, changes in appearance, behavior and mortality. <u>Uterine exam group (GD13)</u> - Ovaries and uterine horns examined for number of copora lutea, number of implantations, number and distribution of viable and nonviable fetuses, and early resorptions. <u>Delivered litters</u> - Litter size, number of still births, number of live births, and gross anomalies were determined. On postnatal day 4, litters were culled to 10 pups to achieve homogenous group size for evaluation of nursing, survival and body weight. Pups weighed on postnatal day 0, 4, 7, 14, and 21. Tissues and organs from all F0 animals were macroscopically observed, with special attention to reproductive organs, and preserved in 10% neutral buffered formalin for potential microscopic evaluation.

Results and Discussion (continued)	There were no treatment related differences in the estrous cycle of female rats. Mortality occurred in 1, 1, 2, and 10 rats in the 0, 100, 500, and 1000 mg/kg day groups, respectively. Macroscopic observations noted in three females that died on study included gastric lesions with thickened tissue indicative of mild gastric irritation. Five males that died in the high dose group had pulmonary lesions suggestive of pneumonia. Test articles was not directly implicated in the deaths. Clinical observations in the mid and high dose groups included excessive salivation and respiratory rales. There were no significant adverse effect on body weights or food consumption. The high dose males showed a slight yet consistent decrease in body weights (4% or less decrease) compared to control animals throughout the study. Uterine exam observations show no difference in the number of viable embryos, postimplantation loss, total implantations or number of corpora lutea. F0 Delivery and F1 Litter Observations - There was no test article effect observed on male or female fertility indices, copulatory indices, gestation length, mean number of live/dead pups on day 0, pup survival to weaning or pup body weight throughout lactation. There were no indications of a treatment related effect on fetal or embryonic growth or survival. Ovulation, implantation, intrauterine development, and embryogenesis were uniform in all study groups.
Conclusion	NOBS administered orally at dosage levels of 100, 500, or 1000 mg/kg/day did not result in adverse effects on fertility, parturition, neonatal viability, growth of the newborn or reproductive performance in rats. The NOEL and NOAEL were 1,000 and 100 mg/kg/day for reproductive and systemic effects, respectively.
Klimisch criterium	1

[4.8] 13 Week Oral (Dietary Administration) Toxicity Study

Study Title	P1407.02: 13 Week Oral (Dietary Administration) Toxicity Study in the Rat
Date	November 1984
Test Facility	Hazelton Laboratories North Yorkshire, ENGLAND
GLP Compliance	Yes
Test Material	Sodium Octanoyloxybenzene Sulfonate (C8 AOBS), 91.3% active
Animal Species	Rat, Sprague-Dawley
Number of Animals	40 rats /group (20 males, 20 females); 4 groups Animals were received at approximately 28 days of age with treatment beginning on approximately 42 days of age.
Dosing	Dietary levels of 0, 0.001, 0.01 and 0.1% (equivalent to 0, 10, 100, or 1000 mg/kg/day) were administered for 13 weeks. Concentration levels were adjusted to provide a constant dose level in relation to increasing body weight.

Observations	Animals were observed daily for overt signs of toxicity and mortality and weekly for systemic effects. Body weight and food consumption were recorded weekly throughout the study. Clinical laboratory studies were performed on blood and urine collected at weeks 12 and 13 and included hematology, blood chemistry and urinalysis. <u>Clinical chemistry</u> assessment included the following parameters: glutamate oxaloacetate transaminase (GOT) glutamate pyruvate transaminase (GPT) alkaline phosphastase blood urea nitrogen glucose sodium potassium calcium inorganic phosphate chloride total bilirubin creatinine total protein albumin albumin/globulin ratio <u>Hematology assessment</u> performed on blood taken into EDTA anticoagulant included the following parameters: hemoglobin mean cell volume red blood cell count total and differential white blood cell count platelets

	Urine analysis included the following parameters: pH volume specific gravity protein hemoglobin glucose ketones bilirubin urobilinogen reducing substances microscopy of centrifuged deposits including epithelial cell count Histology - Samples of the following tissues from all animals were preserved in 10% neutral buffered formalin: adrenals aorta brain (3 sections) caecum colon duodenum epididymides eyes femur with articular surface heart jejunum ileum lachrymal gland kidneys mammary gland liver esophagus lungs pancreas mesenteric lymph node prostate/uterus ovaries/testes salivary gland pituitary skeletal muscle rectum sternum sciatic nerves thymus seminal vesicles trachea spinal cord (3 levels) stomach spleen thyroid urinary bladder Opthalmoscopic examinations were performed on all animals in the control and high dose group prior to start of treatment and at study end. Complete necropsies were performed on all animals. The following tissues were weighed and fixed: adrenals, heart, pituitary, brain, kidney spleen, testes/ovaries, liver and thyroid. With the exception of the eyes, which were fixed in Davidson's solution, an extensive list of tissues as noted above were preserved in 10% neutral buffered formalin. All tissues from control and high dose animals, lung and liver tissue and gross lesions from low and intermediate dose groups were embedded, sectioned, stained and evaluated by a pathologist.

Results and Discussion	Administration of C8 AOBS did not result in any mortalities or induce any compound-related clinical signs of toxicity. There were no significant changes in body weights or food consumption. There were no toxicologically significant treatment related effects in the hematology, clinical chemistry or urine analysis parameters. Statistically significant increases were observed between the control and high dose males for neutrophils, lymphocytes, and BUN levels. In addition creatinine and sodium were statistically significant for the females. However, these changes were within the normal ranges observed in background data compiled at the laboratory. There were no treatment related effects on absolute or relative organ weights. Test article diet preparations were stable, homogeneous and formulated correctly. No treatment-related gross pathological findings or histopathological changes were observed in test animals compared to controls.
Conclusion	The study established 0.11% in diet (approximately 1,100 mg/kg/day) as the no observed adverse effect level (NOAEL). C8 AOBS was not considered to be systemically toxic up to a level of 1,110 mg/kg/day.
Klimisch criterium	1

BEYOND SIDS ENDPOINTS

[4.9] Primary Eye Irritation - Low Volume Eye Test Method

Study Title	Rabbit Eye Irritation (Low Volume Procedure)
Date	September 28, 1982
Test Facility	International Research and Development Corporation
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS)
Animal Species	New Zealand White Rabbits
Number of Animals	Group I - 6 rabbits (3 male, 3 female); Group II - 3 rabbits (1 male, 2 females

Dosing	Group I rabbits received 0.01 ml of test material (low volume procedure), placed directly on the cornea of one eye without rinsing (the eyelid was released immediately after instillation); Group II rabbits received 0.01 ml of test material directly on the cornea with rinsing (approximately 4 seconds after application using 20 ml of water).
Observations	Eyes were examined for corneal opacity, iritis and conjunctivitis and scored according to the methods of Draize (1959).
Results and Discussion	Group I (unrinsed eye) yielded a maximum average score of 33.7 (Day 2). Corneal involvement and iridal effects were observed in 6 of 6 animals at day 1. Conjunctival irritation ranged from mild to severe. All effects observed were reversible and animals returned to normal (1 animal in 3 days, 1 in 4 days, 3 in 7 days and 1 in 14 days). Group II (rinsed eyes) yielded a maximum average score of 20(Day 1). Effects noted include mild corneal involvement 1 animal, mild iridal effects and mild to severe conjunctival irritation. Eyes of all subjects returned to normal within 3-7 days (2 animals in 3 days and 1 in 7 days).
Conclusions	The test substance caused moderate irritation in all eyes, which cleared by Day 7, except for one eye, which cleared by Day 14 (unrinsed).
Klimisch criterium	1

[4.10] Primary Eye Irritation

Study Title	Rabbit Eye Irritation
Date	October 1, 1982
Test Facility	International Research and Development Corporation
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS)
Animal Species	Rabbits, New Zealand White
Number of Animals	Group I - 3 rabbits (2 male, 1 female); Group II - 3 rabbits (2 male, 1 females); Group III - 3 rabbits (1 male, 2 females)
Dosing	Group I rabbits received 3 mg of test material in their right eye (conjunctival sac) without rinsing (eyelid was gently held closed for approximately one second after instillation); Group II rabbits received 3 mg of test material in the conjunctival sac followed by rinsing (approximately 4 seconds after application using 20 ml of water); and Group III rabbits received 0.1 ml per test eye as a 10% w/v solution in the conjunctival sac (eye held closed for approximately 1 sec) without rinsing.
Observations	Eyes were examined for corneal opacity, iritis and conjunctivitis and scored according to the methods of Draize (1959).
Results and Discussion	Group I - (unrinsed) - yielded a maximum average score of 16.7 (Day 1). Corneal involvement was observed in 2 of 3 animals and mild iridal effects. Mild to moderate conjunctival redness and mild swelling was also noted. All effects observed cleared within 4 days (2 animals in 3 days, 1 in 4 days). Group II - (rinsed)- yielded a maximum average score of 5.3 (Day 1). No effects on the corneal. Mild iritis and conjunctivitis was transient and cleared in all 3 animals within 2 days. Group III - (unrinsed) yielded a maximum average score of 28.0 (Day 1). Corneal involvement, mild iritis, and mild to severe conjunctival irritation was observed in all animals. All effects were reversible (2 animals in 4 days and 1 in 21 days).

Conclusion	The test substance caused slight to moderate irritation in all eyes, which cleared by Day 4 (unrinsed), except in the 10% w/v unrinsed group, which cleared by Day 21.
Klimisch criterium	1

[4.11] Primary Skin Irritation

Study Title	Rabbit Skin Irritation (Department of Transportation -DOTP method)
Date	December 13, 1982 (Study I) October 12, 1983 (Study II)
Test Facility	Miami Valley Laboratories, Procter & Gamble Cincinnati, OH USA
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS, administered as a 40% w/v aqueous suspension or a moistened paste)
Animal Species	New Zealand White Rabbits
Number of Animals	Study I - 6 rabbits (5 males, 1 female); Study II - 6 rabbits (3 males, 3 females)
Dosing	Study I - 0.5 ml of the test material (40% w/v suspension in distilled water) was applied to 1 x1 inch gauze patches and occluded for 4 hours on intact, unabraded skin. Study II - 0.5 g of undiluted test material, slightly moistened with 0.9% saline was applied to 1 x 1 inch gauze patches and occluded for 4 hours on intact unabraded skin.
Observations	After 4 hours of exposure, the patches were removed from animals in both studies and the application sites were observed for irritation and corrosion. Readings were made again at the end of 48 hours.
Results and Discussion	Study I - The average dermal irritation scores for animals at 4 hours were 0.54 and 0 for erythema and edema, respectively; whereas at 48 hours the scores were 1.3 and 0 for erythema and edema, respectively. The primary dermal irritation index was calculated to be 0.9, which translated to a slight irritant. Study II - The average dermal irritation scores for animals at 4 and 48 hours were 0 for erythema and edema.
Conclusion	Dilute and undiluted test material was non-irritating and noncorrosive to skin .
Klimisch criterium	1

[4.12] Delayed Contact Hypersensitivity in Guinea Pigs

Study Title	Delayed Contact Hypersensitivity Study in Guinea Pigs (Modified Buehler Method)
Date	October 6, 1982
Test Facility	Miami Valley Laboratories, Procter & Gamble Cincinnati, OH USA
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS)
Animal Species	Guinea Pig (Hartley Albino)
Number of Animals	Test = 20 (10 male, 10 female); Control = 10 (5 male, 5 female)
Dosing	Based on previous skin irritation information for a similar compound, a concentration of 20% aqueous solution (w/v) was used for the three week induction. A screening study was conducted to determine the highest non irritating concentration for challenge. Based on the results, a 20% (w/v) aqueous solution was used as the challenge concentration.
Observations	The test sites were graded for skin responses, including erythema and edema, using a standardized scoring scale at 24 and 48 hours following chamber application at induction. Following the challenge dose, the skin was depilated after 19 hours and at 24 and 48 hours post challenge, depilated animals were scored for erythema severity using a 0-3 scale (0 = no reaction, ± = slight patchy erythema, 1= slight, but confluent or moderate, patchy erythema, 2= moderate erythema, 3= severe erythema with or without edema).
Results and Discussion	Dermal scores of 0 or +/- were observed in all test and control animals. No evidence of skin sensitization was observed.
Conclusion	The test material is not a dermal sensitizer under the conditions of this test.
Klimisch criterium	1

[4.13] Dermal Sensitization in Guinea Pigs - Modified Buehler

Study Title	Delayed Contact Hypersensitivity Study in Guinea Pigs (Modified Buehler Method)
Date	March 12, 1986
Test Facility	Hill Top Research, Inc.
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS)
Animal Species	Guinea Pig (Hartley Albino)
Number of Animals	Test = 20 (10 male, 10 female); Control = 10 (5 male, 5 female), Rechallenge naïve control = 10 (5 male, 5 female)
Dosing	Based on skin irritation screening information, a concentration of 5% in distilled water (w/v) was used for the three week induction (one six hour patch per week). The concentration used for the challenge phase of the study was 2.5% . Test animals were rechallenged and a naïve control group was dosed with a 1% solution of test material in distilled water for six hours.
Observations	The test sites were graded for skin responses, including erythema and edema, at 24 and 48 hours following patch removal. The procedure for grading the skin after the irritation screen and challenge dose included depilatingthe skin after 19 hours and grading at 24 and 48 hours post challenge. For rechallenge, skin was graded at 24 and 44 hours, depilated, and graded again at 48 hours. The standardized scoring scale assessed severity of erythema using a 0-3 scale (0 = no reaction, ± = slight patchy erythema, 1= slight, but confluent or moderate, patchy erythema, 2= moderate erythema, 3= severe erythema with or without edema).
Results and Discussion	Following the primary challenge, 6/20 and 0/10 animals produced dermal scores greater than +/- at 24 and/or 48 hours in test and control animals, respectively. A rechallenge was conducted using a 1% test material in distilled water. The grades for skin response demonstrated 2/20 test animals and 0/10 control animals responded with a score greater than +/- at 24 and/or 48 hours.
Conclusion	These data indicate a contact sensitization response occurred in some of the test animals at the concentrations tested.
Klimisch criterium	1

[4.14] Dermal Sensitization in Guinea Pigs - Modified Buehler

Study Title	A Dermal Sensitization Study in Guinea Pigs-Modified Buehler Design
Date	September, 2000
Test Facility	Procter & Gamble Non-Clinical Testing Laboratory (PGNCTL) Cincinnati, OH
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS extrudate: 78% C9 AOBS)
Animal Species	Guinea Pig (Hartley Albino)
Number of Animals	Test = 20 (10 male, 10 female); Control = 10 (5 male, 5 female) Induction range finder = 4 animals, Challenge range finder = 8 animals.
Dosing	Appropriate concentrations were chosen based on the range finding studies. For induction, 0.3 ml of 10% test material in reverse osmosis water was applied for 6 hours under an occlusive Hilltop patch once per week for three consecutive weeks. Following a two week rest period, challenge phase was conducted under similar conditions at 0.5%.
Observations	The test sites were graded for skin responses, including erythema and edema, using a standardized scoring scale at 24 and 48 hours following chamber application at induction. During challenge, the test sites were graded through hair at 19 hours and then following depilation at 24 and 48 hours after patch removal.
Results and Discussion	Irritation was noted during induction. At the 24 and 48 hr scoring intervals during challenge, dermal score of 1 was noted in 1/20 and 0/10 test and challenge control animals, respectively. All other scores ranged from 0 to ± in all other test and control animals. No evidence of sensitization was observed in guinea pigs exposed to the test material. The results show a response in 1/20 test subjects, which does not equate to a positive response.
Conclusion	The test material is not a dermal sensitizer under the conditions of this study according to global guidelines..
Klimisch criterium	1

[4.15] Local Lymph Node Assay

Study Title	Murine Local Lymph Node Assay
Date	September, 2000
Test Facility	Procter & Gamble Non-Clinical Testing Laboratory (PGNCTL) Cincinnati, OH
GLP Compliance	Yes
Test Material	Sodium Nonanoyloxybenzene Sulfonate (NOBS extrudate: 78% C9 AOBS)
Animal Species	Mice
Number of Animals	5 mice/group 4 dose groups, vehicle control (reverse osmosis water), naïve control
Dosing	For each treatment group, five mice were treated daily for three consecutive days by direct epicutaneous application of 25 µl of test article to each ear. In addition a vehicle control (reverse osmosis water) and a naïve control (no treatment) were evaluated. Approximately 71 hours after final test application, mice were injected i.v. in the tail vain with tritiated thymidine to label proliferating cells.
Observations	Mice were observed immediately prior to and approximately 2-4 hours after dosing for any significant alterations in appearance of the application site. Mice were observed twice daily for general health and mortality. Five hours after injection, lymph nodes were harvested and single cell suspensions prepared and quantitated by liquid scintillation spectrometry.
Results and Discussion	All animals appeared normal throughout the study. Body weight gain was noted for all treatment animals during the day -1 and day 6 interval. The stimulation indices of lymph nodes were calculated for each treatment group compared to controls. The groups treated with 10%, 5.0%, 1.0% and 0.5% demonstrated stimulation indices of 0.5, 0.6, 0.9, and 0.7, respectively. A stimulation index of 3.0 (three fold increase over controls) would be considered a positive immunological response for sensitization.
Conclusion	Treatment with the test article did not result in an increase in lymph node proliferation compared to controls demonstrating the test material is not a dermal contact allergen.
Klimisch criterium	1

[4.16] 28 Day Subchronic Percutaneous Toxicity Study

Study Title	28 Day Subchronic Percutaneous Toxicity Study in Rabbits
Date	October 22, 1982
Test Facility	Springborn Life Sciences Laboratories, Inc. Spencerville, OH USA
GLP Compliance	Yes
Test Material	Sodium Octanoyloxybenzene Sulfonate (C8 AOBS) 50% Sodium Decanoyloxybenzene Sulfonate (C10 AOBS) 50%
Animal Species	New Zealand White Rabbits weighing between 2.0 - 3.0 kg.
Number of Animals	10 rabbits/group (5 males, 5 females); 2 treatment groups and 1 control
Dosing	Water vehicle control, 1.5% or 20% C8/10 AOBS in water (2 ml/kg dosing volume). Dosing on abraded skin for 7 hours/day, 5 days/week for 4 weeks. All test sites are washed with tepid water approximately 7 hours after application.

Observations	Animals were observed daily for overt signs of toxicity, mortality and the skin was graded each day of dosing. Body weights were recorded weekly. At necropsy, liver and kidneys were weighed and a hematological assessment including hemoglobin, hematocrit, white blood cell count, red blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, and differential white blood cell count determined for each animal. All animals were necropsied and gross observations recorded. Tissues listed below were taken at the end of the study for microscopic evaluation. Organ weights were recorded for the liver and kidneys. Histology - A sample of the following tissues were collected, preserved in 10% neutral buffered formalin and examined microscopically: Lung — Heart Aorta — Tongue Trachea, esophagus, thyroid — Submandibular lymph node Ileocecocolic lymph node — Stomach Liver — Gall bladder Duodenum — Jejunum Ileum — Cecum, colon Urinary bladder — Kidneys Prostate & seminal vesicle — Testis & epididymis Ovaries, vagina, uterine horns — Adrenals Thymus — Psoas muscle Spleen — Pancreas Bone — Skin (test site) Brain — Lumbar spinal cord Sciatic nerve — Submandibular salivary gland Pituitary gland — Eyes Gross lesions
Results and Discussion	No mortalities or clinical signs of toxicity occurred except for diarrhea and soft stools (also in control group). There were no changes in body weights, food consumption, ophthalmoscopy, hematology, absolute or relative organ weights or effects in the macroscopic and microscopic pathology, except for skin. Skin responses at the test site, both gross and microscopic, increased with the concentration of test article. Slight erythema and desquamation were observed in the 1.5% group. Exposure to 20% caused slight erythema, edema and desquamation and slight to moderate atonia and fissuring. The microscopic evaluation of the skin from this group revealed dermal effects, which included inflammation, parakeratosis, acanthosis, hyperkeratosis, and vesiculation.

Conclusion	The application of test material at levels up to 20% (0.4 g/kg/day) to the abraded skin of rabbits did not cause any detectable systemic toxicity. The effects of C8/10 AOBS appears to be limited to dermal irritation and microscopic changes at the application site when applied to the skin up to 20% w/v and dosed 5 days/week for 4 weeks. The degree of irritation appears to be dose related.
Klimisch criterium	1

[4.17] Absorption, distribution, metabolism, and excretion (ADME) study

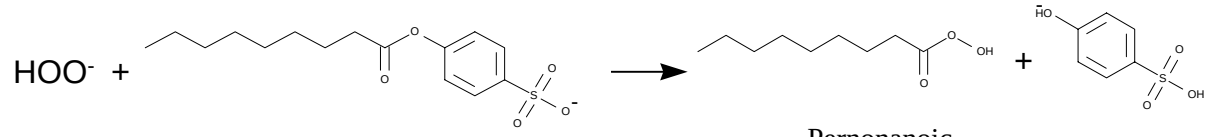
Study Title	The absorption, distribution, metabolism, and excretion of nonanoyloxybenzene sulfonate after oral or dermal dosing
Date	July 15, 1983
Test Facility	Procter & Gamble Company, Miami Valley Laboratories
GLP Compliance	Yes
Test Material	^{14}C Nonanoyloxybenzene Sulfonate (NOBS) - (uniformly ring labeled) The radiochemical purity of the test material was 97%.
Animal Species	Sprague Dawley Rats
Number of Animals	4 male rats/group, each male weighing between 175-225 grams
Dosing	Animals are food-fasted overnight before dosing and for four hours after dosing. Radiolabeled test material was administered by the following exposure routes at a dosage of 10 mg/kg: Oral gavage alone and with bile duct canulation- Vehicle was distilled water with concentration of test material at ~2.0 mg/g (5-10 μCi/g) Dermal - Vehicle was distilled water with concentration of test material at ~20 mg/g (50-100 μCi/g). Approximately 0.1g solution applied.
Observations	Fecal and urine samples were collected at 24, 48 and 72 hours after dosing. Carbon dioxide samples were collected at 8 hour intervals for 72 hours. At the end of the test period, the cage was washed with 0.1N HCl. At necropsy the following tissues and samples were collected and analyzed for radioactivity: Urine, feces, CO2, blood, plasma, liver, kidney, testes, heart, lung, spleen, pancreas, brain, bone marrow, muscle (hink limb), bone (femur), adipose (at the psoas), GI tract, GI tract wash, carcass, cage wash.

Results and Discussion	The dermal ADME study showed there was no significant absorption by this route of exposure. Less than 1% was absorbed with 0.56 ± 0.18% eliminated from urine, < 0.02% via CO2, and < 0.16% via faeces after 72 hours. Recovery from the skin application site and the cage wash was 99.1 ± 1.0% and 0.14 ± 0.06%, respectively. Total recovery was 101.9 ± 0.7%. NOBS was rapidly absorbed and eliminated in the oral (gavage) ADME study. Essentially all of the oral dose was eliminated in 72 hours; 80.2 ± 8% via urine, 1.6 ± 0.1% via faeces, and < 0.22% via CO2, and 19.7 ± 6.1% via the cage wash. At 72 hours after dosing, there was no concentration of the 14C-labelled material in any of the tissues examined including reproductive tissues. Bile duct canulation showed enterohepatic circulation did not occur. Total recovery was 101.8 ± 3.3%. HPLC analysis of the urine showed that no parent compound was excreted. Approximately 99% of the radioactivity in the urine represented a single metabolite consistent in HPLC retention time with hydroxybenzene sulphonate (phenol sulphonate).
Conclusion	These ADME data indicate that NOBS is very poorly absorbed upon dermal exposure (the most relevant route of exposure) and highly absorbed following oral exposure. Absorbed material appears to be rapidly metabolised (via cleavage of the ester linkage) with excretion of the phenol sulphonate moiety and assumed normal catabolism of the fatty acid moiety via the established odd-chain fatty acid pattern (AL Lehninger, Biochemistry, 2nd edition, 1975, chapter 20, p.555).
Klimisch criterium	1

APPENDIX B: Degradation of NOBS in the wash solution [1]

A. Perhydrolysis - major pathway

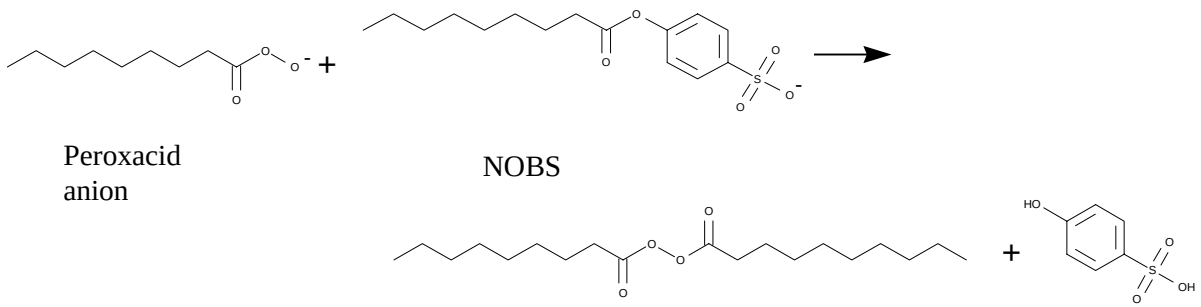
Perhydrolysis is the desired and favored reaction under wash conditions. Under the temperature and pH conditions created by the detergent formula in the wash solution, sodium perborate monohydrate releases hydrogen peroxide that reacts with NOBS to form the peroxy acid, pernonanoic acid, and at the same time releases phenol sulfonate. These reactions are largely complete within the first two minutes of the wash.



Peroxide anion | NOBS | Pernonanoic acid | Phenol Sulfonate

B. Diacylperoxide formation - minor pathway

Detergent formulations containing NOBS are designed to minimize diacyl peroxide formation. Like the peroxide anion, pernonanoic acid can also react with the electrophilic carbonyl carbon of NOBS to form a diacylperoxide. Since diacylperoxide is a less efficient bleach than the peroxy acid, laundry detergents are designed to adjust several conditions in the wash solution to minimize its formation.



Peroxacid anion | NOBS | Diacylperoxide | Phenol Sulfonate

[1] Degradation data on a similar ingredient were published in: Calvin GC (1992) Risk management case history - Detergents. In: Richardson ML (ed) Risk management of chemicals. ISBN 0-85186-467-8. pp: 120-136.

C. Hydrolysis - minor pathway

Detergent formulations containing NOBS are designed to minimize alkaline hydrolysis of the ester bond in NOBS. This reaction can be catalyzed by the hydroxyl ion released from perborate and result in formation of the nonanoic acid and phenol sulfonate. Since neither of these products possess bleaching, sanitizing or other properties beneficial to detergent performance, hydrolysis of NOBS detracts from the efficacy of NOBS.

The *n*-pernonanoic acid is the major bleaching species so the perhydrolysis is the favored reaction. The rate of perhydrolysis is much greater than the rate of hydrolysis because the reaction with the peroxy anion (HOO^-) is approximately 150-fold faster than that with the hydroxyl ion (HO^-) with carbon centered electrophiles. This minimizes the hydrolysis reaction in the wash. The rate of diacylperoxide formation is a function of wash temperature, pH and perborate concentration. Formation of this less efficient bleach is minimized (<10%) by keeping the pH near 10 using sodium carbonate and providing an excess perborate relative to NOBS. Thus, the perhydrolysis reaction predominates.

D. Relative stability of NOBS and pernonanoic acid

1. Dry conditions

Under dry conditions, for example, in the dry detergent granules, the pernonanoic acid will not be present. NOBS will be present and is quite stable.

2. Wet conditions

As soon as the detergent granules are added to the wash water, the reactions described above will be initiated. Under wet conditions, perhydrolysis rapidly occurs and NOBS has a half-life of about 15-30 seconds. The half-life of the pernonanoic bleach is also relatively short depending on the amount of soil in the laundry. Based on consumer data of average soil load in a wash and timed trials, over 90% of the pernonanoic acid bleach is consumed during the first 8 minutes of the wash cycle. Following completion of the wash cycle, wash water would normally be released into the sewer system and a POTW for treatment.

E. Analytical data on degradation of NOBS in wash solution

In the experiment described below, the degradation of NOBS was determined in a detergent solution at 1%, reflecting a typical use concentration washing.

1. Methodology

NOBS concentration:	1% aqueous detergent solution
Time-points:	0, 1, 3 and 5 minutes
Temperature:	40^{o}C
Product:	US detergent with bleach

INGREDIENT	%

SURFACTANTS	
Anionic surfactants	18.25
Nonionic surfactant	1.43
BUILDERS	40.54
BLEACH	
Perborate-monohydrate	2.23
NOBS	1.92
Others	0.49
ENZYMES	0.26
MISCELLANEOUS	
Sodium sulfate	17.48
Others	4.43
PERFUME	0.23

Ten grams of detergent was added to 1 liter of water stirred in a Sotax at 150rpm. Aliquots of 1ml were taken from this solution after 1, 3, or 5 minutes, quenched with acidified water and analyzed by HPLC.

2. Results

The table below presents the concentration of residual NOBS in a wash solution 1 to 5 minutes after the start of a wash cycle.

Time (min)	% of initial
Initial	100.0
1	9.4
3	nd (i.e., < 1%)
5	nd(i.e., < 1%)

3. Conclusion

The degradation of NOBS at 40^{o}C in a 1% aqueous solution of laundry detergent is extremely fast: after 3 minutes, NOBS could no longer be detected.

APPENDIX C: Comparison of P&G to E-FAST Exposure Estimates

To provide a basis for understanding how the results of an assessment conducted by the US EPA for consumer exposure might differ from the P&G assessment, the **E-FAST** model (Exposure and Fate Assessment Screening Tool) was used to evaluate the consumer exposure to NOBS. E-FAST was developed by Versar, Inc. for U.S. EPA's Office of Pollution Prevention, Economics, Exposure and Technology Division. E-FAST provides screening level estimates of concentrations of chemicals released to air, surface water, landfills, and from consumer products and can estimate potential dermal, inhalation and ingestion rates resulting from these releases. Modeled estimates of concentrations and doses are designed to provide high end to bounding estimates of exposure for use in screening level assessments. Information about E-FAST is available via OPPT's Exposure Assessment Tools and Models Web site: www.epa.gov/opptintr/exposure.

NOBS is used in P&G granular and tablet laundry detergents, however, E-FAST does not contain data for estimating exposure from use of a granular laundry detergent; therefore, E-FAST's Liquid Laundry Detergent scenario was used. As discussed in [3.4], the most likely scenarios for consumer exposure to NOBS are skin contact during hand laundering and during use of a concentrated paste for pretreatment of fabric.

Overview of Differences in Assessment Approaches

In conducting these exposure calculations using E-FAST, it must be recognized that there are inherent differences in the ways that the exposure parameters are expressed in E-FAST compared to those in the P&G assessment described in the previous section. For example, rather than using a use concentration of consumer product, E-FAST uses a factor representing the amount retained on skin which is equal to the thickness of the product film on the skin times the dilution fraction of the product in water times the product density. For example, for NOBS hand laundering, the amount retained on skin would be 1.1 x 10-5 g/cm2 (i.e., 0.005 cm thickness of a liquid laundry detergent product film on skin (E-FAST default) times 0.002 dilution fraction for a liquid laundry detergent (E-FAST default) times1.1 g/cm3 for granule product density). Also rather than using a factor representing the area of exposed skin, E-FAST uses a surface area to body weight value. For example for NOBS hand laundering, E-FAST would use 15.6 cm2/kg (i.e., 1,120 cm2 which is the median value for the surface area of hands (E-FAST default) divided by a body weight of 71.8 kg (E-FAST default)).

One major difference between the P&G and the E-FAST exposure calculations is that where available, P&G incorporates a dermal absorption fraction, which for NOBS is 1%. The percent dermal absorption represents the fraction of NOBS that will penetrate the skin and thus the internal dose. However, E-FAST does not allow for the use of a dermal absorption fraction. Therefore, the effect of a dermal absorption fraction less than 100% needs to be calculated by hand from the E-FAST results.

Comparison of Default Values

A comparison of the default values used in the P&G and E-FAST dermal exposure assessments for hand laundry and some of the intermediate calculated values are presented in Table 1.

Table 1. Comparison of Exposure Factors used in P&G and E-FAST exposure calculations for Hand Laundry Scenario

Parameter	EPA default or calculated value	P&G default or calculated value
Frequency of Use -- FQ	52/yr = 0.14/day	0.38/day
Film thickness - FT	0.005 cm	0.0024 cm
Dilution factor - DF	0.002	
Use concentration of product - PC		5 mg/ml
Product density - PD	1.1 g/cm^3	1.1 g/cm^3
Weight Fraction of NOBS in Product - WF	0.06	0.06
Amount Retained on Skin -AQ	1.1 x 10^{-5} g/cm^2-event	1.2 x 10^{-5} g/cm^2 - event (calc)
Body weight - BW	71.8 kg	70 kg
SA/BW ratio	15.6 cm^2/kg	27.1 cm^2/kg (calc)
Surface area exposed – SA [(a)]	1,120 cm^2 (calc)	1,900 cm^2
Concentration of NOBS in solution -- Q	0.00013 g/cm^3 (calc)	0.0003 g/cm^3 (calc)
Amount of solution on skin -- SQ	5.6 cm^3 (calc)	4.56 cm^3 (calc)

[(a)] EPA assumes that hands are exposed and P&G assumes that both hands and forearms are exposed.

Table 2 gives the same comparison for the pre-treatment scenario. However since there is no default pretreatment scenario in E-FAST the exposure factors were entered in the user-defined scenario option. For this reason, many of the parameters entered are consistent with those in the P&G scenario.

Table 2. Comparison of Exposure Factors used in P&G and E-FAST exposure calculations for Pretreatment Scenario

Parameter	EPA default, user defined or calculated value	P&G default or calculated value
Frequency of Use -- FQ	1/day	1/day
Film thickness - FT	0.005 cm	0.0024 cm
Dilution factor - DF	1	1

Use concentration of product - PC	.55 g/cm^3	1.1g/cm^3
Product density - PD	1.1 g/cm^3	1.1 g/cm^3
Weight Fraction of NOBS in Product - WF	0.06	0.06
Amount Retained on Skin -AQ	0.0028 g/cm^2-event	0.0026 g/cm^2 - event (calc)
Body weight - BW	71.8 kg	70 kg
SA/BW ratio	3.9 cm^2/kg (calc)	2.8 cm^2/kg (calc)
Surface area exposed – SA [(a)]	280 cm^2	200 cm^2
Concentration of NOBS in solution -- Q	0.033 g/cm^3 (calc)	0.066 g/cm^3 (calc)
Amount of solution on skin -- SQ	1.4 cm^3 (calc)	0.48 cm^3 (calc)

[(a)] Both use 25% of hands are exposed.

Comparison of Exposure Assessment Results

For both exposure scenarios the respective equations used to calculate the external exposure are for EPA was Exposure (g/kg/day) = FQ x AQ x WF x SA/BW and for P&G was Exposure (g/kg/day) = FQ x Q x SQ / BW and where Q = PC x WF x 10^{-3} , AQ = FT x DF x PD or Q/WT x SQ / SA and SQ = FT x SA. The external exposure assessment results are compared in Table 3.

Table 3. Comparison of External Exposure Calculated by E-FAST and P&G.

Scenario	E-FAST	P&G
Hand Laundry	1.3 x 10^{-6} g/kg/day	7.5 x 10^{-6} g/kg/day
Pretreatment	6.6 x 10^{-4} g/kg/day	4.1 x 10^{-4} g/kg/day

The above estimates conservatively assume 100% absorption. When there is evidence to support less than 100% dermal penetration the resulting internal dose may be determined by multiplying the external exposure by a dermal penetration fraction. The ADME study found that NOBS was poorly absorbed (less than 1%). E-FAST does not allow for the use of a dermal absorption fraction. Therefore, this needs to be calculated by hand from the E-FAST results, and is shown in Table 11.

Table 4. Comparison of Internal Doses Calculated by E-FAST and P&G.

Scenario	E-FAST	P&G
Hand Laundry	1.3 x 10^{-8} g/kg/day	7.5 x 10^{-8} g/kg/day
Pretreatment	6.6 x 10^{-6} g/kg/day	4.1 x 10^{-6} g/kg/day

Conclusion: The consumer exposure estimates from the E-FAST runs are comparable in magnitude to those estimates derived from typical calculations developed by P&G. Both methods arrived at a external dermal exposure without consideration of dermal penetration of less than 0.01 mg/kg/day from hand laundering of fabrics and less than 1 mg/kg/day for pretreatment for a 6% NOBS granular laundry detergent. The resulting internal dose is less than 0.0001 mg/kg/day from hand laundering and less than 0.01 mg/kg/day for pretreatment. Using either method, the exposure estimates demonstrate very low potential for consumer exposure to NOBS from use of a granular laundry detergent.

APPENDIX D: Exposure Summaries

Outline A: Basic Chemical Manufacturing and Use Exposure-Related Information

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
II. Scope	
(2) Activity	Chemical manufacture and use
(3) Coverage	Entire U.S.
III. Chemical information	
(4)Chemical Category	--
(5) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(6) CAS Number (s)	91125-43-8
(7) Other Constituents (If Applicable)	
(8) Physical Form	Extrudate (particles 500 - 1000 μm)
IV. Production, Import and Use	
(9) Estimated Volume	11,100 metric tons
(10) Function/Product Use Categories	Bleach activator in granular and tablet laundry detergents used by consumers (100%)
V. Potential Releases and Exposures	
(11) General description of Potential Releases and Exposures	Potential exposures include manufacturing and formulation plant workers, consumers and the environment.
(12) Discussion of Factors that Mitigate or Exacerbate Releases and Exposures	NOBS is produced in an enclosed, controlled release process. Low volatility and production as an extrudate minimizes potential for inhalation exposure by workers and consumers. Detergents containing NOBS are formulated in continuous operation, dedicated equipment systems, where no releases occur during regular production. For equipment clean-up, hot water is used and disposed via the drain to waste water treatment. Personal protective equipment further minimizes workplace exposure. In its intended use, NOBS is degraded (>99% in 3 minutes) during the laundry wash process, prior to wastewater disposal. Any residual NOBS is rapidly and completely biodegraded and highly removed during wastewater treatment (>95% removal), resulting in negligible aquatic and indirect exposure.
(13) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate surface water concentration following consumer use, disposal and wastewater treatment.
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Following consumer use in laundry detergents, unreacted NOBS is disposed to sewer and waste water treatment. This study models the concentration of unreacted, unremoved NOBS in surface waters.
(10) Exposure Medium Modeled	Aquatic
(11) Input parameters	Per capita water use is 364 l/cap.day, a US population of 2.5×10^8 (EPA defaults), 99% degradation of 11,100 t/y during the wash, no loss of NOBS in the sewage collection and conveyance system, a removal of 95% during waste water treatment
(12) Results	0.003 ng / l (50^{th} %) to 0.040 ng / l (10^{th} %)
(13) Reliability	Assessment conservatively assumes that neither hydrolysis nor perhydrolysis occurs in sewer conveyance system. Removal in wastewater treatment was conservatively assumed to be 95% vs 99+% observed in studies.
(14) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate surface water concentration following manufacturing release and wastewater treatment. (Batesville, AK)
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Manufacturing release due to cleaning and spillage is disposed to sewer and wastewater treatment. This study models the concentration of unremoved NOBS in surface waters.
(10) Exposure Medium Modeled	Aquatic
(11) Input parameters	335 days of operation on site, 0.15 % loss from equipment cleaning (e.g., wash down of the tower, scrubber water) and from spillage (U.S. EPA 1996), all the aqueous release goes to municipal waste water treatment before release to the environment.
(12) Results	16 μg / l
(13) Reliability	Assessment conservatively assumes that neither hydrolysis nor perhydrolysis occurs following discharge at the manufacturing site. Removal in wastewater treatment was conservatively assumed to be 95% vs 99+% observed in studies.
(14) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate surface water concentration following formulation plant release and wastewater treatment. (Augusta, GA)
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Formulation release due to cleaning and spillage is disposed to sewer and wastewater treatment. This study models the concentration of unremoved NOBS in surface waters.
(10) Exposure Medium Modeled	Aquatic
(11) Input parameters	Forty-five % of NOBS produced in the Eastman plant (i.e., 5,001 metric tons/y) is formulated in the Augusta plant.
(12) Results	0.23 μg / l (7Q10, 10^{th} %tile low flow)
(13) Reliability	Assessment conservatively assumes that neither hydrolysis nor perhydrolysis occurs following discharge at the processing site. Removal in wastewater treatment was conservatively assumed to be 95% vs 99+% observed in studies.
(14) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate surface water concentration following formulation plant release and wastewater treatment. (Pineville, LA)
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Formulation release due to cleaning and spillage is disposed to sewer and wastewater treatment. This study models the concentration of unremoved NOBS in surface waters.
(10) Exposure Medium Modeled	Aquatic
(11) Input parameters	Fifty-five % of NOBS produced in the Eastman plant (i.e., 6,112 metric tons/y) is formulated in the Alexandria/Pineville plant.
(12) Results	0.38 μg / l: (7Q10, 10^{th} %tile low flow)
(13) Reliability	Assessment conservatively assumes that neither hydrolysis nor perhydrolysis occurs following discharge at the processing site. Removal in wastewater treatment was conservatively assumed to be 95% vs 99+% observed in studies.
(14) Remarks	

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate consumer exposure during use in laundry detergent-hand laundering scenario for comparison with P&G calculations.
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Consumer dermal exposure to ingredients in granular and tablet laundry detergents can arise from hand laundering of delicate fabrics after dilution in wash water. This study models the external exposure of this scenario.
(10) Exposure Medium Modeled	
(11) Input parameters	EPA's E-FAST model was run using default values in the Liquid Laundry Detergent scenario (model does not contain granule scenario). Parameters included a frequency of 52 times per year, solution concentration of 0.00013 g/cm^3, exposure of both hands and film thickness of 0.005 cm.
(12) Results	1.3×10^{-6} g/kg/day
(13) Reliability	The calculated result is an external exposure estimate. E-FAST assumes 100% dermal penetration. Actual dermal penetration of this substance is less than 1%. The hand laundering task duration is in the range of 5-10 minutes, which is not considered in the calculations. Thus the estimate is very conservative.
(14) Remarks	The purpose of running this model was to compare the results with calculations developed by P&G, which produced a very comparable 7.5×10^{-6} g/kg/day external exposure estimate for this scenario.

Outline C: Modeling Evaluations

I. Identification Information	
(1) Assessment Identification and Date	NOBS—October 2001
(2)Chemical Category	--
(3) Chemical Name (s)	Nonanoic acid, sulfophenyl ester, sodium salt (NOBS)
(4) CAS Number (s)	91125-43-8
II. Modeling Objective	
(5) Modeling Study Objective	Estimate consumer exposure during use in laundry detergent-fabric pretreatment scenario for comparison with P&G calculations.
III. Description of Model	
(6) Tool or Model	E-FAST-US EPA Screening Level Model
(7) Validation/Peer Review	
(8) Availability and Documentation	EPA Website http://www.epa.gov/opptintr/exposure/docs/efast.htm
IV. Description, Inputs and Results	
(9) Description of Modeled Scenario	Consumer exposure to ingredients in granular and tablet laundry detergents can arise from dermal exposure during pretreatment of fabrics, prior to machine washing. This study models the external exposure of this scenario.
(10) Exposure Medium Modeled	
(11) Input parameters	EPA's E-FAST model was run with the user-defined scenario (model does not contain pretreatment scenario). Parameters included a frequency of 365 times per year, solution concentration of 0.033 g/cm^3, exposure to 25% of hands and film thickness of 0.005 cm.
(12) Results	6.6×10^{-4} g/kg/day
(13) Reliability	The calculated result is an external exposure estimate. E-FAST assumes 100% dermal penetration. Actual dermal penetration of this substance is less than 1%. The fabric pretreatment task duration is in the range of 5-10 minutes, which is not considered in the calculations. Thus the estimate is very conservative.
(14) Remarks	The purpose of running this model was to compare the results with calculations developed by P&G that produced a very comparable 4.1×10^{-4} g/kg/day external exposure estimate for this scenario.