Human & Environmental Risk Assessment on ingredients of household cleaning products

- Version 1 –
April 2005

Secondary Alkane Sulfonate (SAS)
(CAS 68037-49-0)

The content of this document has been prepared and reviewed by experts on behalf of HERA with all possible care and from the available scientific information. It is provided for information only. Much of the original underlying data which has helped to develop the risk assessment is in the ownership of individual companies.

1. Executive Summary

General

Secondary Alkane Sulfonate (SAS) is an anionic surfactant, also called paraffine sulfonate. It was synthesized for the first time in 1940 and has been used as surfactant since the 1960ies. SAS is one of the major anionic surfactants used in the market of dishwashing, laundry and cleaning products.

The European consumption of SAS in detergent application covered by HERA was about 66.000 tons/year in 2001.

Environment

This Environmental Risk Assessment of SAS is based on the methodology of the EU Technical Guidance Document for Risk Assessment of Chemicals (TGD Exposure Scenario) and the HERA Exposure Scenario.

SAS is removed readily in sewage treatment plants (STP) mostly by biodegradation (ca. 83%) and by sorption to sewage sludge (ca. 16%). Only around 1% of the mass load from sewage is discharged into surface water and readily biodegraded in river as well.

The Predicted Environmental Concentrations (PECs) for STP, water, sediment and soil were estimated for both scenarios (HERA and TGD). Due to the low volatility of SAS air concentrations are very low and are therefore not considered in this assessment.
For the aquatic compartment acute and chronic data for all three trophic levels are available and the $PNEC_{aquatic}$ was calculated from the $NOEC_{reproduction}$ based on a 21d Daphnia study. As no sediment and terrestrial ecotoxicity data are available the equilibrium partitioning method was used to derive a $PNEC_{sediment}$ and $PNEC_{soil}$. The $PNEC_{STP}$ was derived from a chronic study on bacterial cell growth.

The Environmental Risk Characterisation for all compartments (STP, water, sediment and soil) and both scenarios (HERA and TGD) gave PEC/PNEC quotients below 1. From the comparison of the Predicted Environmental Concentrations with measured data it is obvious that the HERA Scenario is more realistic than the TGD Scenario.

Indirect exposure of humans via the environment was also taken into account. Based on the calculated local and regional doses in drinking water and food indirect exposure for humans can be neglected.

Human Health

The presence of SAS in many commonly used household detergents gives rise to a variety of possible consumer contact scenarios including direct and indirect skin contact, inhalation, and oral ingestion derived either from residues deposited on dishes, from accidental product ingestion, or indirectly from drinking water.

The consumer aggregate exposure from direct and indirect skin contact as well as from inhalation and from oral route in drinking water and dishware results in an estimated total body burden of 3.87 µg/kg bw/day.

The toxicological data show that SAS was not genotoxic in vitro or in vivo, did not induce tumors in rodents after two years daily dosing using both, the oral and dermal route of exposure, and failed to induce either reproductive toxicity or developmental or teratogenic effects. The critical adverse effects identified are of local nature mainly due to the irritating properties of high concentrated SAS.

Comparison of the aggregate consumer exposure to SAS with a systemic NOEL of 180 mg/kg body weigh per day (assuming 90% absorption; adapted from Michael, 1968) which is based on a chronic feeding study, results in an estimated Margin of Exposure (MOE) of 46500. This is a very large Margin of Exposure, large enough to account for the inherent uncertainty and variability of the hazard database and inter species and intra species extrapolations (which are usually conventionally estimated at a factor of 100).

Neat SAS is an irritant to skin and eyes in rabbits. The irritation potential of aqueous solutions of SAS depends on concentration. However, well documented human volunteer studies indicate that SAS up to concentrations of 60% active matter is not a significant skin irritant in humans. Local effects of hand wash solutions containing SAS do not cause concern given that SAS is not a contact sensitizer and that the concentrations of SAS in such solutions are well below 1% and therefore not expected to be irritating to eye or skin. Laundry pre-treatment tasks, which may translate into brief hand skin contact with higher concentrations of SAS, may occasionally result in mild irritation easily neutralized by prompt rinsing of the hands in water. Potential irritation of the respiratory tract is not a concern given the very low levels of airborne SAS generated as a consequence of cleaning spray aerosols or laundry powder detergent dust.

In view of the extensive database on toxic effects, the low exposure values calculated and the resulting large Margin of Exposure described above, it can be concluded that use of SAS in household laundry and cleaning products raises no safety concerns for the consumers.

2. Contents

3. Substance Characterisation

Secondary alkane sulfonate (SAS) is an anionic surfactant and was manufactured by sulfoxidation of n-paraffins already in 1940 (Platz and Schimmelschmidt, 1940). It was introduced as surfactant in the 1960s. Very good water solubility, high wetting action, pronounced foaming power, excellent grease- and soil dispersing properties make SAS an important surfactant ingredient in detergents especially for dish washing (Clariant, 2000).

Several reviews for SAS are available which were used as starting point of this assessment (Painter, 1992; Vollebregt and Westra, 1998; Vollebregt and Westra, 2000; Madsen et al, 2001).
In addition a Life-cycle assessment (LCA) for surfactants exists where SAS is covered as well (Stalmans et al, 1995).

3.1 CAS No. and Grouping Information

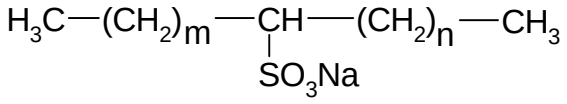
CAS Numbers in use for EU
CAS No. 85711-69-9 and EINECS No. 288-330-3 for "Sulfonic acids, C13-17-sec-alkane, sodium salts" represent the main SAS type used in the European market and are addressed in this risk assessment. The assessment provided in this report also includes other CAS-No. given below in Table 3.1.1 with their respective CAS/EINECS numbers and names:

Table 3.1.1: CAS and EINECS numbers of SAS in the European market

CAS No.	EINECS No.	NAME
85711-69-9	288-330-3	Sulfonic acids, C13-17-sec-alkane, sodium salts
68037-49-0	268-213-3	Sulfonic acids, C10-18-alkane, sodium salts (used in IUCLID)
97489-15-1	307-055-2	Sulfonic acids, C14-17-sec-alkane, sodium salts
85711-70-2	288-331-9	Sulfonic acids, C14-18-sec-alkane, sodium salts
75534-59-7	-	Sulfonic acids, C13-18-sec-alkane, sodium salts

Chemical structure and composition

SAS in the European market is a specific and rather constant mixture of closely related isomers and homologues generated by sulfoxidation of n-paraffins. SAS contains a sulfonate group distributed over the n-paraffin chain and mainly located at one of the secondary C-atoms, as shown below (Clariant, 2000):



m + n = 11-14
Average chain length: $C_{15,9}$
Average Mol weight 328 g/Mol

The linear alkyl chain (linearity > 98%) has typically 14 to 17 carbon units with an average of 15,9 carbon atoms which corresponds to an average molecular weight of 328 Dalton. The C-chain distribution is given in table 3.1.2

Table 3.1.2: C-chain length distribution

Carbon chain	Distribution
< C13	< 2 %
C13 – C15	> 45 %
C16 – C17	< 55 %
> C17	< 4 %

The content of primary alkane sulfonates is < 1 %. The sulfoxidation in the presence of UV light and water results in a mixture of about 90 % mono- and 10 % disulfonic acids (Hauthal, 1995), which contribute favourably to the well-balanced application properties. The paraffin cut used for the sulfoxidation ensures a product characterised by optimum foaming, wetting, emulsifying, washing and cleaning performance. The chemical composition guarantees good solubility, strong surfactant properties and high chemical stability at high and low pH values. The commercial SAS consists of many individual components (Hauthal, 1995). The present risk assessment adopts a category approach, i.e., considers the fate and effects of the SAS mixture as described above, rather than of each isomer and homologue separately. Consequently, calculated values of SAS properties refer to the average carbon chain length of about 16.

The typical composition and the appearance of commercial products is given in table 3.1.3 (Clariant, 2000). While SAS obtained from the sulfoxidation, is a waxy residue, SAS 60 and SAS 30 are aqueous mixtures of SAS.

Table 3.1.3: Typical composition of commercial SAS 60 and 30 (Clariant, 2000)

	SAS 60	SAS 30
Active content	ca. 60 %	ca. 30%
Appearance	yellowish soft paste	clear faintly yellowish liquid
Sodium sulfate	max. 4,2 %	max. 2,1 %
Residual paraffins	max. 0,7 %	max. 0,4 %

Physico-chemical properties

In table 3.1.4 the physico-chemical properties of SAS are given

Table 3.1.4: Physico-chemical data of SAS

Parameter	Value	Reliability	Remark
Physical state	yellowish waxy	1	Clariant, 2003
Bulk density (kg/m^3)	ca. 600	1	Clariant, 2003
Melting point (deg C)	< 200 (softening)	1	Clariant, 2003
Boiling point (deg C)	not determ.	-	Clariant, 2003
Vapour pressure at 25 C (Pa)	$5,3*10^{-11}$	2	calculated for C16 SAS[1] (US EPA, 2000a)
Water solubility at 25 C (g/L)	ca. 300	1	Clariant, 2003
log Kow	2,76	2	calculated for C16 SAS[1] (US EPA, 2000b)
Koc (L/kg)	not applicable	-	see Chapter 4.1.1.6
Henry coefficient (unitless)	$3,6*10^{-5}$	2	calculated for C16 SAS[1] (US EPA, 2000c)

pK_a (25 C)	< 0	2	estimated for C16 SAS[1] based on pKa of Methansulfonic acid (Evans, 2003)
pH (20 C, 10g/L)	ca. 7	1	Clariant, 2003

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable
[1] explanation sees following text on Physico-chemical data

Boiling point and Vapour pressure

As SAS is a sodium salt, a very high boiling point can be expected and was therefore not measured. In addition, the vapour pressure of this salt at room temperature is so low that it could not be experimentally determined; instead, it was estimated for 16C-SAS (see table 3.1.4, US EPA, 2000a).

Octanol- water partitioning coefficient K_{ow}

The K_{ow} of SAS cannot be measured because of its surface active properties (Boethling and Mackay, 2000). Instead the K_{ow} was estimated for 8-Hexadecasulfonic acid , sodium salt (16C-SAS) with the US EPA Property Estimation Program KOWWin (see table 3.1.4, US EPA, 2000b) providing all structural fragments available including the ionic sulfonate group.

Henry's Law Constant (HLC)

The estimated HLC of 16C-SAS is very low due to the negligible vapour pressure of 16C-SAS and its high water solubility. Therefore the ionic SAS is not volatile (see table 3.1.4, US EPA, 2000c).

Acid constant pK_a and pH

A pK_a value for the corresponding acid of SAS and for longchain primary or secondary alkanesulfonic acids is not available. Instead the pK_a of Methanesulfonic acid of – 2,6 (Evans, 2003) determined in DMSO was used to estimate that the longchain alkanesulfonic acid having +I inductive carbon chain would increase the pK_a but would be most likely still below 0. This means that the SAS-based sulfonic acid is a very strong

acid and that these sulfonic acids will be completely deprotonated to sulfonates under environmental conditions. In addition the corresponding bases - the alkanesulfonates - are very weak bases and therefore aqueous solutions of these salts are neutral as is demonstrated with the measured pH of a SAS solution (see table 3.1.4).

3.2 Manufacturing Route and Production/Volume Statistics

3.2.1 Manufacturing Route

Basically, secondary alkane sulfonates (SAS) can be manufactured by sulfoxidation and sulfochlorination.

The alkane sulfonates produced by *sulfochlorination* (Reed, 1933) are mainly used for non-detergent technical purposes as they contain undesirable by-products. SAS manufactured by sulfochlorination are not covered in this HERA risk assessment.

The secondary alkane sulfonates manufactured by *sulfoxidation* (Platz and Schimmelschmidt, 1940) are mainly used in household products and have a low content of undesirable by-products. They are prepared by reacting n-paraffins with sulfur dioxide and oxygen in the presence of water whilst irradiating with ultraviolet light. Secondary Alkane Sulfonates (SAS) obtained from sulfoxidation are a mixture of closely related isomers and homologues of secondary alkane sulfonate sodium salts.

$$RH + 2\,SO_2 + O_2 + H_2O \longrightarrow RSO_3H + H_2SO_4$$

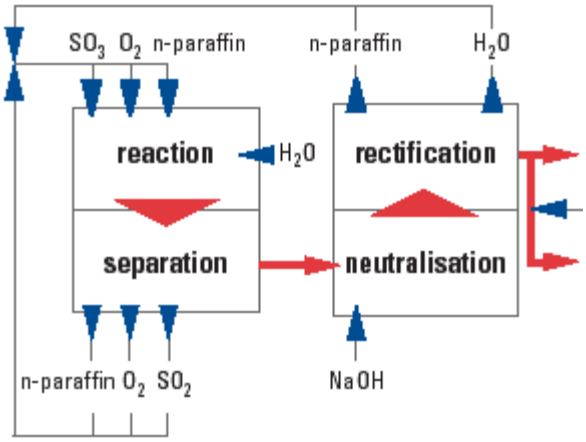
$$RSO_3H + NaOH \longrightarrow RSO_3Na + H_2O$$

The industrial sulfoxidation of n-paraffins is a photooxidation in the presence of water carried out in a multi-lamp reactor. This process does not require any catalyst or solvent. A gaseous mixture of SO_2 and O_2 is introduced into the reaction mixture by gas injection.

The mixture of SO_2, O_2 and n-paraffins is exposed to UV light produced by high-pressure mercury lamps. The reaction gas is circulated and the reaction liquid is removed at the bottom of the reactor. The product phase which is the lower layer is separated and the upper layer which is the (unreacted) paraffin phase, is cooled and replenished with water. The unreacted n-paraffins are returned into the reactor again.

After concentration of the product phase under reduced pressure, separation of the sulphuric acid and neutralization of the concentrate with sodium hydroxide solution, the remaining paraffins are removed from the raw product by steam destillation with superheated steam. The steam distillate is again separated and the paraffins are returned to the reaction mixture. The remaining product melt is finally distributed into water to achieve commercial aqueous SAS products with 60% or 30% SAS content (see figure 3.2.1).

Figure 3.2.1 Sulfoxidation process



3.2.2 Production/Volume statistics

The total alkane sulfonate production capacity in Western Europe (comprising the sulfochlorination and sulfoxidation processes) is estimated to be 81.000 tons/year in 2001 (CESIO, 2003).

Sales and captive use in Western Europe accounts for about 76.000 tons/year in 2001 (CESIO, 2003). According to CESIO (2003), 63 % of the 76.000 tons/year in 2001 are used in household applications (48.000 tons/year). The alkane sulfonates produced via

sulfochlorination are not used in household applications. In addition to the household application, 24 % (18.000 tons/year) alkane sulfonate for Industrial & Institutional use is ultimately released down-the-drain. The remaining 13 % (10.000 tons/year) alkane sulfonate for technical uses (textile, leather, paper, polymers, constructives, paint, coating, inks, minery, metalworking, oil refinery, agriculture, food and feed additives etc.) are basically non-down-the-train applications. For this HERA targeted Risk Assessment the household use (scope of HERA) and Industrial & Institutional use - together 66.000 tons/year - ultimately released down-the-drain, are taken into account.
Most of the commercial SAS is sold as an aqueous solution with 60 % or 30 % active ingredient (see chapter 3.1).

3.3. Use applications summary

Most of the European consumption of SAS is in household cleaning. The far most important use is in dishwashing liquids, other minor applications are laundry detergents, household cleaners, cosmetics hair and body care products, industrial cleaners and special technical sectors (see 5.1.1).

4. Environmental Assessment

4.1. Environmental Exposure Assessment

4.1.1. Environmental Fate

4.1.1.1 Biodegradation in Water

Aerobic biodegradation in water

Results from standard laboratory biodegradation tests

The potential of SAS to biodegrade under aerobic conditions was intensively investigated. The results of these tests were listed in reviews but mostly without sufficient details (e.g. DHI, 2001; Painter, 1992; Schoeberl, 1997; Voolebregth and Westra, 1998). In table 4.1.1.1.1. those biodegradation results were given where sufficient information was available to differentiate between primary and ultimate biodegradation and to check the reliability of the results as well. **Primary biodegradation** (EU, 1999) means alteration in the chemical structure of a substance, brought about by biological action, resulting in the loss of specific properties (e.g. for surfactants surface activity and ecotoxicity). Primary biodegradation of surfactants is often monitored using colorimetric analytical methods (e.g. MBAS Methylene Blue Active Substances). **Ultimate biodegradation** (EU, 1999) is the level of degradation achieved when the test compound is totally utilised by micro-organisms resulting in the production of carbon dioxide (for aerobic conditions), water, mineral salt(s) and new microbial cellular constituents (biomass). Ultimate biodegradation is monitored using analytical methods appropriate for the test method applied (e.g. removal of Dissolved Organic Carbon (DOC), carbon dioxide formation etc). Achieving rapid primary biodegradation for surfactants is required by EU legislation (e.g. EU, 1973; EU, 1982) but only if the surfactant meets the criteria for ready (ultimate) biodegradability it can be concluded that the chemical will undergo rapid and ultimate biodegradation in the environment (EU, 2003b and OECD, 2003).

Table 4.1.1.1.1 Aerobic biodegradation results in standard tests

Ready Biodegradability Tests	**Chain-length**	**Degradability**	**Value (%) (Exposure)**	**Reliability**	**Remark/ Reference**
OECD 301 B (Sturm Test)	C13 - C18	ultimate (CO_2)	56 - 91 (28d)	2	Clariant, 1998
OECD 301 D (Closed Bottle Test)	C12 - C18	ultimate (ThOD)	93 (30d)	2	Hrsak et al, 1981
OECD 301 E (Modif. OECD Screening Test)	C13 - C18	ultimate (DOC)	88 - 96 (28d)	2	Clariant, 1998
	C15 - C17	ultimate (DOC)	98 (28d)	2	Hoechst, 1989a
Inherent Biodegradability Tests	**Chain-length**	**Degradability**	**Value (%) (Exposure)**	**Reliability**	**Remark/ Reference**
OECD 302 B (Zahn-Wellens-Test)	C15 - C17	DOC removal	95 (10d, 28d)	2	Hoechst, 1990
WWTP Simulation Tests.	**Chain-length**	**Degradability**	**Value (%)**	**Reliability**	**Remark/ Reference**
OECD / ISO Confirmatory Test ISO 11733	C14 - C17	primary (MBAS)	97-98	2	Clariant, 1998
	C14 – C17	primary (MBAS)	99,6 – 99,8	2	Hrsak et al, 1981 3 different inocula: sewage, river water and soil microorganisms
OECD 303 A (Coupled Units Test)	C13 - C17	ultimate (DOC)	83 - 96	2	Clariant, 1998
	C13 - C17	ultimate (DOC)	96	2	Hoechst, 1991
	C13 - C17	ultimate (DOC)	99	2	Schöberl, 1997 modern STP settings

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

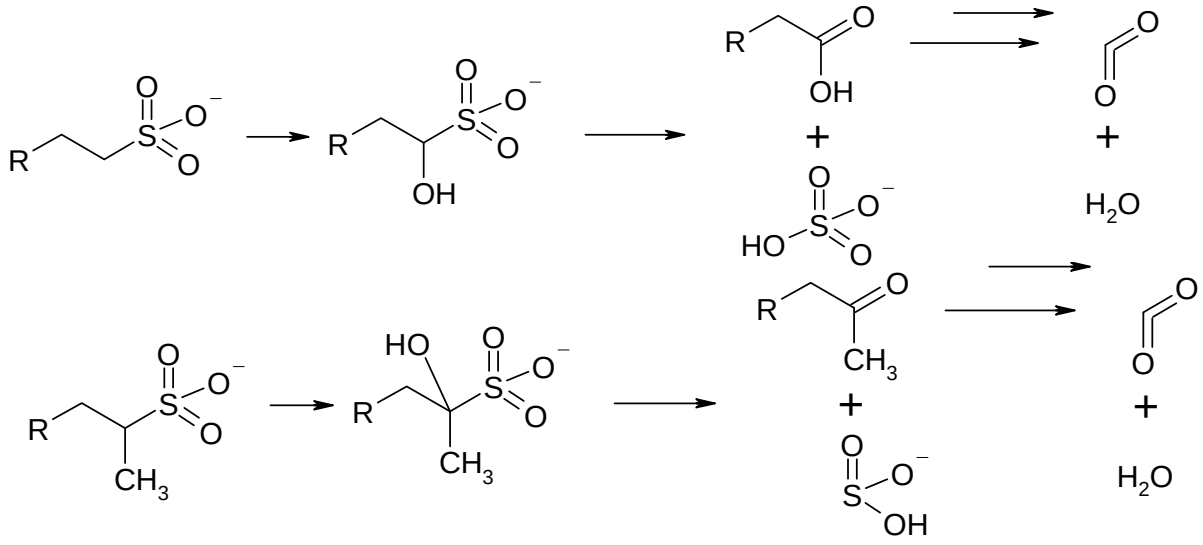
The data show that SAS is ultimately biodegradable and meets the OECD criteria for ready biodegradability. For the following exposure assessment of SAS it is important to note that several comparative studies exist into the biodegradation kinetics of SAS and LAS in standard screening tests. They show unequivocally that primary as well as

ultimate biodegradation of SAS is considerably faster. For instance, MBAS removal in the OECD Screening Test was about 10% after 5 days for LAS while SAS had already attained 85% in this time period (Tegewa, 1989). Similarly, the linear part of the CO_2 evolution kinetics determined in the CO_2 evolution test (OECD 301B) revealed a mineralisation rate of 6.2%/d for SAS and 3.1%/d for LAS (Clariant, 2004). Finally, comparative studies of the CO_2 evolution from radiolabelled (U-^{14}C) SAS and (ring-^{14}C) LAS in a 12-day batch test (Lötzsch et al., 1979) underlined again the faster and more extensive mineralisation of SAS.

The results from the Sewage Treatment Plant Simulation tests show a very high removal. Hrsak et al (1981) have also demonstrated that SAS loadings varying from ca. 50 to 500 mg/L can be fed in to a simulation test system (OECD Confirmatory Test) without any effect on the high primary degradation of SAS.

Metabolic Pathway for SAS

Primary n-alkanesulfonates are metabolised to bisulfite and the corresponding aldehyde (Thysse and Wanders, 1972; Schöberl and Bock, 1980).



R = $C_{10}H_{21}$

The metabolic pathway of SAS is not fully investigated. Thysse and Wanders (1974) isolated an alkane sulfonate hydroxylase which was able to desulfonate n-C12-SAS forming 2-Dodecanone. Swisher (1987) suggested that the first step in metabolism is the

formation of a ketobisulfite, which forms the ketone and bisulfite. The ketone may be further oxidized to an alkylacetate ester. Ester cleavage yields acetate and an alcohol which is further metabolised via ß-oxidation. Based on this metabolic pathway, the formation of recalcitrant metabolites is unlikely. This was also proven experimentally in a special test for the detection of recalcitrant metabolites (Gerike and Jasiak, 1985, 1986).

Biodegradation / Elimination in Continuous Activated Sludge Systems (CAS)

As was shown in table 4.1.1.1.1 SAS is eliminated in Continuous Activated Sludge Systems to a very high extent. Around of 16% SAS is carried over to activated sewage sludge (Field et al., 1995, see Chapter 4.1.2 Removal) and ca. 83% of the elimination determined in CAS Tests can be attributed to biodegradation

Biodegradation and Half-lives of SAS in River water

Schöberl et al. (1998) have measured the primary biodegradation of SAS in river water using a river simulation model (aquatic stair case model) fed with the effluent of a Confirmatory Test and flow rate of 1 m/h. The half-life from the primary degradation in the river simulation model of 0,7 to 0,9 h is in the same order of magnitude as was measured for LAS in a comparable river simulation model ($t_{1/2}$ = 2.2 – 4.7 h) (Steber 1997) and in European rivers (1-3 h) (see HERA, 2002b).

As the LAS data are based on measurements in rivers the half-life for SAS in river water is assumed to be the same and a half-life of 3h is used as realistic worst case.

Anaerobic biodegradation in water

SAS is not biodegraded under strict anaerobic conditions (Field et al., 1995).

4.1.1.2 Biodegradation in Sediment and Soil

Experimental data on the aerobic and anaerobic degradability of SAS in sediment and soil are not available. However, it is justified to make use of the pertinent comprehensive information about LAS (HERA, 2002b) for prediction of the biodegradation kinetics of SAS in sediment and soil. It has been established that primary and ultimate biodegradation of SAS in standard screening tests is faster compared to LAS (see chapter

4.1.1.1). Furthermore, it could be shown (Steber & Richterich, 1993) that the biodegradation of chemicals in screening tests using soil as inoculum is at least as effective as using a standard (sewage) inoculum. Consequently, it can be conservatively concluded that the half-life of LAS in aerated soil ($t_{1/2}$ = 7 d) is also applicable to SAS. In agreement with the EU Technical Guidance Documents on Risk Assessment for Chemical substances (EU, 2003a) the half-life of 7d is also being used in the exposure calculations for aerated sediment.

4.1.1.3 Abiotic Degradation in Air

Due to the very low volatility of SAS degradation in air is not a relevant fate pathway and therefore is not considered in this assessment.

4.1.1.4 Abiotic Degradation in Water, Sediment and Soil

SAS does not hydrolyse in water, sediment and soil. The molecular structure indicates that photolysis in surface water and top soil can be neglected as well.

4.1.1.5 Volatilisation

Based on the Henry coefficient of SAS (see table 3.1.2) volatilisation is not a relevant elimination factor.

4.1.1.6 Sorption to soil, sediment and sludge

The sorption behaviour of SAS was determined for 5 Eurosoils and 1 Sediment (Clariant, 2001a) according to the OECD Guideline 106. Sorption to municipal sewage sludge was determined according ISO Guideline 18749 (Clariant, 2001b). The sorption constants K_d are shown in table 4.1.1.6. The sorptive effects in the different matrices cannot be attributed to the organic carbon content alone as is obvious from the ‘calculated K_{oc}’ values (see table 4.1.1.6) which vary considerably. K_{oc} alone is therefore not an adequate parameter to describe the sorption behaviour of SAS.

Table 4.1.1.6 Measured Sorption constants of SAS to Sediment, Soils and municipal Sewage sludge (Clariant, 2001a & 2001b)

	Sediment	EUROSOIL 4	EUROSOIL 2	EUROSOIL 1	EUROSOIL 3	EUROSOIL 5	Sewage sludge
Description	**sand**	**silt**	**silt loam**	**clay soil**	**loam**	**loamy sand**	**municipal**
% Organic Carbon	**0,31**	**1,36**	**2,39**	**3,29**	**3,32**	**4,43**	**ca. 37**
K_d (v/v)	**23[1]**	**20[1]**	**56[1]**	**50[1]**	**35[1]**	**75[1]**	**270[2]**
K_d (L/kg)	**15[3]**	**13[3]**	**37[3]**	**33[3]**	**23[3]**	**50[3]**	**208[1]**
K_{oc}[4] (calculated)	**7481**	**1453**	**2349**	**1523**	**1068**	**1690**	**730**

[1] **measured values**
[2] **value calculated from measured value assuming a sludge density of 1,3 kg/m^3 d.m. (EU, 2003a)**
[3] **value calculated from measured value assuming a soil density of 1,5 kg/m^3 d.m. (EU, 2003a)**
[4] **values calculated from K_d (v/v) and organic carbon content**

The sorption constants for soil sand sediments are in a range of Kd 13-50 L/kg (average in soil: 34 L/kg) while the value for sewage sludge is considerably higher (208 L/kg).

4.1.1.7 Bioconcentration

Salts of strong acids like sulfonates are known to be poorly absorbed into living cells because the charged species are hindered to cross membranes (Boethling & Mackay, 2000). Bioconcentration studies with radiolabelled homologues of the surfactant Linear Alkylbenzenesulfonate (LAS) gave BCF values allowing calculation of an average BCF= 66 L/kg (HERA, 2002b).

The absorption behaviour of charged species is taken into account by the QSAR calculation programme BCFWin from US EPA (US EPA, 2000d) which uses different Kow dependent equations for ionic compounds. As for SAS no measured BCF values are available a QSAR approach was used and applied to 8-Hexadecansulfonic acid sodium salt (C16-SAS) (see table 4.1.1.7).

Table 4.1.1.7 Bioconcentration of C16-SAS from US EPA BCFWin (US EPA, 2000d)

Bioconcentration	BCF	Reliability	Remark / Reference
Bioconcentration in fish	71	2	US EPA, 2000e

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

The calculated value for C16-SAS is in the same order of magnitude as the value determined for technical LAS suggesting that bioconcentration is not likely to occur.

4.1.2 Removal

Sewer

Laboratory studies have demonstrated that the concentrations of surfactants can be reduced significantly in sewers, depending on the length of the sewer, travel time and the degree of microbial activity present in the sewer (Matthijs et al., 1995). Because of the variability of the removal in sewers this effect will not be considered in the SAS environmental risk assessment.

Sewage treatment plant

CAS Test results

Continuous activated sludge (CAS) test systems simulating municipal sewage treatment plants are suitable to evaluate removal of SAS in sewage treatment plants (see chapter 4.1.1.1). In a CAS study a removal of >= 99% was measured for SAS (primary & ultimate degradation) which is mainly due to biodegradation.

Removal calculated from influent and effluent monitoring data

Removal rates of SAS in municipal sewage treatment plants can be calculated from measured influent and effluent concentration (Field et al., 1994, 1995; Klotz, 1994b; Schroeder, 1995; Schroeder et al., 1999, see Chapter 4.1.3 and Table 4.1.3). Table 4.1.2 lists those monitoring data of Table 4.1.3 assigned as valid and which can be used for the calculation of removal rates of SAS in STPs.

Table 4.1.2 Elimination rates from measured influent & effluent conc. in STPs

Country	Location	Influent conc.	Effluent conc.	Reliability	Calc. Removal	Ref.
Germany	Lüdinghausen	1,2 mg/L	2 µg/L	2	99,8 %	Klotz, 1994b

Germany	Marl-Ost	0,5 mg/L	4 µg/L	2	99,2 %	Klotz, 1994b
Germany	München II (Autumn 1993)	0,3 mg/L	< 1 µg/L	2	> 99,7 %	Klotz, 1994b
Germany	München II (Winter1993)	0,5 mg/L	2 µg/L	2	99,6 %	Klotz, 1994b
Switzerland	Zürich-Glatt	0,54 – 0,89 mg/L	<1-17 µg/L	1	96,9 - >99,9 %	Field et al., 1994
Switzerland	Bülach	0,85 mg/L	< 1 µg/L	1	> 99,9 %	Field et al., 1994
Switzerland	Niederglatt	0,67 mg/L	< 1 µg/L	1	> 99,9 %	Field et al., 1994
Switzerland	Opfikon	0,61 mg/L	< 1 µg/L	1	> 99,8 %	Field et al., 1994

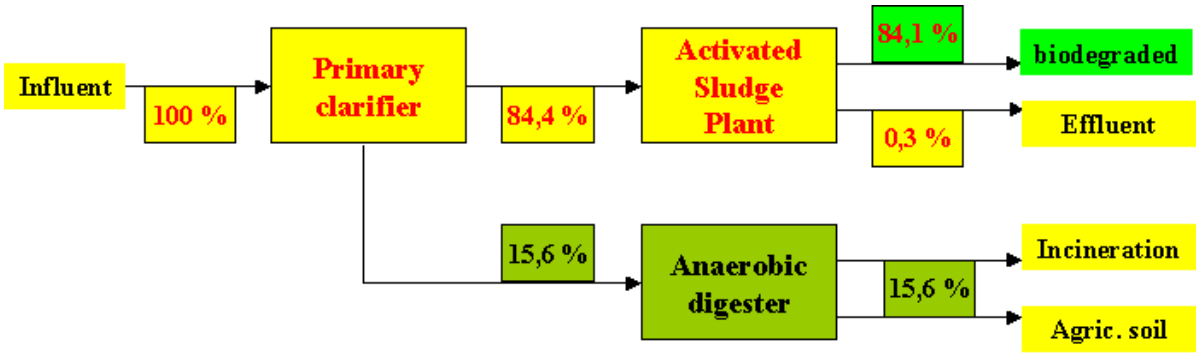
Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

From the data given in table 4.1.2 a removal of SAS in STP of at least 99% can be assumed and this figure is conservatively used in exposure calculations.

Fate of SAS in sewage treatment plants

Field et al. (1995) have carried out a detailed mass balance investigation on the fate of SAS in the municipal sewage treatment plant of Zurich-Glatt (Switzerland) serving 120.000 inhabitants (Figure 4.1.2).

Figure 4.1.2 Simplified Fate of SAS in the Swiss sewage treatment plant Zurich-Glatt according Field et al., 1995



Field et al. (1995) have also investigated the fate of the different SAS homologues in effluent and sludge of the Zurich-Glatt sewage treatment plant and found that the homologues with higher chain-length tend to be biodegraded slower, thus, representing a higher relative amount in sludge.

For exposure calculations the following realistic worst case removal assumptions are assumed: biodegradation 83% and sorption to sludge 16% resulting in 99% removal and 1% discharge in effluent.

4.1.3 Monitoring studies

Influent and effluent concentrations in sewage treatment plants

Monitoring data on influent and effluent concentrations are available for 12 German and Swiss STPs (see Table 4.1.3.1). These effluent and influent concentrations were used to calculate the STP removal and these removal data were given in a summarized form in table 4.1.2 already.

Table 4.1.3.1 Measured influent & effluent conc. in STPs

Country	Location	No. of Locations	Influent conc.	Effluent conc.	Reliability	Reference
Germany	Herrenhausen	1	not determined	8 µg/L	2	Klotz, 1994b
Germany	Lüdinghausen	1	1,2 mg/L	2 µg/L	2	Klotz, 1994b
Germany	Marl-Ost	1	0,5 mg/L	4 µg/L	2	Klotz, 1994b
Germany	München II (Autumn 1993)	1	0,3 mg/L	< 1 µg/L	2	Klotz, 1994b
Germany	München II (Winter1993)	1	0,5 mg/L	2 µg/L	2	Klotz, 1994b
Germany	Monschau Düren	1 1	0,045 mg/L 0,1 mg/L	<= 1 µg/L	4	Schroeder, 1995
Switzerland	Bülach Neuglatt Opfikon Zürich	4	0,690-0,980 mg/L	<1-17 µg/L	1	Field et al., 1994, 1995

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

SAS concentrations in sewage sludge

Field et al. (1992, 1995) and Klotz (1994b) have also measured the concentration of SAS in sludges (see Table 4.1.3.2).

Table 4.1.3.2 Measured sewage sludge concentrations in STPs

Country	Location	Primary sludge	Secondary sludge	Digested sludge	Relia-bility	Reference

Germany	Kriftel (1991)	-	0,05 g/kg dw.	3 g/kg dw.	2	Klotz, 1994b
Germany	Lorsbach (1991)	-	< 0,1 g/kg dw.	0,4 g/kg dw,	2	Klotz, 1994b
Germany	Lüdinghausen (1986)	1,8 g/kg dw.	0,6 g/kg dw.	2,4 g/kg dw.	2	Klotz, 1994b
Germany	Lüdinghausen (1987)	1,2 g/kg dw.	1,7 g/kg dw.	2,9 g/kg dw.	2	Klotz, 1994b
Germany	Essen (1987)	-	-	3,3 g/kg dw.	2	Klotz, 1994b
Germany	München (1987)	-	< 0,1 g/kg dw.	-	2	Klotz, 1994b
Germany	München (1993)	-	< 0,1 g/kg dw.	-	2	Klotz, 1994b
Switzerland	Zürich (1992)	-	-	0,8 g/kg dw.	2	Field, 1992
Switzerland	Opfikon (1992)	-	-	0,8 g/kg dw.	2	Field, 1992
Switzerland	Niederglatt (1992)	-	-	0,3 g/kg dw.	2	Field, 1992
Switzerland	Seegräben (1992)	-	0,4 g/kg dw.	-	2	Field, 1992
Switzerland	Stäfa (1992)	-	0,5 g/kg dw.	-	2	Field, 1992
Switzerland	Zurich (1995)	-	0,5 g/kg dw.	0,7 g/kg dw.	1	Field, 1995

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

SAS in surface waters

SAS monitoring data from six German rivers measured at 13 different locations are available (see Table 4.1.3.3). At 11 locations the measured SAS concentration was =< 1 µg/l which is the limit of detection, at 2 locations higher concentrations were found but the reliability of these measurements cannot be assigned from the available data.

Table 4.1.3.3 Monitoring data for SAS in 6 German rivers at 13 different locations (Detection limit for SAS in surface water is ca. 1µg/L)

River names	No. of Locations	Conc. in river	Reliability	Reference
Isar near STP Munich II (Winter 1993)	1	above STP: < 1 µg/L below STP: 1 µg/L	2	Klotz, 1994b
Main near Frankfurt (Summer 1993)	1	< 1 µg/L	2	Klotz, 1994b
Leine near STP Herrenhausen	1	< 1 µg/L	2	Klotz, 1994b
Rur, Wurm, Inde	8	< 1 µg/L	4	Schulze, 2001
Rur	6	1 µg/L (median)	4	Schroeder, 1995

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

SAS in ground water, sediment and soil

No monitoring data for SAS in ground water, sediment and soil are available.

4.1.4 PEC Calculations

4.1.4.1 Summary of the data used in exposure calculations

In table 4.1.4.1 the data for the exposure calculations with EUSES 1.0 are listed to provide a quick and comprehensive overview. References to the chapters for details are given as well. For the EUSES calculation two exposure scenarios were applied. EU standard Scenario acc. to TGD (EU, 2003a) HERA Scenario (HERA, 2002a)

In the revised EU Technical Guidance Document (EU, 2003a) in Part II (Appendix I, B-Tables, IC5, Private use) the fraction of main source is given as 0,0005 for surfactants with a use of >1000 tons/year. This means that the per capita consumption in the EU Region (20 Million inhabitants) is the same as for the local EU situation (10000 inhabitants). The only difference between the calculations of the HERA Scenario is the

EU regional factor of 7% instead of 10% (see explanation of the 7% factor in HERA, 2002a).

Table 4.1.4.1 Summary of data used in EUSES 1.0 Exposure calculations

Data point	Value	Chapter or Reference
Mol weight	328 g/Mol	Chapter 3.1
Melting point	200 deg C	Chapter 3.1
Vapour pressure	$5{,}3*10^{-11}$ Pa	Chapter 3.1
Water solubility	***300 g/L***	Chapter 3.1
Use volume (HERA)	66.000 tons/year	Chapter 3.2.2
EU Connection degree to Sewage Treatment Plants	80%	EU, 2003a
EU Regional use factor	7 % (HERA) 10 % (TGD)	HERA, 2002a and EU, 2003a
Fraction of Main source Used for HERA & TGD Scenario	***0,0005***	EU, 2003a
Use per capita (regional & local)	***0,63 g/d*capita (HERA)*** ***0,9 g/d*capita (TGD)***	EUSES 1.0 Calculations
K_d sludge	208 L/kg	Chapter 4.1.1.6
K_d suspended matter	***30 L/kg***	double of K_d sediment (see EU, 2003a)
K_d sediment	15 L/kg	Chapter 4.1.1.6
K_d soil	34 L/kg	Chapter 4.1.1.6
$t_{1/2}$ water	3 h	Chapter 4.1.1.1
$t_{1/2}$ aerobic sediment	7 d	Chapter 4.1.1.2
$t_{1/2}$ anaerobic sediment	***70 d***	10 fold of $t_{1/2}$ aerobic sediment (see EU, 2003a)
$t_{1/2}$ soil	7 d	Chapter 4.1.1.2
Removal STP	99%	Chapter 4.1.2
STP fraction to effluent	1,0 %	Chapter 4.1.2
STP fraction in sludge	16 %	Chapter 4.1.2

STP fraction biodegraded	83,0 %	Chapter 4.1.2

In the following the calculation results from EUSES are given in pertinent tables.

4.1.4.2 Aquatic Compartment

Table 4.1.4.2 $c_{local,\ water}$ and PEC_{water} for SAS

	No.	Scenario TGD	Scenario HERA	Remark
$c_{local,\ water}$ (µg/L)	[1]	4,52	3,16	
$PEC_{regional,\ water}$ (µg/L)	[2]	0,19	0,13	
$PEC_{local,\ water}$ (µg/L)	[3]	4,71	3,29	[3] = [1] + [2]

All measured concentrations in surface water which are assigned as reliable (see Table 4.1.3) are below 1 µg/L (see chapter 4.1.3) and therefore the calculated concentrations are somewhat conservative with respect to the measured data.

4.1.4.3 Sediment Compartment

Table 4.1.4.3 $c_{local,\ sediment}$ and $PEC_{sediment}$ for SAS

	No.	Scenario TGD	Scenario HERA	Remark
$c_{local,\ sediment}$ (µg/kg dw)	[4]	87,4	61,2	
$PEC_{regional,\ sediment}$ (µg/kg dw)	[5]	2,0	1,4	
$PEC_{local,\ sediment}$ (µg/kg dw)	[6]	89,4	62,6	[6] = [4] + [5]

4.1.4.4 Soil Compartment

Table 4.1.4.4 $c_{local,\ soil}$ and PEC_{soil} for SAS

	No.	Scenario TGD	Scenario HERA	Remark
$c_{local,\ sludge}$ (mg/kg dw)	[7]	680	476	
$c_{local,\ soil}$ (mg/kg dw)	[8]	0,36	0,25	averaged over 30d
$c_{local,\ agric.\ soil}$ (mg/kg dw)	[9]	0,06	0,04	averaged over 180d
$c_{local,\ grassland}$ (mg/kg dw)	[10]	0,03	0,02	averaged over 180d
$PEC_{regional,\ natural\ soil}$ (mg/kg dw)	[11]	<< 0,001	<< 0,001	
$PEC_{local,\ soil}$ (mg/kg dw) (endpoint terrestr. ecosystem)	[12]	0,36	0,25	[12] = [8] + [11]

$PEC_{local,\ agric.\ soil}$ (mg/kg dw) (endpoint crops for human)	[13]	0,06	0,04	[13] = [9] + [11]
$PEC_{local,\ grassland}$ (mg/kg dw) (endpoint grass for cattle)	[14]	0,03	0,02	[14] = [10] + [11]

Almost all measured concentrations in secondary sludge are in the range of 50 to 500 mg/kg dw. (see Table 4.1.3.2) except for one value (1,7 g/kg dw) and therefore the calculated values are somewhat conservative with respect to the measured data.

4.1.4.5 Sewage Treatment Plant (STP)

As SAS is used continuously (365 d/year) the effluent concentration of the sewage treatment plant is equivalent to the PECstp.

Table 4.1.4.5 PEC_{stp} for SAS

	No.	Scenario TGD	Scenario HERA	Remark
PEC_{stp} (µg/L)	[15]	45,2	31,6	

The calculated PEC_{stp} are somewhat conservative with respect to the measured effluent concentrations in STPs (<1 – 17 µg/L, see table 4.1.3.1).

4.1.4.6 Secondary Poisoning

As the BCF of SAS is very low secondary poisoning is unlikely and therefore not covered in this assessment.

4.1.4.7 Indirect Exposure of Humans via Environment

Based on environmental concentrations and transfer factors EUSES calculates local and regional concentrations in food (vegetables, meat, milk etc), air and drinking water. The estimated daily intakes are highly uncertain as the log K_{ow} used to calculate the transfer between the different media cannot be measured for SAS but only calculated. Nevertheless it can be concluded from these estimates that indirect exposure of humans via the environment is very low and therefore does not need to be taken into account for

the human health exposure assessment. The daily intakes for humans on a local and regional basis are given in table 4.1.4.7.

Table 4.1.4.7 Indirect Exposure of Humans via Environment

Type	***Daily intake for humans (µg/kg*d)***	
	TGD	**HERA**
Local	***0,9***	0,6
Regional	0,07	0,05

4.2. Environmental Effects Assessment

The production process for SAS delivers a product with a well defined distribution in chain length and composition. Therefore the effects found in ecotoxicological test were not related to definitive components in the SAS mixture (e.g by applying toxic units, tox-weighted averages etc) but was only related to the SAS mixture as such. Therefore no further information on the test substance is given in the following chapters and tables but instead it is always referenced to chapter 3.1 where details on the substance were given already.

4.2.1 Ecotoxicity

4.2.1.1 Aquatic Ecotoxicity

Acute Aquatic Ecotoxicity

Data for all three trophic levels (fish, daphnia and algae) as well as for bacteria are available and listed in table 4.2.1.1.1.

Chronic Ecotoxicity

Chronic data are available for fish, daphnia and algae (see table 4.2.1.1.2). The most sensitive species is Daphnia.

Biocenosis studies

Two biocenosis studies are available but not or insufficiently described in order to judge if these data (listed in Table 4.2.1.1) could be used instead of the chronic daphnia NOEC (Huels, 2000; Guhl & Gode, 1989).

Table 4.2.1.1 Results from Biocenosis studies on SAS

	Duration	**LOEC**	**NOEC**	**Reliability**	**Reference**
Biocenosis study 1 (allochthonous biocenosis originating from wildlife)	***12-35 d***	-	0,3 mg/L	4	Guhl & Gode (1989)
Biocenosis study 2 (no details)	***long-term***	***3,5 mg/L***	***1,4 mg/L***	4	Huels (2000)

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

Table 4.2.1.1.1 Acute Aquatic Ecotoxicity

Acute Fish Toxicity					
Species	**Guideline**	**Exposure (h)**	**LC50 (mg/L)**	**Reliability**	**Remark / Reference**
Danio rerio	OECD 203	96	8,4	1	Huels, 2000
Danio rerio	OECD 203	96	1 - 10	2	Hoechst, 1988a
Danio rerio	OECD 203	96	1 - 5	2	Hoechst, 1989b
Danio rerio	OECD 203	96	14,8	2	Hoechst, 1989c
Lepomis macrochirus	-	-	1,3 - 144	4	Clariant, 1998
Leuciscus idus	-	96	11,3	2	Hoechst, 1977
Leuciscus idus	-	96	27,1	2	Hoechst, 1978
Poecilia reticulata	DIN 38412, Part 15	96	NOEC 4 mg/L	4	Hoechst, 1972

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

Acute Toxicity to Invertebrates					
Species	**Guideline**	**Exposure (h)**	**EC50 (mg/L)**	**Reliability**	**Remark / Reference**
Daphnia magna	DIN 38412, Part 11	24	12,5	2	Huels, 2000
Daphnia magna	-	24	2 - 319	4	7 different studies not fully described, see IUCLID file: Clariant, 1998

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

Acute Toxicity to Algae					
Species	**Guideline**	**Exposure (h)**	**EC50 (mg/L)**	**Reliability**	**Remark / Reference**
Scenedesmus subspicatus	OECD 201	72	311	1	BUA, 1997
Scenedesmus subspicatus	OECD 201	72	96	1	Huels, 2000

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

Table 4.2.1.1.1 Acute Aquatic Ecotoxicity (continued)

Acute Toxicity to Aerobic Bacteria					
Species	**Guideline**	**Exposure (h)**	**EC10 (mg/L)**	**Reliability**	**Remark / Reference**
Pseudomonas putida	OECD 209	3	700	2	Clariant, 1998

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

Acute Toxicity to Anaerobic Bacteria					
Species	**Guideline**	**Exposure (h)**	**EC0 (mg/L)**	**Reliability**	**Remark / Reference**
Anaerobic bacteria from STP	ETAD Fermentation Tube Method	24	1000	2	Hoechst, 1972

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

Table 4.2.1.1.2 Chronic Aquatic Ecotoxicity

Chronic Toxicity to Fish					
Species	**Guideline**	**Exposure (h)**	**EC50 (mg/L)**	**Reliability**	**Remark / Reference**
Oncorhynchus mykiss	OECD 204	28d	2,9 (length of fish)	1	BUA, 1997

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

Chronic Toxicity to Invertebrates					
Species	**Guideline**	**Exposure (h)**	**(mg/L)**	**Reliability**	**Remark / Reference**
Daphnia magna	OECD 202, Part 2	22 d	EC50 1,2	1	BUA, 1997
Daphnia magna	OECD 202, Part 2	22 d	NOEC 0,37	1	BUA, 1997

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

Table 4.2.1.1.2 Chronic Aquatic Ecotoxicity (continued)

Chronic Toxicity to Algae					
Species	**Guideline**	**Exposure (h)**	**NOEC(mg/L)**	**Reliability**	**Remark / Reference**
Scenedesmus subspicatus	OECD 201	72	5,3	1	BUA, 1997
Scenedesmus subspicatus	OECD 201	72	20,1	1	Huels, 2000

Reliability criteria of IUCLID are used:
1 valid without restriction 2 valid with restrictions 3 not valid 4 validity is not assignable

Chronic Toxicity to Aerobic Bacteria					
Species	**Guideline**	**Exposure (h)**	**EC10 (mg/L)**	**Reliability**	**Remark / Reference**
Pseudomonas putida	DIN 38412, Part 8 Cell Growth Test	16	> 1000	2	Hoechst, 1988b

4.2.1.2 Sediment and Soil Ecotoxicity

No data on sediment or soil ecotoxicity of SAS are available.

4.2.2 PNEC Calculations

General

The PNECs derived in the following are summarized in table 4.2.2.1.

4.2.2.1 $PNEC_{water}$

The $PNEC_{water}$ can be derived from the lowest chronic NOEC of 370 µg/L of a 21d Daphnia reproduction study. As chronic aquatic ecotoxicity data are available for all three trophic levels an application factor of 10 to this NOEC is applied to derive the **$PNEC_{water}$** of **37 µg/L**.

Due to insufficient information the results from mesocosm studies (see table 4.2.1.1) could not be considered as a basis for the PNEC derivation.

4.2.2.2 $PNEC_{sediment}$

As no sediment ecotoxicity studies are available, the equilibrium partitioning method described in the EU TGD was used (EU, 2003a) to derive the $PNEC_{sediment}$ by means of EUSES. No extra application factor was applied because SAS shows low sorptivity. Based on the $PNEC_{water}$ of 37 µg/L, a **$PNEC_{sediment}$** of **0.6 mg/kg dw.** was calculated for SAS.

4.2.2.3 $PNEC_{soil}$

As no soil ecotoxicity studies are available, the equilibrium partitioning method described in the EU TGD was used (EU, 2003a) to derive the $PNEC_{soil}$ by means of EUSES. No extra application factor was applied because SAS shows low sorptivity. Based on the aquatic PNEC of 37 ug/L a **$PNEC_{soil}$** of **1.3 mg/kg dw.** was calculated for SAS.

4.2.2.4 $PNEC_{stp}$

For SAS the lowest EC10 for bacteria is 700 mg/L (see table 4.2.1.1.1). Using an application factor of 10 a **$PNEC_{STP}$** of **70 mg/L** was calculated for SAS.

Table 4.2.2.1 PNECs for SAS

PNECs for SAS		
	Value	**Remark**
$PNEC_{water}$ (µg/L)	**37**	lowest NOEC 0.37 mg/L, application factor 10
$PNEC_{sediment}$ (mg/kg dw.)	**0,6**	equilibrium partitioning method using assumed aquatic PNEC, no extra application factor
$PNEC_{soil}$ (mg/kg dw.)	**1,3**	equilibrium partitioning method using assumed aquatic PNEC, no extra application factor
$PNEC_{stp}$ (mg/L)	**70**	derived from acute bacteria study, application factor 10

4.3. Environmental Risk Characterisation

In the following the Risk Characterisation for the relevant Environmental Compartments (surface water, sediment, soil and stp) are calculated from the PECs given in chapter 4.1.4 and the PNECs derived in chapter 4.2.2. The PEC/PNECs are summarized in Table 4.3.

Table 4.3 Environmental Risk Characterisation for SAS

	Scenario TGD	**Scenario HERA**	**Remark**
$PEC_{local,\ water}/PNEC_{water}$	0,13	0,09	based on chronic data
$PEC_{local,\ sediment}/PNEC_{sed.}$	0,15	0,10	equilib. partitioning method used
$PEC_{local,\ soil}/PNEC_{soil}$	0,29	0,20	equilib. partitioning method used
PEC_{stp} /$PNEC_{stp}$	$6{,}5*10^{-4}$	$4{,}5*10^{-4}$	

4.4 Discussion and Conclusions

As shown in chapter 4.3, the Risk Characterisation Ratio (RCR) for SAS for both scenarios TGD and HERA is < 1 in all environmental compartments which may be potentially affected by the exposure to SAS (water, sediment, soil, sewage treatment plants). The comparison of the calculated PECs with measured exposure data shows that calculated values are more conservative than the measured ones. In addition, conservative assumptions may have been made in the derivation of $PNEC_{aquatic}$ as data from at least one biocenosis study suggest a higher $PNEC_{aquatic}$.

Similar conclusions can be drawn for the risk characterisation in the sediments compartment. The PNEC value used for this part of the risk characterisation is based on the aquatic toxicity data using the equilibrium partitioning approach according to the TGD.

The assessment of the soil has a higher uncertainty in comparison to the assessments of other compartments due to the fact that no measured degradation in soil is available and instead the data from LAS were used. In addition the ecotoxicity had to be estimated using the equilibrium partitioning method. On the other hand the calculated sludge concentrations fit well to the measured ones.

5. Human health assessment

5.1 Consumer exposure

5.1.1 Product types

SAS is one of the major anionic surfactants used in the market of dishwashing, laundry and cleaning products. In this respect about 63% of the total SAS volume in Western Europe is assigned for the use in household applications. Main uses (>80%) are standard dishwashing liquids (at a typical concentration range of 3% to 29%). Minor uses are laundry detergents at a typical concentration range of 1% to 15%, household cleaners at a typical concentration range of 0.2% to 15%. The SAS volumes used for cosmetics hair, body care products and industrial cleaners are outside the scope of this HERA-Risk assessment.

Table 5.1.1: SAS Applications in Western Europe according AISE, 2004 (data for 2002)

PRODUCT CATEGORIES IN WHICH SUBSTANCE IS CONTAINED		RANGE OF USE LEVELS OF SUBSTANCE AS 100% OF ACTIVE INGREDIENT % weight		
		Minimum	Maximum	Typical
LAUNDRY REGULAR				
	Powder	0	0	0
	Liquid	0	10	8
LAUNDRY COMPACT				
	Powder	0	0	0
	Liquid/gel	0	15	10
	Tablet	0	0	0
	Gel	0	0	0
FABRIC CONDITIONERS				
	Liquid Regular	0	0	0
	Liquid Concentrate	0	0	0
	Others (specify)	0	0	0
LAUNDRY ADDITIVES				
	Powder Bleach	0	0	0
	Liquid Bleach	0	0	0
	Tablet	0	0	0
HAND DISHWASHING				
	Liquid (Regular)	0	25	3.5 - 15
	Liquid	0	29	8 - 25

	(Concentrate)			
	Gel	0	9	8
MACHINE DISHWASHING				
	Powder	0	0	0
	Liquid	0	0.2	0.2
	Tablet	0	0	0
	Gel	0	0	0
SURFACE CLEANERS				
	Liquid	0	9	0.2 - 3
	Concentrate	0	15	3.5 - 15
	Powder	0	0	0
	Gel	0	0	0
	Spray	0	4	2 - 4
	Wipe	0	0	0
TOILET CLEANERS				
	Powder	0	0	0
	Liquid	0	4	0.7 - 3.4
	Gel	0	0	0
	Tablet	0	0	0

5.1.2 Consumer Contact Scenarios

Based on the product types, the consumer contact scenarios that were identified and considered in this assessment include mainly direct and indirect skin contact by using dishwashing liquids and to a minor extent laundry detergents or household cleaners, as well as oral ingestion derived either from residues deposited on dishes, from accidental product ingestion, or indirectly from drinking water. Based on the main application area in dishwashing liquids, potential inhalation of SAS is of insignificant relevance, will however be considered during the exposure assessment. Accordingly the following potential exposure scenarios will be assessed (Table 5.1.2):

Table 5.1.2: exposure scenarios

Product Type	Exposure scenario
Dishwashing	Direct skin contact from hand dishwashing
	- Standard dishwashing liquids
	- Dishwashing liquid concentrates
	Oral exposure to residues deposited on dishes
	Oral exposure from drinking water and food
Laundry	Direct skin contact from hand washed laundry
	Direct skin contact from laundry tablets
	Direct skin contact from pre-treatment of clothes

	Indirect skin contact from wearing clothes
	Inhalation of detergent dust during washing
Household cleaners	Direct skin contact from floor cleaners
	Inhalation of aerosols from cleaning sprays
	Accidental or intentional overexposure

5.1.3 Consumer exposure estimates

There is a consolidated overview concerning habits and practices of use of detergents and surface cleaners in Western Europe which was tabulated and issued by AISE (Table of Habits and Practices for Consumer Products in Western Europe, AISE 2002). This Table reflects the consumer's use of detergents in g/task, tasks/week, duration of task as well as other intended uses of products if applicable. The following exposure estimates were calculated using the most relevant data from that Table.

5.1.3.1 Direct skin contact from hand dishwashing

A) Standard dishwashing liquids

The contact time with SAS in the course of hand dishwashing is relatively short (max. duration of about 45 minutes) using both, standard liquids or liquid concentrates (Table of Habits and Practices for Consumer Products in Western Europe, AISE 2002) and the percutaneous absorption of ionic substances has also been reported to be very low (Schaefer and Redelmeier, 1996). Therefore, it can be assumed that the amount of SAS systemically available via percutaneous absorption, if any, is quite low. For the exposure scenario a dermal penetration rate of one percent is assumed.

1) Based on the Table of Habits and Practices for Consumer Products in Western Europe (HERA, 2002), a maximum of 10 grams regular liquid per 5 L water for hand dishwashing is used. This corresponds to about 2 mg/mL or a 0.2% detergent concentration in the washing solution.
2) The highest concentration of SAS in standard dishwashing liquids is about 25% (see Table 5.1.1). Thus, the highest concentration of SAS in dishwashing solutions is approximately 0.5 mg/mL.
3) Immersion of hands and forearms into solution would expose about 1980 cm^2 (EU, 2003a).

4) Assuming a film thickness of 100 μm (0.1 mm or 0.01 cm) (EU, 2003a) on the hands and an assumed percutaneous absorption of 1% for SAS in 24 hr exposure time, the following amount of SAS absorbed via skin can be calculated:

1980 cm^2 · 0.01 cm · 0.01 (fraction absorbed) · 0.5 mg/mL (cm^3) = **0.1 mg SAS absorbed in 24 hours**

Assuming 45 min contact time per task and a very conservative maximum task frequency of 21 washes per week (3 per day) (Table of Habits and Practices for Consumer Products in Western Europe, 2002) the total daily contact time adds to 135 min. Assuming such very conservative daily duration of exposure and taking a dermal absorption rate of 1% into account, the amount of absorbed SAS per day can be calculated as [(0.1 mg/day) · (135/60 hr) · (1/24 day/hr)] = 9.375 μg. Assuming a body weight of 60 kg, the resulting estimated systemic dose is:

$Exp_{sys\ (direct\ skin\ contact)}$ = 0.15 μg/kg BW /day

B) Dishwashing liquid concentrates

In the case of using dishwashing liquid concentrates (typical concentration range of SAS 8% to 29%), the above calculated potential systemic body burden is not changing significantly. Although the highest concentration of SAS in such formulations is increased to 29%, the maximum applied amount to the washing solution is reduced to about 5 grams per 5 L washing solution (corresponding to about 0.1%). Thus, the highest SAS concentration in the washing solution is approximately 0.29 mg/mL. Using the same conservative parameters as described above, this results in a potential systemically body burden of SAS via dermal absorption **of 0.09 μg/kg body weight per day**. Since this

value is lower than for using standard dishwashing formulations and because it is unlikely to use both dishwashing liquid formulations in parallel, the calculated body burden for standard dishwashing liquids is used for the assessment.

5.1.3.2 Direct skin contact from hand washed laundry

The use of SAS in laundry detergents is of minor importance since only about 2% of the total production volume is going into this application. However, taking the same conservative assumptions into account like for dishwashing, the following worst case scenario may reflect this situation:

1) The highest concentration of laundry detergents in hand washing solutions according to AISE 2002 is approximately 1% (corresponding to about 10 mg/mL)
2) The highest concentration of SAS in laundry detergents amounts to 15% (internal data). Thus, the highest concentration of SAS in dishwashing solutions is approximately 1.5 mg/mL.
3) Immersion of hands and forearms into solution would expose about 1980 cm^2 (EU, 2003a).
4) Assuming a film thickness of 100 μm (0.1 mm or 0.01 cm) (EU, 2003a) on the hands and an assumed percutaneous absorption of 1% for SAS in 24 hr exposure time, the following amount of SAS absorbed via skin can be calculated:

$$1980\ cm^2 \cdot 0.01\ cm \cdot 0.01\ (\text{fraction absorbed}) \cdot 1.5\ mg/mL\ (cm^3) =$$
0.3 mg SAS absorbed in 24 hours

Assuming 10 min contact time per task and a very conservative maximum task frequency of 21 washes per week (3 per day) (Table of Habits and Practices for Consumer Products in Western Europe, AISE 2002) the total daily contact time adds to 30 min. Assuming such very conservative daily duration of exposure the amount of absorbed SAS per day

can be calculated as [(0.3 mg/day) · (30/60 hr) · (1/24 day/hr)] = 6.25 µg. Assuming a body weight of 60 kg, the resulting estimated systemic dose is:

$Exp_{sys\ (direct\ skin\ contact)}$ = 0.1 µg/kg BW /day

5.1.3.3 Direct skin contact from laundry tablets

Contact time is so low and area of contact with skin is so small that the amount absorbed percutaneously is considered insignificant. Therefore this scenario will not be considered for the risk assessment.

5.1.3.4 Direct skin contact from pre-treatment of clothes

Direct skin contact with SAS is possible when clothing stains are being removed by spot-treatment with a detergent paste (SAS concentration about 15%), or neat liquid (SAS concentration about 15%). As only a fraction of the skin surface area of the hands (~ 840 cm^2 (EU, 2003a)) is exposed, treatment time is very short (10 minutes or less (Table of Habits and Practices for Consumer Products in Western Europe, AISE 2002)) and percutaneous absorption of ionic substances has been reported to be very low (Schaefer and Redelmeier, 1996), it can be assumed that the amount of SAS systemically available via percutaneous absorption, if any, is quite low.

The following worst case estimate should address this scenario:

- The highest amount of SAS in hand washing paste (SAS concentration about 9%) is approximately 90 mg/ml. The highest concentration of SAS in liquid laundry detergents amounts to 15% (150 mg/ml) (internal data). Because liquid detergents may be used neat for pre-treatment, the worst case value of 150 mg/ml will be used in the calculation
- The contact of hands into solution would expose a maximum of 840 cm^2 (EU, 2003a). This value is very conservative because only a fraction of the two hands surface skin will be exposed.

- Assuming a film thickness of 100 μm (0.1 mm or 0.01 cm) (EU, 2003a) on the hands and an assumed percutaneous absorption of 1% for SAS in 24 hr exposure time, the following amount of SAS absorbed via skin can be calculated:

840 cm^2 · 0.01 cm · 0.01 (fraction absorbed) · 150 mg/ml (cm^3) = **12.6 mg SAS absorbed in 24 hours**

Under the very conservative assumption of 10 minute highest contact time per task and a maximum task frequency of 1 wash pre-treatment per day, the total daily contact time adds to 10 minutes. Assuming such conservative daily duration of exposure the amount of absorbed SAS per day can be calculated as [(12.6 mg/day) · (10/60 hr) · (1/24 day/hr)] = 87.5 μg. Assuming a body weight of 60 kg, the resulting estimated systemic dose is:

$Exp_{sys\ (direct\ skin\ contact)}$ = 1.45 μg/kg BW /day

5.1.3.5 Indirect skin contact from wearing clothes

Residues of components of laundry detergents may remain on textiles after washing and could come in contact with the skin via transfer from textile to skin. Although no experimental data for SAS are available, the amount of a comparable anionic surfactant deposited on fabric remaining after 10 repeats of a typical washing process with typical laundry detergents, was measured to be in the order of 2.5 mg per g of fabric (Rodriguez et al., 1994). Thus, this value will be also used for SAS in the following calculations.

Assuming a worst case scenario, the exposure to SAS can be estimated according to the following algorithm recommended by the HERA Guidance Document (2002a):

$$\mathbf{Exp_{sys} = F_1 \cdot C` \cdot S_{der} \cdot n \cdot F_2 \cdot F_3 \cdot F_4 / BW} \quad [\text{mg/kg BW/day}]$$

For this exposure estimate the terms are defined with the following values for the calculation:

F_1 percentage (%) weight fraction of substance in product: not used, = 1

C` product (SAS) load in [mg/cm²]: C' was determined multiplying the experimental value of the amount of anionic surfactant deposited on fabric after a typical wash (2.5 mg of SAS per 1000 mg of fabric times an estimated value of the fabric density (FD = 10 mg/cm^2) (P&G, 1996). The resulting estimated value is $2.5 \cdot 10^{-2}$ mg/cm^2 of SAS deposited on fabric surface.

S_{der} surface area of exposed skin in [cm²] = 17,600 cm^2 (excludes head and hands) (EU, 2003a)

n product use frequency in number [events/day]: not used, = 1

F_2 percentage (%) weight fraction transferred from medium to skin: = 1% (Vermeire et al.,1993)

F_3 percentage (%) weight fraction remaining on skin: = 100% (worst case assumption)

F_4 percentage (%) weight fraction absorbed via skin: = 1%

BW body weight in [kg]: = 60

$$\mathbf{Exp_{sys\ (indirect\ skin\ contact)}} = \textit{[(2.5} \cdot 10^{-2} \textit{ mg/cm}^2\textit{)(17,600 cm}^2\textit{) (1/100)(1 /100)] / 60 kg} = \textit{7.4} \cdot 10^{-4} \textit{ mg/kg/day} = \mathbf{0.74\ \mu g\ /kg/day}$$

5.1.3.6 Inhalation of aerosols from cleaning sprays

SAS is present in some surface cleaning spray products (e.g. glass cleaners) at a typical concentration range of 0.1% to 2% (internal data). Assuming a worst case scenario, the exposure to SAS from aerosols derived from usage of such products can be estimated according to the following algorithm recommended by the HERA Guidance Document (2002a):

$$\mathbf{Exp_{sys} = F_1 \cdot C` \cdot Q_{inh} \cdot t \cdot n \cdot F_7 \cdot F_8 / BW} \quad [\text{mg/kg BW/day}]$$

F_1 weight fraction (percentage) of substance in product: = 2 % (worst case assumption).

C' product concentration, in mg/m^3: = 0.35 mg/m^3. This value of C' was obtained from experimental measurements of the concentration of aerosol particles under 6.4 microns in size which are generated upon spraying with typical surface cleaning spray products (Procter & Gamble, 2001).

Q_{inh} ventilation rate of user, in m^3/hr: = 0.8 m^3/hr (EU, 2003a)

t duration of exposure, in hr: = 0.17 hr (10 min) (Table of Habits and Practices for Consumer Products in Western Europe, 2002)

n product use frequency, in number of events per day: = 1 (Table of Habits and Practices for Consumer Products in Western Europe, 2002)

F_7 weight fraction (percentage) respirable: = 100% given that the experimentally determined value of C' refers to the fraction of respirable particles.

F_8 weight fraction (percentage) absorbed or bio available: = 75% (EU, 2003a)

BW body weight, in kg: = 60

$$\mathbf{Exp_{sys\ (inhalation\ of\ aerosols)}} = [(2/100) \cdot (0.35\ mg/m^3) \cdot (0.8\ m^3/hr) \cdot (0.17\ hr) \cdot 1 \cdot (75/100)] / 60\ kg \quad [\text{mg/kg BW/day}] = \mathbf{0.012\ \mu g\ /kg/day}$$

This amount is judged not to contribute significantly to the total systemic exposure of SAS and is therefore not considered further in the risk assessment.

5.1.3.7 Oral Exposures to SAS

5.1.3.7.1 Oral Exposure from drinking water and food

Oral exposures can be assumed to originate from drinking water, food and from residues on eating utensils and dishes washed in hand dishwashing detergents (machine dishwashing products do not contain SAS).

For the oral intake from drinking water, the Environmental Risk Assessment for SAS, presented in Section 4.1.4.7, revealed that indirect exposure of humans via the environment including drinking water as well as potential intake via agriculture food products is very low and therefore need not to be taken into account in the human health

exposure assessment.

5.1.3.7.2 Oral Exposure to residues deposited on dishes

The potential daily exposure to SAS from eating with utensils and dishware that have been washed in hand dishwashing detergents can be estimated assuming a worst case scenario as follows:

$$\mathbf{Exp_{sys} = F1 \cdot C` \cdot Ta' \cdot Sa / BW \quad [mg/kg\ BW/day]}$$

F_1 weight fraction (percentage) of substance in product: = 29 % (worst case assumption) (internal data).

C' concentration of product in dish wash solution in mg/cm^3: C' was determined dividing the amount of product per task (worst case assumption, maximum amount 5,000 mg (Table of Habits and Practices for Consumer Products in Western Europe, 2002)) over the volume of wash water volume (5,000 cm^3 (Table of Habits and Practices for Consumer Products in Western Europe, 2002)). The resulting estimated value is 1 mg/cm^3

Ta' amount of water on dishes after rinsing in ml/cm^2: According to Schmitz (Schmitz, 1973), Ta' is approximately 10% of the amount of water left in non-rinsed dinnerware. The amount of water left in non-rinsed dinnerware was estimated to amount to $5.5 \cdot 10^{-4}$ ml/cm^2 (Official publication French legislation, 1990). Therefore Ta' = $5.5 \cdot 10^{-5}$ ml/cm^2.

Sa area of dishes in daily contact with food: = 5,400 cm^2 (Official publication French legislation, 1990)

BW body weight, in kg: = 60

$$\mathbf{Exp_{sys\ (oral\ dish\ deposition)}} = [(29/100) \cdot (1\ mg/cm^3) \cdot (5.5 \cdot 10^{-5}\ ml/cm^2) \cdot (5400\ cm^2)] \ / \ 60\ kg$$

[mg/kg BW/day] = **1.43 µg /kg/day**

5.1.3.8 Accidental or intentional overexposure

Accidental or intentional overexposure to SAS may occur via household detergent products, which may contain up to 25% of SAS.

No fatal cases or serious injuries arising from accidental ingestion of SAS by humans are known. The accidental or intentional overexposure to SAS directly is not considered a likely exposure route for consumer. Regarding household products, the German Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV, **1999**)

published a report on products involved in poisoning cases. No fatal case of poisoning with detergents was reported in this document. Detergent products were not mentioned as dangerous products with a high incidence of poisoning.
Equally, in the UK, the Department of Trade and Industry (DTI) produces annual reports of the home accident surveillance system (HASS). The data in these reports summarizes the information recorded at accident and emergency (A&E) units at a sample of hospitals across the UK. It also includes death statistics produced by the Office for National Statistics for England and Wales. The figures for 1998 show that for the representative sample of hospitals surveyed, there were 33 reported accidents involving detergent washing powder (the national estimate being 644) with none of these resulting in fatalities (DTI, 1998). In 1996 and 1997, despite their being 43 and 50 reported cases, respectively, no fatalities were reported either.
Accidental exposure of the eye to SAS may occur in consumers only via splashes or spills with a formulated product.

5.2 Hazard assessment

5.2.1 Summary of the available toxicological data

5.2.1.1 Acute toxicity

5.2.1.1.1 Acute oral toxicity

The acute oral toxicity of SAS was investigated in several studies, both in rats and mice, using different grades of concentration. In total 4 tests in rats (Hoechst 1971; Hoechst 1977a; Hoechst 1979; Hüls 1983) and one test in mice (Hoechst 1975a) are available. Although most of the studies have been conducted not according to GLP and/or existing OECD-Guidelines, there are no methodological deficiencies which may alter the reliability of the test results. All studies are well documented and followed the principles of the OECD 401 method. The acute median lethal doses (LD50) revealed in these studies, are reflecting the different grades tested in a concentration dependent manner.

The acute oral toxicity of SAS (60% active matter) was investigated in rats using water as vehicle. 10 female SPF-Wistar rats each was administered the test compound via gavage at dose levels of 1600, 2500 or 4000 mg/kg body weight. After application the animals were observed for 7 days. In the highest dose all animals died and in the mid-dose 3 out of 10 animals. Fatal intoxicated animals showed the following gross pathology: Intestinal tract mucosa reddened and enlargement of the caecum. The LD50 was calculated to be 2890 mg/kg body weight (Hoechst 1971).

In another study groups of 5 male and 5 female rats received via gavage doses of 1990, 2510, 3980 or 5010 mg SAS (60% active matter) per kg body weight. Clinical symptoms of intoxication (coat bristling, ataxia, sedation, squatting posture, diarrhea) were apparent until 96 hours after treatment. Based on the study results, a combined LD50 of 2250 mg/kg body weight was calculated (Hüls 1983).

The acute oral toxicity of SAS (30% active matter) was investigated in female SPF-Wistar rats. 10 rats each was administered the test compound by single-dose gavage at dose levels of 4000, 5000, 6300 or 8000 mg/kg body weight. Lethality occurred in the high-dose (10 out of 10) and the group having received 6300 mg/kg body weight (9 out of 10). At 5000 mg/kg body weight 2 animals died and at 4000 mg/kg body weight one animal out of 10. Fatal intoxicated animals showed a squatting posture. The LD50 was calculated to be 5322 mg/kg body weight (Hoechst 1977a).

Using SAS (25% active matter), an acute oral toxicity study in female SPF-Wistar rats was performed. Groups of 10 female rats each were administered Hostapur SAS 25 by single-dose gavage at dose levels of 4000, 5000, 6300 or 8000 mg/kg body weight. All animals of the highest dose and 9 out of 10 animals of the group receiving 6300 mg/kg body weight died. At 5000 mg/kg body weight 4 out of 10 and in the lowest group 2 out of 10 animals died. Fatal intoxicated animals exhibited squatting posture, passivity, disequilibrium, and narrow palpebral fissure. In the highest dose group additionally

motor excitation as well as prone- and lateral position was observed. The LD50 was calculated to be 4970 mg/kg body weight (Hoechst 1979).

The acute oral toxicity of SAS (60% active matter) was also investigated in mice using a 25% aqueous solution at variable volume-dosages. 5 male and 5 female CD-1 mice each were administered SAS via gavage at dose levels of 1740, 2080, 2500, 3000, 3600, 4320 or 5180 mg/kg body weight. Signs of toxicity included hypoactivity, hypersensitivity, prostration and dyspnoea at dosages of 2080 mg/kg body weight and above. Convulsions were seen just prior to death at dosages of 3600 mg/kg body weight and above. In survivors, complete recovery was visible within 19 hours. Mortality was associated with dosages of 2080 mg/kg body weight and above. The acute oral median lethal dosages (LD50) were calculated as 2130 mg/kg body weight for males and 2550 mg/kg body weight for females (Hoechst 1975a).

Conclusion

The LD_{50} for rats and mice revealed in these studies are reflecting the different grades tested in a concentration dependent manner. The acute median lethal dose of SAS (60% active matter) revealed values from 2130 (male mice) to 2890 (female rats) mg/kg body weight, thus reflecting the different grades tested in a concentration dependent manner. Clinical signs of toxicity were only observed at doses near the LD_{50} values, and included squatting posture, passivity, disequilibrium, and narrow palpebral fissure.

5.2.1.1.2 Acute inhalation toxicity

There are no data available to evaluate the acute inhalation toxicity of SAS. Given the irritant nature of neat SAS, it is expected that high SAS aerosol concentrations may be irritating to the respiratory tract. However, due to the very low aerosol / dust generation during realistic use conditions, risks for consumers are regarded to be negligible.

5.2.1.1.3 Acute Dermal Toxicity

There are no data available to evaluate the acute dermal toxicity of SAS. However, in all tests with dermal exposure, including a subacute dermal toxicity study (see 5.2.1.5.3), no indications of acute and/or systemic toxic effects have been observed. Therefore it can be concluded that, beside irritative effects, acute toxic effects of SAS concerning this exposure route are very unlikely.

5.2.1.2 Skin Irritation

Tests on Animals

Several skin irritation studies on rabbits are available for SAS at various concentrations of up to 60% (Hoechst 1989d; ProTox 2002). All studies have demonstrated a significant skin irritating potential of Hostapur SAS at higher concentrations which proved to be concentration dependent. Whereas in a recent study, high concentrated SAS (60% active matter) reflecting todays commercial standard was used, in former studies SAS with a different paraffin basis was tested.

The most reliable study (ProTox 2002) was performed on three female New Zealand White rabbits with a semi-occlusive application for 4 hours. According to the OECD Guideline 404 the animals were treated with 0.5 mL of undiluted SAS (60% active matter). The SAS used was identical to todays commercial product and the study followed the principles of GLP. Well-defined up to severe erythema as well as very slight up to moderate oedema were observed up to 7 days after removal of the patches. Additionally, the skin surface of all animals was indurated, brown discolored and chapped. 14 days after removal of the patches all signs of irritation had resolved completely in all animals (ProTox 2002).

In another study, SAS (60% active matter) was tested for skin irritation in an occlusive patch-test (GLP not mentioned). Three male rabbits were dermally exposed for 4 hours and readings were performed up to 22 days. According to the authors strong irritative but reversible skin reactions were observed (Hüls 1986a).

SAS (30% active matter) was tested for primary dermal irritation properties in rabbits according to OECD 404 and GLP. Three rabbits were treated with 0.5 mL undiluted SAS. Following a dermal exposure period of 4 hours, the semi-occlusive dressing was removed and readings were performed up to 14 days. One hour up to 72 hours after patch removal the treated skin sites exhibited well-defined to moderate erythema and slight oedema. In addition, a dry, rough skin was observed. The skin surface was indurated, lumpy, chapped and discolored light brown. 14 days after removal of the patches, all irritative skin effects were almost completely reversible (Hoechst 1989f).
In an older study, SAS (20% active matter) was tested for primary skin irritation in 6 rabbits. 0.5 mL of undiluted SAS was applied to the intact and abraded skin of all animals. Following a dermal exposure period of 4 hours, the occlusive dressing was removed and readings were performed up to 14 days p.a. One hour up to 72 hours after removal of the patches, the treated skin surface was dry, rough, indurated, lumpy and discolored light brown. All signs of irritation were almost completely reversible after 14 days (Hoechst 1981).

Tests on Human Volunteers

Decades of manufacturing experience with occasional incidental dermal contact of workers with SAS have not revealed a significant skin irritating potential of SAS in humans. This is supported by a series of dermal irritation studies, divided in pilot and main studies, which were conducted in human volunteers. In these investigations, diluted and undiluted SAS (60% active matter) was used as test substance. All studies of this series were performed at the dermatological hospital of the University of Göppingen (Germany) between May 1990 and November 1990.

To screen the skin compatibility of SAS (60% active matter), 15 test volunteers with healthy skin (type I and II) were dermally exposed in an open patch test for 15 minutes. The volunteers were adviced to report any discomfort at once. Two test volunteers reported a very slight itching whereas in the remaining 13 volunteers no adverse effects occurred. Skin changes were not observed at all. After this screening study, a second screen was conducted using 1:100 and 1:10 dilutions of SAS (60% active matter) in water. 40 healthy test volunteers having a skin type I or II were patch-tested for 24 hours

under occlusive conditions. Afterwards three subsequent readings were performed. As a result, both dilutions were tolerated by the volunteers without significant skin reactions (Ippen, 1990a).

Based on these screening tests, an open patch test with undiluted SAS (60% active matter) was performed in 10 female test volunteers (skin type I and II) 26 to 52 years old. About 0.5 mL of the undiluted test material was dermally applied to the flexor side of the left forearm for 4 hours. Readings were performed every 15 minutes as well as 24 hours after exposure. No discomfort was reported by the test volunteers and no skin effects occurred. Thus it was concluded that SAS up to concentrations of 60% active matter is not a skin irritant in humans (Ippen, 1990b).

A human covered patch test was carried out with SAS (10%, 30% or 60% active matter) to further evaluate potential skin irritation in humans under GCP conditions which mimics the standard Draize rabbit skin test. For ethical reasons and to ensure safe test conditions for the volunteers, at first a pilot phase was conducted using diluted SAS (10% active matter) and after that SAS at 30% and 60% active matter. The test materials were applied to the left arm of three volunteers at first for one hour. In every case, only after there were no unacceptable responses or results observed, testing with the higher active product was initiated. Since no significant skin reactions were observed in the pilot phase, a subsequent dermal exposure for 4 hours took place (again first with the 10% sample following the 30% sample). After that SAS (60% active matter) was tested under semi-occlusive conditions in 10 human volunteers. The exposure period was 4 hours. After removal of the test patches the treated skin sites were gently wiped with a moist cotton wool ball and than graded one hour later. Further skin readings were made after a further 24, 28 and 72 hours. Throughout the study there was no evidence of oedema or encrustation in any of the pilot or main group subjects. Some of the human volunteers exhibited very slight, but transient erythema. Based on the low irritation levels obtained, SAS in concentrations up to 60% active was not regarded to be a skin irritant in humans even under conditions comparable to animal experiments (ISC, 2000).

Conclusion

Based on the most reliable studies available, SAS in concentrations up to 60% active matter is regarded to present significant skin irritating properties in rabbits. Also when tested as 30% active material, SAS has to be considered a skin irritant in animals. However, well documented human volunteer studies indicate that SAS up to concentrations of 60% active matter is not a significant skin irritant in humans.

5.2.1.3 Eye irritation

Four eye irritation studies on rabbits are available for SAS at various concentrations of 15 up to 60% (Hüls, 1986b; Hoechst 1989g; RCC 1990; RCC 1994). Findings of all the studies were consistent and demonstrated concentration dependent irritant effects. With the exception of one study (Hüls 1986b) which was not conducted according to GLP, all other studies are regarded to be valid without restrictions although in one study the so-called `low volume procedure` had been applied.
SAS (30% active matter) was tested for primary eye irritation according to OECD 405 and GLP. Because of the observed skin irritating potential in rabbits, testing for eye irritation was conducted in only one rabbit. 0.1 mL of undiluted SAS was applied into the left conjunctival sac of this rabbit. The right eye served as a control. Assessments were made 1, 24, 48 and 72 hours p.a. as well as 7 days after treatment. From one hour up to seven days moderate irritations including corneal and iridial effects were reported. After seven days a clear vascularisation of the cornea was observed. Based on the results of this study, SAS was considered to be severely irritating to eyes and thus no further animals were included in the test (Hoechst 1989g). Additionally, no higher concentrated SAS was tested as the same result can be expected.

In another GLP study, SAS 15 (15% active matter) was tested according to OECD Guideline 405 for primary eye irritation in three rabbits. On test day 1, 0.1 mL of the undiluted test article was placed into the conjunctival sac of the left eye of each animal. The right eye remained untreated and served as the reference control. Readings were performed after 1, 24, 48 and 72 hours as well as after 7, 14 and 21 days. Under the conditions of this experiment, SAS was found to cause a primary irritation score of 3.50. Slight opacity of the cornea was observed in all animals from 1 hour to 7 days and in one

animal from 14 to 21 days after treatment. However, a clear tendency of reversibility was observed in all animals between 72 hours and 21 days after application. Based on the results of this study and the clear tendency of reversibility, SAS in concentrations up to 15% active matter is considered to be only slightly irritating to eyes (RCC 1990).

In a non-GLP conform test, SAS (60% active matter) was tested for acute eye irritation. Based on the study results, the authors concluded that SAS is moderately irritating to eyes. However, irreversible effects in form of progressive vascularisation occurred in the eyes at the end of observation period of 21 days (Hüls 1986b).

In a further study, SAS 30 (30%active matter) was tested for primary eye irritation in rabbits using the low volume test procedure. 0.01 mL of the undiluted test material was applied into the left conjunctival sac of three rabbits. Readings were performed after 1, 24, 48, and 72 hours as well as 7 days after application. From one hour up to 48 hours p.a. slight to moderate redness and chemosis of the conjunctivae were observed. 72 hours after application one animal exhibited still slight redness of the conjunctivae. After 7 days all signs of irritation were reversible. Based on the results of this study and following the low-volume procedure SAS up to 30% active matter is not causing significant eye irritation (RCC 1994).

Conclusion
SAS is slightly irritating to eye at 15%. It is irritating to eye at concentrations of 30% and above. However, even at 30% active matter, SAS is not causing significant eye irritation when the low-volume technique is applied.

5.2.1.4 Sensitisation

There are two studies available with regard to skin sensitization (Hüls, 1986c; Hoechst 1974). Although both studies were not carried out according to the criteria of GLP, both tests are of acceptable validity for the evaluation of a skin sensitizing potential.

In the first study (Hoechst, 1974), SAS (60% active matter) was examined for its capacity to cause contact allergy by the maximization test according to Magnusson and Kligman with guinea pigs. Based on a screening using groups of 6 male guinea pigs the highest non-irritating concentration of SAS was established to be 5% in water. In the main study 15 male guinea pigs were used. Induction exposure included 10 intracutaneous injections of 0.05 mL of a solution of 500 mg SAS in 10 mL of Freund`s complete adjuvant. Challenge was made 14 days after the last injection using 0.1 mL of SAS at 5% test concentration. Readings performed 24 and 48 hours after the challenge treatment revealed no signs of skin reactions (sensitization incidence = 0%). Additionally, also a second challenge treatment using the same test conditions like in the first challenge revealed no signs of skin reactions (sensitization incidence = 0%). Thus it was concluded, that SAS is not a skin sensitizer (Hoechst 1974).

In a second study (Hüls 1986c), SAS (60% active matter) was tested for skin sensitization according to OECD Guideline 406 but without GLP using the maximization test protocol of Magnusson and Kligman. Based on prescreening, the primary irritating as well as non-irritating concentration was 5% and 1% respectively. 20 guinea pigs in the test group and 10 guinea pigs as control were used. Intradermal induction was performed using 0.1 mL of a 0.05% solution of SAS in Freud`s complete adjuvant. Dermal induction was performed one week later by dermal exposure with a 5% solution of SAS in water. 14 days after the dermal induction phase challenge treatment was conducted using a 1% solution of the test material in water. Readings performed after 24 and 48 hours after challenge treatment revealed no signs of skin reactions (sensitization incidence = 0%). Based on the test results, the authors concluded that SAS is not a skin sensitizer (Hüls 1986c).

Conclusion

No sensitisation potential was found for SAS (60% active matter) when tested in guinea pigs according to the maximization protocol of Magnusson and Kligman.

5.2.1.5 Repeated Dose Toxicity

5.2.1.5.1 Oral route

There is one chronic feeding study available for SAS (60% active matter). Although not conducted according to GLP, the study followed the scientific standards at this time and is regarded to be valid with restrictions. Groups of 30 male and 30 female Sprague-Dawley rats were fed diets containing 0.08, 0.4 or 2.0% (w/w) corresponding to approximately 62.5, 200 or 1000 mg/kg bw/day SAS (60% active matter) for 52 weeks. A similar sized group received a control diet and served as controls. 10 male and 10 female rats from each group were killed after 26 weeks of treatment for interim pathological examination. Throughout the study no mortality occurred. A lack of grooming activity was observed throughout the treatment period in both sexes given 2% (w/w). By the end of the fourth week, the leaner body conformation of rats at the high dose level was discernible on handling. No signs of reaction to treatment were seen at treatment levels of 0.4 % and below. Food intake was reduced in weeks 1 to 19 in males given the highest level. Females at this level and rats of both sexes at lower levels were unaffected in this respect. Bodyweight developments were reduced in rats of both sexes given 2% SAS, but not below. Marginal increases in serum alkaline phosphatase and glutamate-pyruvate transaminase activity, seen at 26 and 52 weeks in animals receiving the highest dietary concentration, did not associate with structural changes in any tissue. Therefore they were not considered to be manifestations of adverse reactions. Haematological characteristics, urinalysis and urine concentrating ability were unaffected by treatment at 2%: No disturbances of absolute and relative organ weights relating to treatment with SAS were seen in rats killed after 26 or 52 weeks of treatment. Macro- and microscopic examinations of rats killed after 26 or 52 weeks similarly revealed no changes in organ morphology attributable to treatment. Based on all results, it was concluded that the only detectable evidence of adverse reaction in rats receiving 2% SAS in their diet for one year was impaired grooming activity and retarded weight gain relating only in part to reduced food consumption. These non-specific changes were not accompanied by any significant functional or structural changes (Hoechst 1978a). Based on the study results the NOAEL

was conservatively placed at 0.4 SAS (60 % active matter) which aprroximates 200 mg/kg bw/day.

5.2.1.5.2 Inhalation

Long-term inhalation studies with SAS are not available. Given the irritant nature of SAS, it is expected that repeated inhalation of SAS might be irritating to the respiratory tract. However, due to the very low aerosol / dust generation during realistic use conditions, risks for consumers are regarded to be negligible.

5.2.1.5.3 Dermal route

A subacute dermal toxicity study with SAS (60% active matter) was performed in CD-1 mice using aqueous solutions of SAS at different concentrations. 4 groups of 25 female mice were topically administered 0.1 mL of 0% (group 1), 0.1% (group 2), 0.5% (group 3) or 1.0% (group 4) SAS (w/v). After 3 weeks of exposure the concentration applied to group 3 was increased to 8.0% and after 4 weeks to 16% (w/v). The concentration of the test solution applied to group 4 was increased after one week to 2% and after 3 weeks to 32% (w/v). Treatment was continued 5 days per week for 4 consecutive weeks in the case of groups 2 and 4, and for 5 weeks in groups 1 and 3. Encrustation, skin thickening, erythema and skin sloughing were observed at the treated skin sites in all mice within two days of commencement of treatment with solutions containing 32% (w/v). Mice given 16% showed skin thickening after one week of treatment. Mice treated with solutions containing 8% (w/v) SAS and below showed no detectable reactions at the exposed skin sites. Weight losses, without concomitant reduction of food intake, were seen in all mice receiving 32% in the first week of treatment. However, a return to normal growth was observed during the second week of exposure at this level. Mice dermally treated at 8% or below showed no weight retardation. Organ weight analysis showed increased absolute and relative spleen weights in mice given 32%. This was considered a secondary response to the inflammatory and infective skin condition due to the irritating properties of SAS at the site of application.

Absolute and relative weights of liver and kidneys in mice given 32% as well as spleen, liver and kidneys at lower levels of administration were unaltered by the treatment (Hoechst 1975b).

Conclusion

SAS (60% active matter) was tested for systemic toxicity using both, the oral and the dermal route of exposure. With regard to oral uptake, a chronic feeding study has demonstrated that concentrations of SAS in the diet up to 0.4% have been tolerated by the animals without any significant effect. As a first approximation this concentration corresponds to about 200 mg/kg body weight per day. Even at the highest level of 2% in the diet (approximately 1000 mg/kg body weight per day) only unspecific effects not accompanied by any functional or structural changes have been observed. In view of the results of a 2-year bioassay in rats, dietary concentrations of up to 2% SAS (w/w) (approximately 1000 mg/kg bw/day) were tolerated without any significant toxicological side effects (see 5.2.1.7).

Repeated dermal application on mice of SAS solutions as high as 32% (w/v) for 4 respectively 5 weeks, resulted neither in mortality nor any substance related systemic toxicity. The only changes noted were local skin effects due to irritative properties. SAS solutions up to 8% (w/v) proved to be without any effects.

NOAEL for systemic toxicity

Based on all available information, an oral NOEL of 200 mg/kg body weight per day is conservatively proposed for this risk assessment, although no significant changes have been reported even at dietary levels of up to 2% (w/w).

5.2.1.6 Genetic Toxicity

5.2.1.6.1 *In vitro*

One bacterial mutagenicity test with SAS is available (Hoechst 1977b), which was not conducted according to GLP and OECD Guidelines. However, it followed the scientifical standard at this time and is regarded to be valid with restrictions. In this test, SAS (30% active matter) was investigated for point mutagenic effects in the *Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537 using the methodology of Ames. The tests were performed in the presence and in the absence of a metabolizing system derived from rat liver homogenate (S9-mix). A dose range of 0.001 to 5 µL per plate was used. Based on the results obtained, SAS is not mutagenic in these bacterial test systems either with or without exogenous metabolic activation (Hoechst 1977b).

Conclusion

Based on the available *in vitro* data, no indications of a point mutagenic effect of SAS exist.

5.2.1.6.2 *In vivo*

There are two different *in vivo* micronucleus assays with SAS in different strains of mice available (Hoechst 1975c; 1978b). Although not according to GLP and OECD Guidelines, both studies can be used for an evaluation of potential mutagenicity of SAS.

In the first study, SAS (60% active matter) was investigated for possible chromosomal aberration effects in CD1-mice. Groups of 5 male and 5 female mice were administered the test compound orally by gavage at dose levels of 280, 580 or 1170 mg/kg body weight for two consecutive days. A fourth group, serving as negative controls, received distilled water, whilst a fifth group, serving as positive controls, received thio-tepa at a dose level of 10 mg per kg body weight for two days by the intraperitoneal route. In the group given thio-tepa, a significant increase in the incidence of erythrocytes containing micronuclei was recorded. On the contrary, the administration of SAS to mice at dose levels up to 1170 mg/kg body weight for two days was without effect on the incidence of erythrocytes containing micronuclei. On the basis of the results obtained, SAS was not mutagenic in the micronucleus test (Hoechst 1975c).

In another micronucleus-test, groups of 5 male and 5 female NMRI-mice were administered SAS (60% active matter) orally by gavage at dose levels of 0, 600, 1200 or 2400 mg/kg body weight. The animals were treated twice in an interval of 24 hours and sacrificed 6 hours after the last application. All animals of the high-dose group died after the second application. In the mid and low dose groups the incidence of micronucleated polychromatic erythrocytes was not increased in comparison with controls. On the basis of the results obtained, SAS was not mutagenic in the micronucleus-test in NMRI-mice (Hoechst 1978b).

Conclusion

Based on all available test data, no indications regarding a mutagenic potential for SAS (60 % active matter) exist.

5.2.1.7 Carcinogenicity

5.2.1.7.1 Oral route

Groups of 50 male and 50 female CD rats were fed diets containing 0.08, 0.4 or 2% (w/w) SAS (60% active matter) for two years. A similar constituted group received diet without added SAS and acted as controls. Body weight developments (and food intake in weeks 0 to 52 for males and weeks 0 to 12 for females) were reduced (approximately 10 to 15%) in animals of both sexes receiving diets containing 2% SAS (w/w), but not at lower concentrations. Apart from an initial dishevelled appearance indicative of impaired grooming in rats receiving the highest dietary concentration of 2%, treated and control rats remained indistinguishable from another throughout the treatment period in respect to appearance, general health condition, behaviour, locomotor function and faecal characteristics. Compared with controls, survival in the two-year treatment period was improved in animals of both sexes receiving 2% and in males receiving 0.4% SAS in the diet (w/w). The cellular and chemical characteristics of blood and urine were undisturbed by treatment when examined after 26, 52, 78 and 104 weeks. The incidence, onset times and multiplicity of externally palpable masses was not affected by treatment. Macroscopic findings at necropsy of decedents or of survivors at termination were

considered to reflect the normal range of spontaneous pathology associated with the strain of rats employed. Non-neoplastic and neoplastic pathology were undisturbed by treatment with SAS for two years. Based on the results, there was no indication of a carcinogenic potential of SAS (60% active matter) after oral administration for two years (Hoechst 1978c).

Conclusion

The study was not conducted according to GLP but followed formerly accepted scientific guidance. The results of both, the chronic toxicity study as well as the bioassay in rats revealed comparable results and have not shown any evidence of carcinogenicity. Thus, the study can be regarded as valid with restrictions and the NOEL for tumorigenic effects therefore can be placed at 2% SAS in the diet, which approximately corresponds to about 1000 mg/kg body weight per day for rats.

5.2.1.7.2 Dermal route

SAS (60% active matter) was administered three times each week to the shaved backs of groups of 100 male and 100 female CD-1 mice at concentrations of 0 (untreated), 0 (vehicle alone (distilled water)), 0.1, 0.5 or 1.0% (w/v) in distilled water over a scheduled period of 80 weeks. This treatment was followed by an observation period lasting 24 weeks. No signs of reaction to treatment were recorded at any time during the total 104 week period. A total of 982 mice (496 males and 486 females) died or were killed in extremes (18 mice were lost due to cannibalism). Neither, their distribution among the groups, nor the causes of death displayed any relationship to treatment. Predominant macropathological entities, and thos detected by microscopy, were recognized as those that commonly occur in mice of this age and strain. All findings were not considered to be related to treatment. Although subject to some variation, body weight gains in the treated and control groups were throughout the study essential identical. Food and water consumption of mice receiving dermal applications of SAS remained closely comparable with those of untreated controls. Histopathological examination of skin samples taken from areas receiving the highest concentration of 1% (w/v), or the lowest concentration of 0.1% (w/v) of SAS and similar samples taken from untreated animals or from animals

receiving the vehicle alone, revealed no treatment related abnormalities. The neoplasmata diagnosed were those which arise spontaneously in this strain of mouse. There was no evidence to suggest that SAS had displayed oncogenic potential under the conditions of this study (Hoechst 1978d).

Conclusion

The study was not conducted according to GLP but followed formerly accepted scientific guidance and can be used for an evaluation of this endpoint. Based on the results SAS did not show any evidence of carcinogenicity. Thus, the study can be regarded as valid with restrictions and the NOEL after dermal exposure over 80 weeks to mice can be placed at 1% SAS (w/v) in distilled water.

5.2.1.8 Reproductive toxicity

The influence of SAS (60% active matter) upon reproductive function and fertility was assessed over two generations in rats of the Charles River CD strain. For this purpose, SAS was administered in the diet to both the F_0 and F_1 generations at levels of 1000, 3000 or 10000 ppm. Treatment was given either continuously to both sexes for 60 days prior to mating and throughout three successive pregnancies (F_1A, F_1B, F_1C, F_2A, F_2B and F_2C) or to females only during the organogenesis stage of three successive pregnancies. Animals were randomly selected from the F_1B litters to form the second generation. In both the F_0 and F_1 generations, haematological investigations were carried out after 60 days of treatment on five males and five females in each group, prior to carbon dioxide asphyxiation and subsequent macroscopic and histopathological examination. The remaining animals were paired, within groups, on a one to one basis on three consecutive occasions. After the first two matings (F_1A, F_1B, F_2A, F_2B) the females were allowed to litter naturally and rear their young to weaning. Following the third mating (F_1C, F_2C) half of the dams in each group were killed on day 13 of gestation, and the remainder were killed on day 21 of gestation, to permit examination of their uterine contents. After termination of

each generation, all parent animals were examined macroscopically. Five males and five females from each of the continuously treated groups, together with five females only from each of the groups treated during organogenesis, were randomly selected for histopathological evaluation. In both generations prior to mating, food intake, haematological parameters, absolute and relative organ weights and histopathological evaluation of tissues showed no adverse treatment-related effects. In the F_0 generation, a slight but not statistical significant depression of body weight gain was observed in males treated continuously with SAS at 10000 ppm. A similar reduction was observed in F_0 females treated prior to mating at 10000 ppm and statistical significance was achieved here in week 8 of treatment. During the three subsequent pregnancies, some fluctuation in body weight gain was recorded in treated females, but no significant inter-group variation was observed. In both generations, oestrous cycles, mating performance and conception rates were unaffected by treatment. In the F_0 and F_1 generation no alterations in duration of gestation were observed. Neither generation, during the first two pregnancies (F_1A, F_1B, F_2A, F_2B), showed any treatment-related effects in the number of litters containing at least one viable young, the litter size at birth, or the live birth index. The viability index was significantly depressed in the F_1A litters of females receiving 3000 or 10000 ppm continuously, and in the F_2B litters of the females receiving 3000 ppm continuously. In all other groups, the viability index was comparable with that of the control group. The body weight of offspring at day 1 post partum showed no significant inter-group variations. However, the bodies weight gain of offspring from females receiving 10000 ppm continuously was depressed in the F_1A, F_1B, F_2A and F_2B litters. All other treated offspring gained weight at a similar rate to the controls. In both generations, the sex ratio at day 4 post partum and the weaning were unaffected by treatment. Macroscopic examination, absolute and relative organ weights and histopathological evaluation of F_0 and F_1 parent animals showed no adverse treatment-related effects. It was concluded from these investigations that continuous treatment with SAS (60% active matter) at a level of 10000 ppm gave rise to a slight depression of somatic growth in parent animals and offspring in both generations, and to a marginal interference with survival of F_1A offspring. At the intermediate dose level of continuous treatment (3000 ppm) slight depression of somatic growth of F_1 males was observed and there was marginal interference with survival of F_1A

and F_2B offspring. At the lowest level of continuous treatment as well as in animals treated at all levels during organogenesis, no treatment-related adverse effects were observed. There were no indications for an embryotoxic or teratogenic effect related to treatment in any dose groups (Hoechst 1978e).

Based on the results of the available expanded two-generation study including segment two phase testing, no indications for embryotoxic and / or teratogenic properties of SAS (60% active matter) were observed. The NOEL for this endpoint therefore was placed at 10000 ppm SAS in the diet which approximately corresponds to about 500 mg/kg body weight per day.

5.2.2 Identification of critical endpoints

5.2.2.1 Overview on hazard identification

SAS at concentrations up to 60% active matter, the usual concentration sold to formulators, exhibits low acute oral toxicity (LD50 > 2000 mg/kg bw). Indications of acute dermal toxicity do not exist. Conclusive data on acute inhalation toxic effects of SAS are not available.
Regarding primary irritation, indications from animal experiments exist that high concentrated SAS (30% active matter and above) is irritating to the skin. However, a series of well documented human volunteer studies have not revealed signs of significant skin irritation of SAS (up to 60% active matter). With regard to mucous membrane tolerability, concentrated SAS (30% active matter and above) is severely irritating to eyes. However, below a threshold of up to 15% active matter, no significant eye irritation is observed.

Based on two independent maximization tests, SAS is not a skin sensitizer.

SAS shows a very low level of systemic toxicity using both, the oral and dermal exposure route. Based on a chronic feeding study, an oral NOEL was conservatively placed at

0.4% (w/w) SAS in the diet (corresponding to approximately 200 mg/kg body weight per day) although even concentrations up to 2% (w/w) in the diet (corresponding to approximately 1000 mg/kg body weight per day) can be regarded as a NOAEL. The only effects seen at the 2% level was retarded weight gain and impaired grooming activity.
According to results from mutagenicity studies, both in vitro and in vivo, SAS exhibited no pointmutagenic and/or chromosomal mutagenic effect.
Potential carcinogenicity of SAS was investigated in a 2-year feeding study in rats. Based on the results of this bioassay, no indications of non-neoplastic and/or neoplastic pathology have been revealed using dietary SAS levels of up to 2% (w/w) corresponding to about 1000 mg/kg body weight per day. Likewise, using the dermal route of exposure no carcinogenic potential was revealed in a 104 week study in mice up to 1% SAS (w/v) in distilled water.
With regard to potential reproductive toxic effects, a multigeneration study including an in life segment II testing revealed that SAS in dietary concentrations of up to 10000 ppm has no effect on reproductive performance and does not elicit a teratogenic response.
Based on the summarized toxicological profile, the predominant intrinsic hazard of SAS is of direct nature on skin and mucous membranes, and consists of potential local irritating effects of high concentrated SAS formulations. Indications for systemic toxic effects including a carcinogenic potential were not observed.

5.2.2.2 Adverse effects related to accidental exposure

Accidental exposure has to be evaluated as an acute event. Thus identified hazards after acute exposure (i.e. acute toxicity after oral, dermal and/or inhalation exposure, primary irritating effects) have to be considered under this aspect. The acute oral toxicity of high concentrated SAS (60% active matter) is greater than 2000 mg/kg body weight. Although no acute dermal toxicity studies are available, there are no indications of significant toxicity from results of dermal toxicity studies with repeated administration. Although accidental skin exposure or inhalation of concentrated SAS may lead to irritation responses of the skin, eyes and respiratory tract, this exposure scenario is not very realistic for consumers using diluted formulations. Amongst these exposure scenarios,

contact of high concentrated SAS formulations with the eyes seem to be the most critical one. However, in most detergent formulations SAS is present at concentrations between 1 and 15% and thus, below the threshold where significant eye irritation may be expected.

5.2.3 Determination of NOAEL or quantitative evaluation of data

Repeated dose toxicity

With regard to repeated dose toxicity a chronic (1-year) oral toxicity study is available which has demonstrated no significant toxicological effects up to the highest dietary SAS concentration of 2% (approximately 1000 mg/kg body weight per day). The only substance related effects seen at this dose level was impaired grooming activity and slight retardation of body weight gain. Although this dose level can be regarded to be a NOAEL (also supported by the oral carcinogenicity study), the actual NOEL was placed conservatively at 0.4% SAS in the feed which corresponds to about 200 mg/kg body weight per day. Based hereupon, this NOEL is used for the risk characterization. It should be pointed out, however, that this NOEL is coming from a chronic toxicity study. Additional extrapolation factors to account for a duration extrapolation therefore are not necessary.

Carcinogenicity

Based on the available oral bioassay, no indications for potential carcinogenicity of SAS were observed. Up to a dietary SAS concentration of 2% (corresponding to about 1000 mg/kg body weight per day) neither non-neoplastic nor neoplastic findings occurred. Histopathological findings were also not observed. Thus the NOEL for tumorigenic effects was placed at 1000 mg/kg body weight per day.

No signs of carcinogenic properties were also revealed in a 104 week study using the dermal exposure route in mice. The NOEL of this study was 1% SAS (w/v) in distilled water as the highest concentration tested.

Reproductive toxicity

With regard to potential reproductive toxic effects of SAS, a multigeneration study including an in life segment II testing revealed that SAS in dietary concentrations of up to 10000 ppm (approximately 500 mg/kg bw per day) has no effect on reproductive

performance and does not elicit a teratogenic response. Based on this study, an oral NOAEL of 500 mg SAS per kg body weight per day, corresponding to the highest dose tested was assessed.

5.3 Risk assessment

5.3.1 Margin of exposure calculation

The Margin of Exposure (MOE) is the ratio of the No Observed (Adverse) Effect Level [NO(A)EL] or an appropriate substitute (e.g. LOAEL) to the estimated or actual level of human exposure to a substance. A systemic NOEL for SAS can be determined using the oral NOEL of 200 mg/kg body weight per day in the rat derived from a chronic (1-year) oral toxicity study (see 5.2.3) and an conservatively assumed bioavailability after oral uptake of 90% (adapted from Michael, 1968). The resulting value of **180 mg SAS per kg body weight per day** is used as the "**systemic NOEL"** to calculate the MOE values in the different exposure scenarios detailed below.

Exposure scenario: direct skin contact from hand dishwashing
For calculation of the MOE, the systemic NOEL of 180 mg/kg body weight per day was divided by the daily systemic dose of 0.15 µg/kg body weight per day estimated for the dermal exposure to SAS from hand dishwashing:

$$\mathbf{MOE_{direct\ skin}} = \text{systemic oral NOEL /estimated systemic dose} = 180000/0.15\ [\mu g/kg\ BW/day] = \mathbf{1200000}$$

Exposure scenario: direct skin contact from hand washed laundry
For calculation of the MOE, the systemic NOEL of 180 mg/kg body weight per day was divided by the daily systemic dose of 0.1 µg/kg body weight per day estimated for the dermal exposure to SAS from hand washed laundry:

$$\mathbf{MOE_{direct\ skin}} = \text{systemic oral NOEL /estimated systemic dose} = 180000/0.1\ [\mu g/kg\ BW/day] = \mathbf{1800000}$$

Exposure scenario: direct skin contact from pre-treatment of clothes

For calculation of the MOE, the systemic NOEL of 180 mg/kg body weight per day was divided by the daily systemic dose of 1.45 µg/kg body weight per day estimated for the dermal exposure to SAS from pre-treatment of clothes:

$MOE_{direct\ skin}$ = systemic oral NOEL /estimated systemic dose = 180000/1.45 [µg/kg BW/day] = **124000**

All other possible direct and indirect skin contact scenarios, such as short direct contact with laundry powder or laundry tablets result in even lower estimated systemic doses and will give larger MOE. Additionally, also all other exposure scenarios like direct skin contact from `rinse off cosmetics` and potential oral exposures from accidental ingestion result in negligible MOE`s. These are not further considered in this risk assessment.

Exposure scenario: indirect skin contact from wearing of clothes

For calculation of the MOE, the systemic NOEL of 180 mg/kg body weight per day was divided by the daily systemic dose of 0.74 µg/kg body weight per day estimated for the dermal exposure to SAS from wearing of clothes:

$MOE_{indirect\ skin}$ = systemic oral NOEL /estimated systemic dose = 180000/0.74 [µg/kg BW/day] = **240000**

Exposure scenario: oral route from residues left on dishware

For calculation of the MOE, the systemic NOEL of 180 mg/kg body weight per day was divided by the daily systemic dose of 1.43 µg/kg body weight per day estimated for the oral route from residues left on dishware:

$MOE_{oral\ route}$ = systemic oral NOEL /estimated systemic dose =

180000/1.43 [µg/kg BW/day] = **125000**

Exposure scenario: oral route from accidental ingestion and accidental contact with the eyes

Occasional ingestion of a few milligrams of SAS as a consequence of accidental ingestion of laundry and cleaning products is not expected to result in any significant adverse health effects to humans given the low toxicity profile of SAS. This view is reinforced by the fact that poison control centers, such as for example those in Germany and the UK, have not reported a case of lethal poisoning with detergents containing SAS.

Contact of hand wash solutions containing SAS with the skin is not a cause of concern given that SAS is not a contact sensitiser and that the concentrations of SAS in such solutions are well below 1%. As reported in section 5.2.1.2 of this assessment, aqueous solutions of SAS at concentrations up to 2.5% failed to show any irritation effects on rabbit skin after 24 hours of occlusive application.

Accidental contact of hand wash solutions containing SAS with the eyes is not expected to cause more than a mild irritation on the basis of the experimental data as reported in section 5.2.1.3.

Total consumer exposure

Based on a.m. exposure scenarios, the estimated total body burden of consumers for SAS can be calculated as follows:

Direct skin contact from hand dishwashing: 0.15 µg/kg body weight per day

Direct skin contact from hand washed laundry: 0.10 µg/kg body weight per day

Direct skin contact from pre-treatment of clothes: 1.45 µg/kg body weight per day

Indirect skin contact from wearing clothes: **0.74 µg/kg body weight per day**

Oral ingestion from residues left on dishware: **1.43 µg/kg body weight per day**

The consumer exposure to SAS from the identified most relevant sources thus results in an estimated total body burden of 0.15 + 0.10 + 1.45 + 0.74 + 1.43 = 3.87 µg/kg body weight per day. Comparison with the systemic NOEL of 180000 µg/kg body weight per day yields an MOE of approximately 46500.

$\mathbf{MOE_{total}}$ = systemic oral NOEL /estimated total systemic dose = 180000/3.87 [µg/kg BW/day] ≅ 46500

5.3.2 Risk characterization

5.3.2.1 Systemic toxicity

Scenarios relevant to the consumer exposure to SAS have been identified and assessed using the `Margin of exposure` (MOE) or equivalent assessments. The MOE for the combined estimated systemic dose is calculated to be about 46500.
This `Margin of Exposure` is thus large enough to account for the inherent uncertainty and variability of the hazard database and inter species and intra species extrapolations, (which is conventionally estimated at a factor of 100). In addition, the estimated Margin of Exposure is based on very conservative estimations of both exposure and the underlying NOEL (which is a systemic NOEL by assuming 90% absorption). Moreover, given that the identified and used NOEL is coming from a chronic oral toxicity study, no corrections for duration extrapolation are necessary. Taking into account that the NOEL reflects a dose level at which no negative health effects were observed at all, the use of the NOAEL (1000 mg/kg body weight per day) would have resulted in an even fivefold higher MOE. The only adverse effect identified associated to the NOAEL was an

impaired grooming activity and slight retardation in body weight gain. Using the NOAEL for the calculations, the MOE for the combined estimated systemic dose of SAS would have been 235000. Other than that, the toxicological data show that SAS was not genotoxic in vitro or in vivo, did not induce tumors in rodents after two years daily dosing, and failed to induce either reproductive toxicity or developmental or teratogenic effects at the highest doses tested. Based on the above, the presence of SAS in consumer products does not raise any safety concerns associated to systemic toxicity.

5.3.2.2 Acute effects

Occasional ingestion of a few milligrams of SAS as a consequence of accidental ingestion of laundry and cleaning products is not expected to result in any significant adverse health effects to humans given the low toxicity profile of SAS. This view is reinforced by the fact that poison control centers, such as for example those in Germany and the UK, have not reported any case of significant poisoning with detergents containing SAS.

5.3.2.3 Local effects

Neat SAS is an irritant to skin and eyes in rabbits. The irritation potential of aqueous solutions of SAS depends on the concentration. However, well documented human volunteer studies indicate that SAS up to concentrations of 60% active matter is not a significant skin irritant in humans.

Contact of hand wash solutions containing SAS with the skin is not a cause of concern given that SAS is not a contact sensitiser and that the concentrations of SAS in such solutions are well below 1%. As reported in section 5.2.1.5.3 of this assessment, aqueous solutions of SAS at concentrations up to 8% failed to show any irritant effects on the skin of mice treated dermally for 4 to 5 weeks.

Accidental contact of hand wash solutions containing SAS with the eyes is not expected to cause more than a mild irritation on the basis of the experimental data as reported in section 5.2.1.3.

In the course of laundry pre-treatment, skin contact with concentrated powder paste or neat liquid detergent (in the worst case containing up to 29% SAS) may occur. If it does, contact is confined to a fraction of the skin of the hands (palms or fingers), is of very short duration (typically a few minutes) and the initial high SAS concentration is usually diluted out rapidly in the course of the pre-treatment task. Contact with concentrated powder paste or neat liquid may result in transient skin irritation of the hands, which is expected to be mild in nature and effectively avoided by prompt washing with water.

Potential irritation of the respiratory tract is not a concern given the very low levels of airborne SAS generated as a consequence of cleaning sprays aerosols or laundry powder detergent dust (see sections 5.1.3).

SAS is present in household liquid detergent products at concentrations that range from 0.1% to 15%. As described in section 5.2.1.3 the threshold for eye irritating effects in rabbits is 15%. Nevertheless, accidental spillage of neat product into the eye should be avoided as it may result in slight irritation. However, no severe and/or irreversible eye irritation is to be expected and immediate rinsing of the eyes with water following accidental spillage of neat product will further reduce any signs of irritation. The experience from many years of marketing of household liquid detergent products containing SAS is that accidental eye spillage results at worst in transient irritation, with no irreversible effects to the eye.

5.3.3 Summary and conclusions

SAS is mainly used in household products for dishwashing. Although the main exposure possibility for consumers therefore is from dishwashing, also potential consumer exposure from other minor sources is considered in the context of this risk assessment. However, it should be pointed out that more than 97% of the calculated overall SAS body

burden of 3.87 µg/kg body weight per day is coming from sources other than dishwashing. This demonstrates that the overall risk characterization is following very conservative assumptions and reflects a real worst-case scenario.

The estimated consumer aggregate exposure from identified sources results in an estimated total body burden of approximately 3.87 µg/kg body weight per day.

The toxicological data show that SAS is not genotoxic in vitro or in vivo, does not induce tumors in rodents after two years of feeding up to 2% SAS in the diet, and failed to induce either reproductive toxicity or developmental or teratogenic effects at dietary levels of up to 10000 ppm. The only adverse effects identified after chronic (1-year) oral exposure of rodents were impaired grooming activity and a slight retardation of body weight gain at the highest tested dietary dose level of 2% (corresponding to approximately 1000 mg/kg body weight per day). Although this can be regarded to represent a NOAEL, the more conservatively defined NOEL of 0.4% SAS in the diet (corresponding to approximately 200 mg/kg body weight per day) was chosen for the risk characterisation and MOE calculations. Assuming 90% absorption after oral application, this value corresponds to a systemic NOEL of 180 mg/kg body weight per day.

The comparison of the total potential consumer exposure to SAS with the systemic NOEL results in an estimated `Margin of Exposure` of approximately 46500. This `Margin of Exposure` is large enough to account for the inherent uncertainty and variability of the hazard database and inter species and intra species extrapolations. In addition, the estimated `Margin of Exposure` is based on very conservative estimations of both exposure and the underlying NOEL (which is a systemic NOEL by assuming 90 % absorption after oral application). Moreover, given that the identified and used NOEL is coming from a chronic oral toxicity study, no corrections for duration extrapolation are necessary. Taking into account that the NOEL reflects a dose level at which no negative health effects at all were observed, the use of the NOAEL (1000 mg/kg body weight per day) would have resulted in a fivefold higher MOE. The only adverse effect identified associated to the NOAEL was an impaired grooming activity and slight retardation in

body weight gain. Using the NOAEL for the calculations, the MOE for the combined estimated systemic dose of SAS would have been 235000. Other than that, the toxicological data show that SAS was not genotoxic in vitro or in vivo, did not induce tumors in rodents after two years daily dosing using both, the oral and dermal route of exposure, and failed to induce either reproductive toxicity or developmental or teratogenic effects at the highest doses tested. Based on the above, the presence of SAS in consumer products does not raise any safety concerns associated to systemic toxicity.

With regard to local effects, technical grade SAS is an irritant to skin and eyes. However, the irritation potential of aqueous solutions of SAS depends on it`s concentration. Local effects of hand wash solutions containing SAS do not cause concern given that SAS is not a contact sensitiser and that the concentrations of SAS in such solutions are well below 1% and therefore not expected to be irritating to eye or skin. Laundry pre-treatment tasks, which may translate into brief hand skin contact with higher concentrations of SAS, may occasionally result in mild irritation easily avoided by rinsing of the hands in water. Potential irritation of the respiratory tract is not a concern given the very low levels of airborne SAS generated as a consequence of using cleaning sprays or laundry powder detergent dust.

In view of the extensive database with regard to the toxicity profile of SAS, the low exposure values calculated and the resulting large `Margin of Exposure` described above, it can be concluded that use of SAS in dishwashing, laundry and cleaning products raises no safety concerns for consumers.

6. References

AISE (2002)	AISE, Table of Habits and Practices for Consumer Products in Western Europe, 2002
BgVV (1999)	BgVV (Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin), Ärtzliche Mitteilungen bei Vergiftungen, 1999, ISBN 3-931675-59-9
Boethling and Mackay (2000)	Boethling, R.S., Mackay, D., Handbook of Property Estimation Methods for Chemicals, CRC Press, Boca Raton, 2000, ISBN 1-55670-456-1
BUA (1997)	BUA Report No. 206, Ecotoxicology of selected surfactants for the detergent and cleanser sector (May 1997), S. Hirzel, ISBN 3-7776-0847-5
CESIO (2000)	CESIO, Classification and Labelling of Surfactants for Human Health Hazards according to the Dangerous Substances Directive, 2000
CESIO (2003)	CESIO, Alkane sulphonates – consumption and uses in Western Europe, Brussels, August 7, 2003
Clariant (1998)	Clariant IUCLID Datasheet, Sulfonic acids, C10-18 alkane, sodium salts, CAS No. 68037-49-0, May 11, 1998
Clariant (2000)	Clariant Product Brochure Hostapur SAS™, May 2000
Clariant (2001a)	Clariant, Report No. CAD 75631, Hostapur SAS 60, Adsorption – Desorption using a Batch Equilibrium Method acc. OECD Guideline 106 (2000). 2001-06-01, Dr. Noack Test Lab, Sarstedt
Clariant (2001b)	Clariant, Report No. CAB75632, Hostapur SAS 60, Water Quality – Adsorption of substances on activated sludge – Batch Test using specific analytical methods acc. Guideline ISO/CD 18749 (2001-08-14), 2001-11-29, Dr. Noack Test Lab, Sarstedt
Clariant (2003)	Internal data compilation on SAS, 2003
Clariant (2004)	Clariant, Report No. K001, 2004-02-19, Div. FUN, RQA-AL/BI, unpublished
DHI (2001)	DHI Water & Environment and Danish Toxicology Center, Report No.615, 2001, Environmental and Health Assessment if Substances in Household Detergents and Cosmetic Detergent Products, 201 pages & annexes, published on Web Site (http://www.mst.dk/udgiv/publications/2001/87-7944-596-9/pdf/87-7944-597-7.pdf)
DuPont (1992)	DuPont Chemical, Initial submission: approximate lethal concentrations by inhalation of sodium lauryl sulfate & sodium dodecylbenzene sulfonate, TSCA 8ECP Doc ID 880920008936, NTIS/OTS0546357 (LIT), 1992
EU (1973)	EU Council Directive 73/405/EEC of November 22, 1973 on the approximation of the law of the member states relating to methods of testing the biodegradability of anionic surfactants
EU (1982)	EU Council Directive 82/243/EEC of March 31, 1982 amending the Directive 73/505/EEC on the approximation of the law of the member states relating to methods of testing the biodegradability of anionic surfactants
EU (1999)	Opinion of the Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) on a Proposed "ready biodegradability" approach to update detergents legislation - adopted at the 12th CSTEE plenary meeting of 25 November 1999. published on Web Site (http://europa.eu.int/comm/food/fs/sc/sct/out51_en.html)
EU (2003a)	EU Technical Guidance Document Risk Assessment New Notified and Existing Substances, Part II, Environment, Updated version 2003, published on Web Site http://ecb.jrc.it Section Documents
EU (2003b)	Draft Proposal for a Regulation of the European Parliament and of the Council on Detergents, 2003-05-03

(http://europa.eu.int/comm/enterprise/chemicals/legislation/detergents/publicconsult/reg.pdf)

Evans (2003) Evans, D., pKa Data, Methansulfonic acid, Harvard University, 2003 published on Web Site http://daecr1.harvard.edu/pKa/pKa.html

Field et al (1992) Field, J.A., Miller, D.J., Field, T.M., Hawthorne, S.B., Giger, W., Quantitaitve Determination of Sulphonated Aliphatic and Aromatic Surfactants in Sewage Sludge by Ion-Pair/Supercritical Fluid Extraction and Derivatization Gas Chromatography/Mass Spectrometry, Anal Chem 1992, 64, 3161-3167

Field et al (1994) Field, J.A., Field, T.M., Poiger, T., Giger, W., Determination of Secondary Alkane Sulfonates in Sewage Wastewaters by Solid-Phase Extraction and Injection-Port Derivatization Gas Chromatography/Mass Spectrometry, Environ Sci Technol 1994, 28, 497-503

Field et al (1995) Field, J.A., Field, T.M., Poiger, T., Siegrist, H., Giger, W., Fate of Secondary Alkane Sulfonate Surfactants during Municipal Waste Water Treatment, Wat. Res. 1995, 29 (5), 1301-1307

Gerike and Jasiak (1985) Gerike, P. and Jasiak, W., Tenside im Test zur Erkennung stabiler Metabolite, Tenside Det 1985, 22 (6), 305-310

Gerike and Jasiak (1986) Gerike, P. and Jasiak, W., How completely are surfactants biodegraded ?, Tenside Det 1986, 23 (6), 300-304

Guhl and Gode (1989) Guhl, W. and Gode, P., Correlations between lethal and chronic / biocneotic effect concentrations of surfactants, Tenside Surf Det 1989, 26 (4), 282-287

Hauthal (1995) Hauthal, H.G., Alkanesulfonates in Anionic Surfactants, pp 143-221, Ed. Stache, H., Marcel Dekker, New York, 1995, ISBN 0-8247-9394-3

HERA (2002a) HERA Guidance Document Methodology, Updated version April 2002 published on Web Site: http://www.heraproject.com/files/Guidance_document_22_April_2002.pdf

HERA (2002b) HERA, Draft Risk Assessment Linear Alkylbenzene Sulphonates (LAS), CAS No. 68411-30-3, July 2002, published on Web Site http://www.heraproject.com/files/HERA_LAS_RA-nal_draft_for_publication_August_4_.pdf

Hoechst (1971) Hoechst AG (Clariant GmbH), Report No. 71.0015, Unpublished results, 1971

Hoechst (1972) Hoechst AG, Unpublished report, January 13, 1972

Hoechst (1974) Hoechst AG (Clariant GmbH), Report No. 74.0294, Unpublished results, 1974

Hoechst (1975a) Hoechst AG (Clariant GmbH), Report No. 75.0646, Unpublished results, 1975a

Hoechst (1975b) Hoechst AG (Clariant GmbH), Report No. 75.0650, Unpublished results, 1975b

Hoechst (1975c) Hoechst AG (Clariant GmbH), Report No. 75.0647, Unpublished results, 1975c

Hoechst (1977) Hoechst AG, Unpublished report No. 77.0868, Leuciscus idus

Hoechst (1977a) Hoechst AG (Clariant GmbH), Report No. 77.0191, Unpublished results, 1977a

Hoechst (1977b) Hoechst AG (Clariant GmbH), Report No. 77.0644, Unpublished results, 1977b

Hoechst (1978) Hoechst AG, Unpublished report No. 78.0095, Leuciscus idus

Hoechst (1978a) Hoechst AG (Clariant GmbH), Report No. 78.0554, Unpublished results, 1978a

Hoechst (1978b) Hoechst AG (Clariant GmbH), Report No. 78.0310, Unpublished results, 1978b

Hoechst (1978c) Hoechst AG (Clariant GmbH), Report No. 78.0414, Unpublished results, 1978c

Hoechst (1978d) Hoechst AG (Clariant GmbH), Report No. 78.0441, Unpublished results, 1978d

Hoechst (1978e) Hoechst AG (Clariant GmbH), Report No. 78.0415, Unpublished results, 1978e

Hoechst (1979) Hoechst AG (Clariant GmbH), Report No. 79.0752, Unpublished results, 1979

Hoechst (1981)	Hoechst AG (Clariant GmbH), Report No. 81.0223, Unpublished results, 1981
Hoechst (1988a)	Hoechst AG, Unpublished report No. 88.1360, OECD 203, Danio rerio
Hoechst (1988b)	Hoechst AG, Unpublished report No. V88-0933, Pseudomonas putida
Hoechst (1989a)	Hoechst AG, Unpublished report No. 167/89, OECD 301E
Hoechst (1989b)	Hoechst AG, Unpublished report No. 89.0146, OECD 203, Danio rerio
Hoechst (1989c)	Hoechst AG, Unpublished report No. 89.0369, OECD 203, Danio rerio
Hoechst (1989d)	Hoechst AG (Clariant GmbH), Report No. 89.0345, Unpublished results, 1989d
Hoechst (1989f)	Hoechst AG (Clariant GmbH), Report No. 89.0182, Unpublished results, 1989f
Hoechst (1989g)	Hoechst AG (Clariant GmbH), Report No. 89.0856, Unpublished results, 1989g
Hoechst (1990)	Hoechst AG, Unpublished report; Kalle Albert, August 3, 1990
Hoechst (1991)	Hoechst AG, Unpublished report No. 220/91
Huels (1983)	Huels, Report No. 0135, Unpublished results, 1983
Huels (1986a)	Huels, Report No. 0619, Unpublished results, 1986a
Huels (1986b)	Huels, Report No. 0620, Unpublished results, 1986b
Huels (1986c)	Huels, Report No. 0636, Unpublished results, 1986c
Huels (2000)	Huels IUCLID Datasheet, Sulfonic acids, C13-17 sec-alkane, sodium salts, CAS No. 85711-69-9, February 19, 2000
Hrsak et al (1981)	Hrsak, D., Bsonjak, M., Johanides, V., Kinetics of linear alkylbenzene sulphonate and secondary alkane sulphonate biodegradation, Tenside Det 1981, 18 (3), 137-140
Ippen (1990a)	Ippen, Unpublished results, 1990a
Ippen (1990b)	Ippen, Unpublished results, 1990b
ISC (2000)	ISC, Report No. 0555, Unpublished results 2000
Klotz (1994a)	Klotz, H., The determination of Secondary Alkane Sulfonates in Environmental Samples, Lecture at EC Comett Course on Determination of Surfactants in the Environment, University of Venice, 1994
Klotz (1994b)	Klotz, H., GDCh-Fachgruppe Waschmittelchemie, Symposium 'Tensid-Monitoring', Bestimmung von sek. Alkansulfonat in der Umwelt, Hannover, 24.11.1994
Lötzsch et al (1979)	Lötzsch, K., Neufahrt A., Täuber, G., Comparative Study of the Biodegradation of SAS using Carbon-14 labeled Preparations, Tenside Detergents 1979, 16 (3), 150-155
Madsen et al (2001)	Madsen, T., Boyd H.B., Nylen, D., Pederson A.R.,Peterson, G.I., Simonsen, F., Environmental and Health Assessment of Substances in Household Detergents and Cosmetic Detergent Products, Danish EPA, CETOX (Centre for Integrated Environment and Toxicology), Report No. 615, 2001 published on Web Site: http://www.mst.dk/udgiv/publications/2001/87-7944-596-9/pdf/87-7944-597-7.pdf
Matthijs et al (1995)	Matthijs, E., Debaere, G., Itrich, N., Masscheleyn, P., Rottiers, A., Stalmans, M., Federle, T.W., The fate of detergent surfactants in sewer systems, Wat. Sci. Tech. 1995, 31, 321-328
Michael (1968)	Michael, W.R., Metabolism of LAS and alkylbenzene sulfonate in albina rats, Toxicol.Appl.Pharmacol.12: 473-485, 1968
OECD (2003)	OECD, Introduction to the OECD Guidelines for Testing of Chemicals, Section 3, Part 1: Principles and Strategies related to the testing of Degradation of Organic Chemicals, July 2003 (http://www.oecd.org/dataoecd/38/2/5598432.pdf)
Official publication French legislation (1990)	Official publication of the French legislation ("Journal Officiel de la Republique Francaise") concerning substances used in dish care products which may come in contact with foods, 1990
Painter (1992)	Handbook of Environmental Chemistry, Ed. Hutzinger, O., Volume 3 Part F, Volume

	Ed. de Oude, N.T., Painter, H.A., Anionic Surfactants, pp 2-88, Springer, New York, ISBN 3-54053797-X
Platz and Schimmelschmidt (1940)	Platz, C. and Schimmelschmidt, K., Verfahren zur Herstellung von Sulfonsäuren, DRP 735096, 1940
Procter & Gamble (2001)	Procter & Gamble, Unpublished data, 2001
Procter & Gamble (1996)	Procter & Gamble, Unpublished data, 1996
ProTox (2002)	ProTox, Report No. PT02-0380, Unpublished results, 2002
RCC (1990)	RCC, Project 266523, Unpublished results 1990
RCC (1994)	RCC, Project 388225, Unpublished results 1994
Reed (1933)	Reed, C., Method of halogenating compounds and products resulting thereof , Patent US 2046090
Rodriguez C (1994)	Rodriguez C, G Calvin, C Lally, JM Lachapelle, Skin effects associated with wearing fabrics washed with commercial laundry detergents, *Journal of Toxicology-Cutaneous & Ocular Toxicology* 13: 39-45, 1994.
Schaefer and Redelmeier (1996)	Schaefer H and TE Redelmeier, Skin barrier. Principles of percutaneous absorption, S Karger AG, P.O. Box, CH-4009 Basel (Switzerland), ISBN 3-8055-6326-4, 1996
Schmitz (1973)	Schmitz J, *Tenside Surf. Det.*, 10: 11-13, 1973.
Schöberl and Bock (1980)	Schöberl, P. and Bock, K.J., Tensidabbau und dessen Metaboliten, Tenside Det 1980, 17 (5), 262-266
Schöberl (1997)	Schöberl, P., Ökologische Bewertung von Tensiden, Tenside Surf Det 1997, 34 (1), 28-36
Schöberl et al (1998)	Schöberl, P., Guhl, W., Scholz, N., Taeger, K., Simulation method for determining biodegradation in surface waters, Tenside Surf Det 1998, 35 (4), 279-285
Schroeder (1995)	Schroeder, F.R., Concentrations of anionic surfactants in receiving riverine water, Tenside Surf Det 1995, 32 (6), 492-497
Schroeder et al (1999)	Schroeder, F.R., Schmitt, M., Reichensperger, U., Effect of waste water treatment technology on the elimination of anionic surfactants, Waste Managem 1999, 19, 125-131
Schulze (2001)	Schulze, C., Modelling and evaluating the aquatic fate of detergents, Doctorial Thesis, 2001-01-03
Stalmans et al (1995)	Stalmans, M. et al, European Life Cycle Inventory for Detergent and Surfactants Production, Tenside Surf Det, 1995, 32 (2), 84
Steber J., Richterich K. (1993)	Biologische Abbaubarkeit pflanzlicher Öle und Schmierstoffe. In: Biologisch schnell abbaubare Schmierstoffe und Arbeitsflüssigkeiten (ed. W.J. Bartz). pp. 81-96. Expert Verlag, Ehningen (Germany)
Steber J. (1997)	Biodegradation kinetic data for environmental risk assessment in surface waters and soil. In: Biodegradation kinetics: Generation and use of data for regulatory decision making (ed. S.G. Hales et al.), pp. 81-85. Proceedings of SETAC Europe Workshop, Port Sunlight, 4 –6 September 1996. SETAC-Europe, Brussels
Swisher (1987)	Swisher, Surfactants biodegradation, Surfactant Science Series, Volume 18, Marcel Dekker, New York, 1987
Table of habits (2002)	Table of habits and practices for consumer products in western Europe. Developed by A.I.S.E. (Association Internationale de la Savonnerie, de la Détergence et des Produits

d' Entretien) within the HERA project in 2002.

TEGEWA (1989) Datensammlung für den Sachstandsbericht 'Ökologisch relevante Daten von Tensiden in Wasch- und Reinigungsmitteln', 1989

Thysse and Wanders (1972) Thysse, G.J.E. and Wanders, T.H., Mikrobiologischer Abbau von n-Alkan-1-sulfonaten, Fette, Seifen, Anstrichmittel 1972, 74, 413 and

Thysse, G.J.E. and Wanders, T.H., Degradation of n-Alkane-1 sulfonates by Pseudomonas, Antoine van Leevenhoek 1972, 38, 53-63

Thysse and Wanders (1974) Thysse, G.J.E. and Wanders, T.H., Initial Steps in the degradation of n-Alkane-1-sulfonates by Pseudomonas, J. Microbiol and Serol 1974, 40, 25-37

Van de Plassche et al. (1999) Van de Plassche EJ, P Bont, J Hesse, Exploratory report. Fluorescent whitening agents (FWAs). National Institute of Public Health and the Environment. The Netherlands. Report No. 601503013, 1999

Vollebregt and Westra (1998) Vollebregt, L.H.M., Westra, J., Environmental effects of surfactants, University of Amsterdam, The Netherlands, 1998

Vollebregt and Westra (2000) Vollebregt, L.H.M., Westra, J., Environmental effects of surfactants – a risk assessment of frequently used surfactants (the Durch situation), Univ. of Amsterdam, NL, contribution at 47th SEPAWA Congress, 2000

US EPA (2000a) US EPA OPPT EPI Suite Property Estimation Software, 2000, MPBPWin Version 1.40 (http://www.epa.gov/opptintr/exposure/docs/episuite.htm)

US EPA (2000b) US EPA OPPT EPI Suite Property Estimation Software, 2000, KOWWin Version 1.66 (http://www.epa.gov/opptintr/exposure/docs/episuite.htm)

US EPA (2000c) US EPA OPPT EPI Suite Property Estimation Software, 2000, HENRYWin Version 3.10 (http://www.epa.gov/opptintr/exposure/docs/episuite.htm)

US EPA (2000d) US EPA OPPT EPI Suite Property Estimation Software, 2000, PCKOC Version 1.66 (http://www.epa.gov/opptintr/exposure/docs/episuite.htm)

US EPA (2000e) US EPA OPPT EPI Suite Property Estimation Software, 2000, BCFWin Version 2.14 (http://www.epa.gov/opptintr/exposure/docs/episuite.htm)

7. Contributors to this report

This report has been prepared by Clariant GmbH, Germany with the assistance of the members of the HERA Environmental Task Force and the HERA Human Health Task Force.