HERA

Human & Environmental Risk Assessment on ingredients of household cleaning products

Hydrotropes

CAS No.	NAME
12068-03-0	Toluene sulfonate, sodium salt
16106-44-8 30526-22-8	Toluene sulfonate, potassium salt
827-21-4 1300-72-7	Xylene sulfonate, sodium salt
30346-73-7	Xylene sulfonate, potassium salt
26447-10-9	Xylene sulfonate, ammonium salt
28088-63-3	Xylene sulfonate, calcium salt
28348-53-0 32073-22-6	Cumene sulfonate, sodium salt
37475-88-0	Cumene sulfonate, ammonium salt

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2. *Executive Summary*

Hydrotropes are used as coupling agents to solubilize the water insoluble and often incompatible functional ingredients of household and institutional cleaning products and personal care products. These hydrotropes are not surfactants but are used to solubilize complex formulations in water. They function to stabilize solutions, modify viscosity and cloud-point, limit low temperature phase separation and reduce foam. This assessment considers salts of toluene, xylene and cumene sulfonates. Hydrotropes are amphiphilic substances composed of both a hydrophilic and a hydrophobic functional group. The hydrophobic part of the molecule is a benzene substituted apolar segment. The hydrophilic, polar segment is an anionic sulfonate group accompanied by a counter ion (i.e., ammonium, calcium, potassium or sodium).

Hydrotropes are produced by sulfonation of an aromatic hydrocarbon solvent (i.e., toluene, xylene or cumene). The resulting aromatic sulfonic acid is neutralized using an appropriate base (e.g., sodium hydroxide) to produce the sulfonate or hydrotrope. The hydrotropes are 'pure' substances but are produced and transported in either aqueous solutions, typically at a 30-60% level of activity, or in granular solids typically at 90-95% level of activity. The other components of granular solids include sodium sulphate and water.

The consumption of hydrotropes in laundry detergent and household cleaning product applications is 17,000 tonnes in 2002 according to a survey of hydrotrope producers and formulators that are HERA members in Europe. This HERA-reported consumption is believed to account for at least 80% of total hydrotrope tonnages used in HERA applications in Europe (the basis of the 80% default can be obtained from HERA). Important HERA application products are household laundry and cleaning products, such as laundry powders and liquids, liquid fabric conditioners, liquid and powder laundry bleach additives, hand dishwashing liquid, machine dishwashing liquid, liquid and gel toilet cleaners, and liquid, powder, gel and spray surface cleaners. This HERA assessment is based on the 17,000 tonnes consumption figure.

For the purposes of this assessment, it is assumed that the entire 17,000 tonnes/year volume is in products that are ultimately released down-the-drain, and following wastewater treatment, the ingredient may be released into the environment.

Environmental assessment

The present environmental risk assessment of hydrotropes is based on the revised HERA methodology document (HERA, 2002), which in its turn is based on the revised EU Technical Guidance Document (TGD, 2003). It makes use of the EUSES 2.02 programme (EUSES, 2005) which is now compatible with the HERA detergent scenario. Hydrotrope concentrations modelled in the various environmental compartments were compared with extrapolations of the available eco-toxicity data or modelled eco-toxicity values leading to PNEC values protective of each compartment.

- The modelled hydrotropes concentration in raw sewage is 1.16 mg/l. Approximately 87% of hydrotropes are removed in activated sludge sewage treatment plants (STP) yielding a modelled effluent concentration of 0.147 mg/L. Hydrotropes are readily biodegraded under aerobic conditions.

- Dilution of the STP effluent in the receiving waters results in a local estimated concentration of 0.0205 mg/L hydrotropes. The corresponding regional surface water estimate is 0.006 mg/L.

- Predictions for the other local PECs are: 0.002 mg/kg in dry sewage sludge; 2.07E-06 mg/kg wet weight in soil; and 0.0161 mg/kg wet weight in freshwater sediments.

- Fugacity modelling supports the prediction that 99+% of hydrotropes will reside in the water compartment and that negligible amounts will end up in soil, sediments, air or biota. Hydrotropes have a very low measured octanol-water partition coefficient and will therefore not bioaccumulate.

- Aquatic ecotoxicity data are available and well documented for representatives of the hydrotropes category. The aquatic PNEC value is 0.23 mg/L

- Corresponding PNEC values for other environmental compartments are: 0.180 mg/kg for freshwater sediments, 0.027 mg/kg for soils, and 160 mg/L for STPs.

- The risk characterisation, as expressed by the PEC/PNEC ratio, was far below 1 for all environmental compartments. It was therefore concluded that the use of hydrotropes in household laundry and cleaning products does not pose a risk for the environment. Further, the margin of safety would accommodate any additional hydrotrope volumes/uses not accounted for in the HERA assessment.

Human health assessment

The presence of hydrotropes in many commonly used household detergent and cleaning products gives rise to a variety of possible consumer contact scenarios including direct and indirect skin contact, inhalation, and oral ingestion derived either from hand washing of clothes and dishes, residues deposited on dishes and clothes, from accidental product ingestion, or indirectly from drinking water. A standard risk assessment methodology was used to derive Margins of Exposure.

- 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 1.42 µg/kg bw/day. The consumer aggregate external exposure from direct and indirect skin contact is 87 µg/kg bw/day using worst case assumptions.

- Toxicological data are available and well documented for representative tolune, xylene and cumene sulfonates (including sodium, potassium, ammonium and calcium salts). These data demonstrate that hydrotropes have a low order of acute toxicity by all relevant routes (LC50s range from 100s to 1000s mg/kg), are not genotoxic *in vitro* or *in vivo*, show no evidence of a carcinogenic response (or any other systemic toxicity) in 2-year dermal exposure studies, and failed to induce developmental, teratogenic or fertility (sex organ) effects.

- Adverse effects after repeated long term dosing of hydrotropes to animals included epidermal hyperplasia at the site of application in dermal studies, and decreased relative spleen weight in females in oral studies. The critical adverse effect and corresponding systemic NOAEL is 763 mg a.i./kg bw based upon decreased relative spleen weight in female rats in a 90-day oral study. The NOAEL for local effects, based on epidermal hyperplasia at the site of application, was 440 mg a.i./kg bw for mice in 90-day dermal studies.

- Comparison of the aggregate internal consumer exposure to hydrotropes (1.42 µg/kg bw) with the systemic NOAEL (763 mg a.i./kg bw) results in an estimated Margin of Exposure (MOE) of >500,000. Comparison of the aggregate external consumer exposure (87 µg/kg bw) with the epidermal hyperplasia NOAEL (440 mg a.i/kg bw) results in an estimated MOE of >5,000.

Both of these MOEs are very large MOE; 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.

- Hydrotropes can be classified as a negligible-to-slight irritant to skin and a slight-to-moderate irritant to eyes. The irritation potential of aqueous solutions of hydrotropes depends on concentration, and the irritation is lessened with rinsing. Hydrotropes are not considered to be skin sensitizers.

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

3. Substance Characterisation

Hydrotropes are used as coupling agents to solubilize the water insoluble and often incompatible functional ingredients of household and institutional cleaning products and personal care products. In this function they stabilize solutions, modify viscosity and cloud-point, limit low temperature phase separation and reduce foam. Although not being surfactants, hydrotropes are amphiphilic substances composed of both a hydrophilic and a hydrophobic functional group. The hydrophobic part of the molecule is a benzene substituted (i.e., methyl [common name: toluene], dimethyl [common name: xylene] or methylethyl [common name: cumene]) apolar segment. The hydrophilic, polar segment is an anionic sulfonate group accompanied by a counter ion (i.e., ammonium, calcium, potassium or sodium).

3.1 CAS No. and grouping information

The hydrotropes used in the European market and covered in this focused risk assessment, are shown on the list in Table 1. The HERA assessment focuses on levels of these substances in household detergent and cleaning products used in the European market and potentially reaching the various environmental compartments.

Table 1 : CAS and EINECS numbers of Hydrotropes covered in this assessment

CAS No.	EINECS No.	NAME
12068-03-0	2350881	Toluene sulfonate, sodium salt
16106-44-8 30526-22-8	2402735 2502281	Toluene sulfonate, potassium salt
827-21-4 1300-72-7	2125673 2150909	Xylene sulfonate, sodium salt
30346-73-7	2501403	Xylene sulfonate, potassium salt
26447-10-9	2477109	Xylene sulfonate, ammonium salt
28088-63-3	2488299	Xylene sulfonate, calcium salt
28348-53-0 32073-22-6	2489387 2509135	Cumene sulfonate, sodium salt
37475-88-0	2535191	Cumene sulfonate, ammonium salt

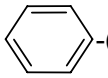
Note that three of the compounds (xylene and cumene sulfonate, sodium salts and toluene sulfonate, potassium salt) have more than one CAS number. This is a result of differences in industry

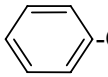
nomenclature practice and/or use patterns across geographical regions at the time of notification. This practice has lead to differences in how some substances are identified on national and regional chemical inventories. The structures as well as the physical/chemical and toxicological properties of these chemical entities are essentially the same although the CAS numbers are different.

3.2 Chemical structure and composition

Commercial toluene sulfonates and cumene sulfonates consist of mixtures of 3 isomers (ortho-, meta- and para-). Commercial xylene sulfonates consist of mixtures of 6 isomers. Diagrams of sodium salts for each of the three hydrotropes (without isomer orientation) are depicted below. An ortho-isomer would have adjacent attachment points to the benzene ring; a para-isomer would have attachments at opposite ends of the benzene ring; and a meta-isomer would have one open carbon between attachments on the benzene ring as depicted in Table 2.

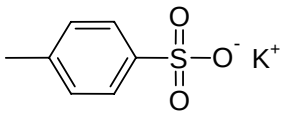
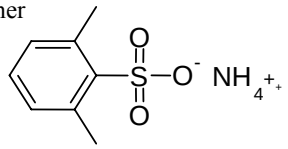
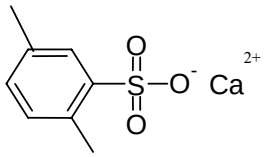
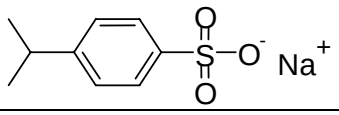

$-CH_3$ $-SO_3Na$ toluene sulfonate, sodium salt


$-(CH_3)_2$ $-SO_3Na$ xylene sulfonate, sodium salt


$-CH.(CH_3)_2$ $-SO_3Na$ cumene sulfonate, sodium salt

In general, on the basis of the evidence documented here, the presence of one or two methyl groups or a methylethyl group on the benzene ring is not judged to have a significant influence on chemical reactivity. Alkyl substituents are known to be weak ortho- and para-directing activators, and the difference between methyl and methylethyl will be negligible. On going from methylbenzene (toluene) to dimethylbenzene (xylene) and to methylethylbenzene (cumene), the number of carbon atoms – and thus the organic character - increases. This will improve solubility in apolar solvents and reduce solubility in polar solvents like water. Hence, reactivity in aqueous solutions may differ somewhat for the hydrotropes. However, the decisive factor determining water solubility of these compounds will be their ionic character, not the number and identity of the alkyl substituents on the benzene ring. The difference in counter ion (i.e., Na^+, NH_4^+, Ca^{++}, or K^+) is expected to have some limited effect on the physical and chemical behaviour of the substances and their chemical reactivity. Generally speaking, it is expected that these hydrotropes will behave similarly (predictably) in solution and that members from one sub-group (i.e., toluene, xylene and cumene sulphonates) may be useful for read across to other sub-groups and to the overall group (category) as a whole.

Table 2 : Representative structures of Hydrotropes with isomer identified

CHEMICAL NAME	CAS No.	STRUCTURE
Toluene sulfonate, potassium salt	16106-44-8	para isomer 
Xylene sulfonate, ammonium salt	26447-10-9	ortho,ortho isomer 
Xylene sulfonate, calcium salt	28088-63-3	meta,ortho isomer 
Cumene sulfonate, sodium salt	28348-53-0 32073-22-6	para isomer 

The data on the physical-chemical properties of hydrotropes presented in Table 3 consist of the available measured values and estimated ones using the EPIWIN model available at http://www.epa.gov/opptintr/exposure/docs/episuite.htm for those properties lacking measured values. Hydrotropes are solid at room temperature. Melting points are 182 degrees C or higher and measured boiling points are at or above 100 degrees C (which is likely attributed to the presence of water). Measurements show hydrotropes to be highly soluble in water. Measured values are 330 g/L or greater. Commercial products are available in aqueous solutions and these products are hydrolytically stable. The salts are expected to dissociate completely in water. Hydrotropes are slightly more dense than water with measured relative densities of just above 1.0. A single measured vapour pressure result of $<2.0 \times 10^{-5}$ Pa is consistent with a 2000 IUCLID data sheet indicating "non-volatile". The low measured value is also consistent with the modelled estimates of vapour pressure values ranging from 1.2×10^{-11} to 3.47×10^{-9} Pa. The single measured low octanol:water partition coefficient (logKow of -2.7) is consistent with the modelled estimates that range from -2.4 to -1.5**.**

Table 3 : Measured and modelled physical chemical properties

Property	Compound	CAS No.	Predicted Data (EPI)	Measured Value	Reference*
Physical state	Pure	All	-	Solid at room temperature	1, 42, 43, 44, 45
Molecular weight	Toluene sulfonate, Na	12068-03-0	194	-	Derived from Molecular formula
	Xylene sulfonate, Na	1300-72-7	208	-	
	Xylene sulfonate, NH_4	26447-10-9	203	-	
	Xylene sulfonate, Ca	28088-63-3	226	-	
	Cumene sulfonate, Na	28348-53-0	222	-	
Melting point	Xylene sulfonate, Na	1300-72-7	233° C	>300° C	42
	Xylene sulfonate, Ca	28088-63-3	"	>375 ° C	29
	Cumene sulfonate, Na	28348-53-0	236° C	182° C	1
	"	"	"	>300° C	44
	Toluene sulfonate, Na	12068-03-0	228 ° C	-	-
Boiling point	Xylene sulfonate, Na	1300-72-7	545° C	100° C	3
	Xylene sulfonate, NH_4	26447-10-9	468° C	101° C	43
	Toluene sulfonate, Na	12068-03-0	533° C	-	-
Relative density	Xylene sulfonate, Na	1300-72-7	-	1.02-1.08 kg/L	3
	Xylene sulfonate, Ca	28088-63-3	-	1.3 kg/L	28
Vapour pressure	Xylene sulfonate, Na	1300-72-7	1.52 x10^{-9} Pa	"non-volatile"	3
	Xylene sulfonate, Na	1300-72-7	1.52 x10^{-9} Pa	<2.0 x10^{-5} Pa	57
	Xylene sulfonate, Ca	28088-63-3	1.2 x10^{-11} Pa	-	-
	Toluene sulfonate, Na	12068-03-0	3.47 x10^{-9} Pa	-	-
	Cumene sulfonate, Na	28348-53-0	1.09 x10^{-9} Pa	-	-
Water solubility	Toluene sulfonate, Na	12068-03-0	1000 g/L	"soluble"	45
	Xylene sulfonate, Na	1300-72-7	1000 g/L	400 g/L	3
	Xylene sulfonate, Na	1300-72-7	-	"soluble"	42
	Xylene sulfonate, NH_4	26447-10-9	54 g/L	"soluble"	43
	Xylene sulfonate, Ca	28088-63-3	-	553 g/L	31
	Cumene sulfonate, Na	28348-53-0	635 g/L	330 g/L	1
	"	"	"	400 g/L	10
	"	"	"	"soluble"	44
Partition coefficient n-octanol /water	Xylene sulfonate, Na	1300-72-7	log Kow = -1.86	-	-
	Xylene sulfonate, Ca	28088-63-3	-	log Kow = -2.7	30
	Toluene sulfonate, Na	12068-03-0	log Kow = -2.4	-	-
	Cumene sulfonate, Na	28348-53-0	log Kow = -1.5	-	-
pH	Xylene sulfonate, Na	1300-72-7	-	7-9 as 40% soln	42
	Xylene sulfonate, NH^4	26447-10-9	-	7-9 as 40% soln	43
	Cumene Sulfonate, Na	28348-53-0	-	6-9 as 45% soln	44
	Toluene sulfonate, Na	12068-03-0	-	6-9 as 40% soln	45

Note 1: The Predicted data (EPI) are based on EPIWIN modelling.
Note 2: Reference numbers are identical with the OECD HPV Dossier references (Hydrotropes SIAR, 2005)

3.3 Manufacturing route and production/volume statistics

Hydrotropes are produced by sulfonation of an aromatic hydrocarbon solvent (i.e., toluene, xylene or cumene). The resulting aromatic sulfonic acid is neutralized using an appropriate base (e.g., sodium hydroxide) to produce the sulfonate or hydrotrope. The hydrotropes are 'pure' substances but are produced and transported in either aqueous solutions, typically at a 30-60% level of activity, or in granular solids typically at 90-95% level of activity. The other components of granular solids include sodium sulphate and water. Liquid product is produced in a closed system. Granular

product is produced by spray drying that includes source control and dust collection. Hydrotropes are manufactured for industrial/professional and consumer use and are not used as intermediates/derivatives for further chemical manufacturing processes or uses.

3.4. Consumption scenario in Europe

The consumption of hydrotropes in laundry detergent and household cleaning product applications is 17,000 tonnes in 2002 based on 100% active ingredient. This estimate comes from a HERA survey (conducted by AISE) of hydrotrope producers and formulators that are HERA members in Europe.As HERA formulator companies represent approximately 80% of the European market, this HERA-reported consumption is believed to accout for at least 80% fo the total hydrotrope tonnages used in HERA applications in Europe.

The present focused risk assessment models the use of the 17,000 metric tonnes per year of hydrotropes available for the household detergent and cleaning products. The implications for any additional volumes are addressed in the environmental risk assessment summary and conclusions.

3.5 Use application summary

The 17,000 tonnes per year of hydrotropes that are within the scope of the HERA are used in a variety of household detergent and cleaning products including laundry powders and liquids, liquid fabric conditioners, liquid and powder laundry bleach additives, hand dishwashing liquid, machine dishwashing liquid, liquid and gel toilet cleaners, and liquid, powder, gel and spray surface cleaners. For the purposes of the HERA it is assumed that the entire 17,000 tonnes/year volume is in products that are ultimately released down-the-drain, where depending upon treatment it may reach the environment. The personal care product uses (e.g., face and hand soaps and shampoos) are outside the scope of HERA.

4. Environmental Assessment

A SIDS Initial Assessment Report (SIAR) for hydrotropes is nearing completion as part of the ICCA HPV Program. It presents the available environmental fate, exposure and ecotoxicity data for hydrotropes, as well as a preliminary risk characterization for Australia (sponsor country) and U.S. use scenarios. Many of these data are presented in the following pages to describe both the environmental exposure (Section 4.1) and the environmental effects (Section 4.2) of hydrotropes. Robust summaries and an evaluation of the data quality for representative studies are available as part of the SIAR document (Hydrotropes SIAR, 2005).

4.1 Environmental exposure assessment

Releases to the Environment Following Consumer Use

Environmental releases from down-the-drain discharges following product use could lead to an exposure of the aquatic compartment. Based on their physical chemical properties, hydrotropes are predicted to partition almost exclusively to the water compartment. The results of EUSES modelling of continental and regional steady state percentages of hydrotropes in different environmental compartments are shown in Table 4. The vast majority of hydrotropes (99%) are predicted to reside in the water compartment. This same result is predictd using other fugacity models, for example, the EQC Model available from the Canadian Environmental Modeling Centre (Trent University) at http://www.trentu.ca/cemc/welcome.html .

Table 4: Fugacity model output from EUSES 2.02 [1,2]

	Water (%)		Air (%)	Soil (%)	Sediment (%)	
	Freshwater	Seawater			Freshwater	Marine
Continental	**86.0**	**13.4**	**Negligible**	**Negligible**	**0.66**	**0.002**
Regional	**91.1**	**8.2**	**Negligible**	**Negligible**	**0.70**	**0.02**

Notes: (1) Input data the same as in Table 4a. (2) Calculated from the regional and continental steady state masses for each compartment given as outputs in EUSES 2.02, divided by the sum of the steady state masses in the region or continent as appropriate.

4.1.1 Environmental fate: biotic and abiotic degradability

Biodegradation

Hydrotropes are readily biodegradable in water under aerobic conditions according to OECD criteria. Studies with toluene, xylene and cumene sulfonates are available and are summarized in Table 5.

Table 5: Biodegradation properties

Compound	CAS No.	Aerobic aquatic biodegradation	Method	Reference*
Toluene sulfonate	12068-03-0	100% after 3 days	Pre-OECD** ; raw sewage inoculum	6 [2]
Xylene sulfonate, Na	1300-72-7	69% degraded in 5 days, 100% in 8 days	Pre-OECD; raw sewage inoculum	6 [2]
Xylene sulfonate, Na	1300-72-7	74% degraded in 15 days, 88% in 28 days	Modified Sturm; OECD301B	46 [2]
Xylene sulfonate, Na	1300-72-7	74% degraded in 15 days, 84% in 28 days	Modified Sturm, OECD301B	33 [1]
Xylene sulfonate, Ca	28088-63-3	>50% degraded in 15days, >80% in 29days	Modified Sturm, OECD301B	27 [1]
Xylene sulfonate, NH_4	26447-10-9	71% degraded in 26 days	Ultimate biodegradation	17, 50 [4]
Cumene sulfonate, Na	28348-53-0	94% degraded	OECD301E screening	7 [4]
Cumene sulfonate, Na	28348-53-0	100% degraded	Zahn Wellens	10 [4]
Cumene sulfonate, Na	28348-53-0	73% degraded	Pre-OECD, Not specified	50 [4]

* Reference numbers refer to the OECD HPV Dossier references

** These 1965 to 1970 studies pre-date OECD standard methodology

*** value in brackets [ ] indicates Klimisch score

There is no known anaerobic biodegradation data on hydrotropes. Due to the presence of the sulphonated aromatic group, hydrotropes are not expected to biodegrade to a significant extent under anaerobic conditions. However, considering their ready aerobic biodegradability and their low potential for adsorption to sediment solids (log Kow), the presence of hydrotropes in anaerobic environments is expected to be negligible.

Photolysis

No experimental data are available for photodegradation of hydrotropes. Photodegradation rates were estimated for the toluene, xylene and cumene sulfonates using AOPWIN™ (in EPIWIN 3.11). The predicted atmospheric oxidation half lives were of the order of 40 to 105 hours, indicating a

significant atmospheric degradation potential (Reference #15). As hydrotropes are not volatile, the importance of atmospheric photodegradation as an environmental fate mechanism is low. Therefore no further consideration is given to the air compartment in this assessment.

Hydrolysis
No measured data are available for hydrolysis of hydrotropes. However, considering the fact that commercial products are available in aqueous solutions and these products are stable it can be expected that dydrolytic degradation is negligibily low.

4.1.2 Removal

Removal of hydrotropes from secondary activated sludge sewage treatment has been calculated with Simpletreat, as incorporated in EUSES 2.02, using the SimpletTreat 3.0 defaults for a readily biodegradable chemical. This model predicts a default 87% removal in wastewater treatment plants, which is derived following EU TGD standard tables for a readily biodegradable substance, and assuming a log Kow value of -2.7 and calculated Henry's Law constant of 4.90E-18 Pa.m3.mol-1. This output is conservative compared to the measured removal of >94% measured in a modified SCAS (OECD 302A) study with calcium xylene sulfonate (34). In addition, secondary literature data indicates up to 91.5% carbon removal in a Coupled Units study (7).

4.1.3 Monitoring studies

There are no monitoring studies reported for hydrotropes.

4.1.4 Exposure modelling: scenario description

The HERA environmental risk assessment of hydrotropes is based on the estimated hydrotropes tonnage of 17,000 t/y in HERA applications and follows the Technical Guidance Document for new and existing substances (TGD, 2003). At screening level the approach makes use of the EUSES programme (EUSES 2.02, 2005) to calculate the local and regional exposure to hydrotropes. The total hydrotropes tonnage produced for detergents was assumed to follow the down-the-drain pathway to the environment. The calculations did not apply the previous HERA exposure scenario (HERA, 2002) assigning 7% of the EU tonnage to the standard EU region, instead of the TGD default 10%, and increasing the emissions at local level by a factor of 1.5, instead of the TGD default factor of 4. Instead, the revised HERA methodology document (HERA, 2005 www.heraproject.com) was taken into account following the revised TGD (2003).

4.1.5 Substance data used for the environmental exposure calculations

Data used for exposure calculations following the TGD (2003) and EUSES calculations are taken from Tables 3 and 5 and summarized in Table 6.

The biodegradation rates used in the calculations for hydrotropes correspond to the default values as assumed by TGD (2003) for readily biodegradable substances.

Table 6: Input Data and selected intermediate results for EUSES exposure calculations

		References
General name	Hydrotrope	-

Description	-	-
Average molecular weight (g/mole)	226	Based on CaXS; see Table 3
Melting point (°C)	375	Based on CaXS; see Table 3.
Vapour pressure at 25 C° (Pa)	$1.2x\ 10^{-11}$	EPIWIN derived for CaXS
Water solubility (g/l)	553	Based on CaXS; see Table 3
Henry's constant (atm·m^3/mole)	3.06E-09	EPIWIN derived for non neutralised XyleneSulphonate (=2,5-dimethylbenzenesulfonic acid
Octanol-water partition coefficient, log K_{ow}	-2.7	Based on CaXS; see Table 3
Soil -water partition coefficient, Kp-soil (m3.m-3)	0.2	EUSES derived (QSAR based on predominantly hydrophobics)
Sediment -water partition coefficient, Kp-sed (L/kg)	0.8	EUSES derived (QSAR based on predominantly hydrophobics)
Suspended matter-water partition coefficient, Kp-SM (m3.m-3)	0.9	EUSES derived (QSAR based on predominantly hydrophobics)
Biodegradation rate in STP	$k = 24\ d^{-1}$	EUSES default based on 1st order, standard OECD/ EU tests for readily biodegradable substances
Biodegradation rate in surface water (primary)	$k = 0.046\ d^{-1}$ (12°C)	EUSES default for readily biodegradable substance
Biodegradation rate in soil (primary)	$k = 0.023\ d^{-1}$ (12°C)	EUSES default for readily biodegradable substance
Biodegradation rate in oxic sediments	$k = 0.023\ d^{-1}$ (12°C)	EUSES default for readily biodegradable substance
Biodegradation rate in bulk sediments	$k = 2.31E\text{-}03\ d^{-1}$ (12°C)	EUSES default for readily biodegradable substance
STP removal (%)	87.3	EUSES derived
Total yearly hydrotropes use in household (HERA scope), tons	17,000	HERA estimate
Hydrotropes continental usage going to standard EU region, %	10	EUSES default
Percentage of Hydrotrope production in standard EU region	10	EUSES 1 default – considered a good estimate for HERA

4.1.6 PEC calculations

PEC calculations based on modelling data are presented in Table 7. Values reported are as calculated by EUSES 2.02 (2005) on the basis of (i) data in Table 5 and 6, and (ii) considering the tonnage used in household applications (17,000 t/y).

Table 7: PEC Results – EUSES 2.02 derived

Parameter calculated by EUSES	Value
Fraction of emission directed to air by STP	2.14E-20
Fraction of emission directed to water by STP	0.127
Fraction of emission directed to sludge by STP	7.74E-07
Fraction of the emission degraded in STP	0.873
Local concentration in untreated wastewater, influent, mg/L	1.16

Local PEC for micro-organisms in the STP, mg/L	0.147
Local concentration in dry sewage sludge, mg/kg	0.002
Annual average local PEC in surface water (total, mg/L)	0.0205
Local PEC in soil (30 d), mg/kg wwt	2.07E-06
Local PEC in fresh-water sediment during emission episode, mg/ kg wwt	0.0161
Regional PEC in surface water (dissolved), mg/L	0.006
Regional PEC in agricultural soil (30 d), mg/kgwwt	7.51E-09
Regional PEC in fresh-water sediment during emission episode, mg/kg wwt	0.004

4.1.7 Bioaccumulation potential

No test data are available for bioaccumulation. A conservative approach in modeling bioconcentration, using the highest logKow value for hydrotropes, derived for sodium cumene sulfonate (log kow of –1.5) and BCFWIN, calculates a bioconcentration factor of approximately 3 (15). Thus the potential for bioaccumulation of hydrotropes in aquatic organisms is predicted to be very low.

4.2 Environmental effects assessment

4.2.1 Ecotoxicity

Reliable data are available on all SIDS-endpoints for representative xylene and cumene sulfonates. The data cover fish, invertebrates and algae for xylene sulfonate (sodium, ammonium and calcium salts) and cumene sulfonate (sodium salt). Chronic toxicity to *Daphnia magna* and bacterial toxicity was also reported for sodium cumene sulfonate. While the toluene sulfonate is not represented in the available data set, the xylene and cumene sulfonate results are consistent and comparable. This and the fact that toluene sulfonate is the hydrotrope representative with the lowest hydrophobicity provides confidence that these data can be conservatively extrapolated to the toluene sulfonates.

4.2.1.1 Aquatic acute toxicity

The hydrotropes demonstrate a low level of acute aquatic toxicity to fish, invertebrates, algae and bacteria exhibiting EC50 and LC50 values > 100 mg/L (see Table 8). Green algae are considered the most sensitive species with EC_{50} values of 230-236 mg/L active ingredient (a.i.) and No Observed Effect Concentrations (NOECs) of 31-75 mg a.i./L when tested with the sodium and calcium salts of xylene sulfonate, respectively. Xylene and cumene sulfonates (ammonium, calcium and sodium salts) had no acute toxicity towards fish and invertebrates at concentrations tested (>318 mg/L). However some sublethal effects were noted in two of the studies at the higher concentrations and included surfacing, loss of equilibrium, swimming on the bottom of the tank, dark discoloration, labored respiration and quiescence in some fish.

Table 8: Acute Aquatic Toxicity

Compound	CAS No.	Acute Toxicity Endpoint Species and Duration EC50 / LC50 (mg/L)[1]	Method	Reference*

		Fish		
Xylene sulfonate, Na	1300-72-7	Rainbow trout 96-hr LC50 >408 a.i.	EPA 797.1400	48 [2]
Xylene sulfonate, Na	1300-72-2	Fathead minnow 96-hr LC50 >400 a.i.	EPA 797.1400	20 [2]
Xylene sulfonate, NH_4	26447-10-9	Bluegill 96-hr LC50 = 1060	Not specified	17 4]
Xylene sulfonate, Ca	28088-63-3	Rainbow trout 96-hr LC50 >490 a.i.	EPA 797.1400 (flow through)	40 [1]
		Invertebrate		
Xylene sulfonate, Na	1300-72-7	*Daphnia magna* 48-hr EC50 >408 a.i.	EPA 797-1300	49 [2]
Xylene sulfonate, Na	1300-72-7	*Daphnia magna* 48-hr EC50 >400 a.i.	EPA 797-1300	39 [2]
Xylene sulfonate, Na	1300-72-7	*Artemia sp.* 48-hr EC50 >400	Not specified	3 [4]
Xylene sulfonate, Ca	28088-63-3	*Daphnia magna* 48-hr EC50 >318 a.i.	EPA 797-1300 (flow through)	23 [1]
		Algae		
Xylene sulfonate, Na	1300-72-7	*Selenastrum* 96-hr EC50 = 230 NOEC = 31	EPA 797.1050	47 [2]
Xylene sulfonate, Ca	28088-63-3	*Selenastrum* 96-hr EC50 = 236 a.i. NOEC = 75	EPA 797.1050	25 [1]
		Fish		
Cumene sulfonate, Na	28348-53-0	Fathead minnow 96-hr LC50 >450 a.i.	EPA 797.1400	41 [2]
Cumene sulfonate, Na	28348-53-0	*Leuciscus idus* 48-hr LC50 >1000	DIN 38412, T15	7, 10 [4]
		Invertebrate		
Cumene sulfonate, Na	28348-53-0	*Daphnia magna* 48-hr EC50 >450 a.i.	EPA 797-1300	19 [2]
Cumene sulfonate, Na	28348-53-0	*Daphnia magna* 24-hr EC50 >1000	DIN 38412, T11	10 [4]
Cumene sulfonate, Na	28348-53-0	Algae	Algenwachstums-hemmtest - UBA	10 [4]
		Scenedesmus 72-hr EC50 >1000		

[1] "a.i." indicates active ingredient for those studies where test substance purity was reported.
EC50 = Effect concentration for 50 percent of organisms tested
LC50 = Lethal concentration for 50 percent of organisms tested.
* Reference numbers refer to the OECD HPV Dossier references
** value in brackets [ ] indicates Klimisch score

4.2.1.2 Aquatic chronic toxicity

Chronic algal toxicity data on hydrotropes are available for sodium and calcium xylene sulfonates while a single chronic study with *Daphnia magna* is reported for sodium cumene sulfonate (see Table 9). There are limited details of presumably the same chronic daphnid study in both a journal article citation (7) and an IUCLID file for sodium cumene sulfonate (10). Both references have Klimisch reliability ratings of 4 (not assignable). The study is described as a 21-day exposure study with reproduction endpoint following method "Verlaengerter Toxizitaetstest bei Daphnia magna nach UBA (1984 standard)" with no analytical monitoring. The 21-day EC50 is reported as 154 mg/L and the NOEC is reported as >30 mg/L in Greim et al. (7) and <30 mg/L in the IUCLID (10). The study sponsor does not have a full laboratory report but did indicate that "Testing was done in 1987 without formal GLP but that GLP certification of the laboratory was received in 1989/1990. Test substance concentrations were 30, 100 and 300 mg/L as active ingredient (with no analysis performed)." The sponsor also provided tables summarizing the number of parent animals and offspring during the course of the study. The tables show no significant test substance related mortality of parent animals over the 21-day exposure period. The average number of offspring produced per day was 43 in the controls, 38 at 30 mg/L, 29 at 100 mg/L and 13 at 300 mg/L. These equate to 88% of control, 67% of control and 30% of control at 30, 100 and 300 mg/L, respectively. There are insufficient data to establish a statistically derived NOEC. It is uncertain whether the 88% of control response is a significant reduction in the number of young produced, but the data in these tables indicate that the "NOEC >30 mg/L" as reported in Greim et al. (7) appears to be an error. The NOEC could be 30 mg/L or < 30 mg/L. A chronic NOEC of approximately 30 mg/L would be consistent with the lowest algal chronic NOEC value of 31 mg/L. Nevertheless, due to the

deficiency of a reliable daphnia chronic NOEC, the PNEC for hydrotropes is derived from the existing acute data (see Sectin 4.2.2).

Table 9: Chronic Aquatic Toxicity

Compound	CAS No.	Chronic Toxicity Endpoint Species and Duration	 NOEC (mg/L)	Method	Reference*
Cumene sulfonate, Na	28348-53-0	*Daphnia magna 21-day*	~30	"1984 standard"	10, 7 [4]
Xylene sulfonate, Na Xylene sulfonate, Ca	1300-72-7 28088-63-3	*Selenastrum* 96-hr *Selenastrum* 96-hr	31 75	EPA 797.1050 EPA 797.1050	47 [2] 25 [1]

***** value in brackets [ ] indicates Klimisch score

4.2.1.3 Terrestrial and sediment ecotoxicity

No terrestrial or sediment toxicity data are reported for hydrotropes. Given the low potential for hydrotropes reaching the terrestrial and sediment compartments (EQC modelling results), the lack of persistence (ready biodegradability under aerobic conditions) or bioaccumulation (BCFWIN modelling results), and the low likelihood of these chemicals partitioning to soil and sediments (EQC modelling results), the lack of ecotoxicity data is not considered a deficiency.

4.2.1.4 Microbial toxicity

Results of a microbial toxicity test are reported for sodium cumene sulfonate. The 48-hr EC10 for the bacteria *Pseudomonas putida* exposed in a Bringmann-Kuehn-Test is reported as >16,000 mg/L (10). The reliability rating is a 4.

4.2.2 PNEC calculations

4.2.2.1 Aquatic PNEC

Aquatic toxicity data are available for representative xylene and cumene sulfonates (including sodium, ammonium and calcium salts). While the toluene sulfonate is not represented in the available data set, the xylene and cumene sulfonate results are consistent and comparable, providing confidence in the ability to extrapolate to the toluene sulfonates. The acute aquatic ecotoxicity data given for the hydrotropes in Table 8 indicate that algae are the most sensitive species. Based on the acute data, using the lowest EC50 (230 mg/L) and dividing by an application factor of 1000 (TGD, 2003), the PNEC is 0.23 mg/L. The limited available chronic data support this PNEC. Taking the lowest algal NOEC (31 mg/L) and dividing by an application factor of 50 (TGD, 2003) gives a PNEC of 0.62 mg/L.

Conclusion: PNEC in water = 0.23 mg/L

4.2.2.2 Terrestrial PNEC

There are no terrestrial ecotoxicity data and hydrotropes are not expected to have significant partitioning to soil.

Soil PNEC of hydrotropes can be calculated by using the TGD equilibrium partitioning method (TGD, 2003, Part II: eq. 72, page 117). On the basis of a local PNEC in water of 0.23 mg/l and the partition coefficient value of -2.7, (see Section 3.2, Table 3), a value of 0.027 mg/kg can be obtained. No additional safety factor is required for hydrotropes due to the log K_{ow} value being less than 5.

Conclusion: PNEC in soil = 0.027 mg/kg

4.2.2.3 Freshwater sediment PNEC

There are no sediment ecotoxicity data and hydrotropes are not expected to have significant partitioning to sediment.

As for soil, sediment PNEC can be calculated using the TGD equilibrium partitioning method (TGD, 2003: Part II, eq. 70, page 113). The resulting PNEC is 0.180 mg/kg.

Conclusion: PNEC in sediment = 0.180 mg/kg

4.2.2.4 STP PNEC

The 48-hr EC10 value is >16,000 mg/l for *Pseudomonas putida*. This value with an application factor of 100, as recommended by the TGD, gives a conservative PNEC of 160 mg/l.

Conclusion: PNEC in STPs = 160 mg/l

4.3 Environmental risk assessment

PEC and PNEC values with the corresponding PEC/PNEC ratios are summarized in Table 10.

Table 10a: Environmental risk characterization – local scenario

Hydrotropes	PEC	PNEC	PEC/PNEC
freshwater, mg/l	0.0205	0.23	0.0891
Soil (30 d), mg/kgwwt	2.07E-06	0.027	7.66E-05
Freshwater sediment, mg/kgwwt	0.0161	0.180	0.0894
STP, mg/l	0.147	160	2.49E-04

Table 10b: Environmental risk characterization – regional scenario

Hydrotropes	PEC	PNEC	PEC/PNEC

freshwater, mg/l	0.006	0.23	0.026
Agricultural soil (30 d), mg/kgwwt	7.51E-09	0.027	2.78E-07
Freshwater sediment, mg/kgwwt	0.004	0.180	0.022

The risk characterization ratios derived by EUSES 2.02 modelling are far below one (1.0) for all environmental compartments. It is therefore concluded that the use of hydrotropes in household laundry and cleaning products does not pose a risk for the environment. Further, the margins of safety would accommodate any additional hydrotrope volumes/uses not accounted for in the HERA assessment.

5. Human Health Assessment

5.1 Consumer exposure

5.1.1 Product types

Hydrotropes are used in many household detergents including powder laundry detergents (maximum concentration 0.66%), liquid laundry detergents (maximum concentration in regular and compact formulations 2%), fabric conditioners (maximum concentration 0.66%), laundry bleach liquids (maximum concentration 1%), hand dishwashing liquids (maximum concentration 3%), machine dishwashing rinse aids (maximum concentration 11.9%) and hard surface and bathroom cleaners (maximum concentration: 6%), hard surface trigger sprays (maximum concentration 2%), and toilet cleaners (maximum concentration 1.9%). The personal care product uses (e.g., face and hand soaps and shampoos) are outside the scope of HERA. They are not evaluated in this assessment.

5.1.2 Consumer contact scenarios

Based on the product types, the following consumer task and the related exposure scenarios were identified:

Fabric Washing:
Direct skin contact with diluted consumer product (hand-washed laundry) or with neat product (laundry pre-treatment)
Indirect skin contact via release from clothes fibers to skin
Inhalation of powder formulation detergent dust

Dishwashing
Direct skin contact (hand dishwashing)
Oral ingestion of residues deposited on dishes

Surface cleaning
Direct skin contact with diluted consumer product
Inhalation of aerosols generated by spray cleaners

Other scenarios
Oral ingestion of residues in drinking water and food
Accidental or intentional overexposure

Overall, exposures routes can be categorized as
Skin contact – direct and indirect
Inhalation - direct
Oral – indirect

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 the European Soap and Detergent Industry Association, AISE [AISE/HERA Table of H&P (2002)]. This table reflects consumers' use of detergents in g/task, use frequency, duration of task and other uses of products and is largely the basis for the exposure estimates in the following paragraphs. In some instances, e.g. habits & practices of pre-treatment of clothes, the information provided by the AISE/HERA table was not detailed enough for a targeted exposure assessment and the H&P information was directly provided by the member companies of AISE.

5.1.3.1 Direct skin contact

A. Hand-wash laundry. Hand-washing of laundry is a common consumer habit. During this procedure, the hydrotrope-containing laundry solution comes in direct contact with the skin of hands and forearms. A hand-washing task typically takes 10 minutes [AISE/HERA (2002)]. The exposure to hydrotrope is estimated according to the following algorithm from the HERA guidance document:

$$\mathbf{Exp_{sys} = F_1 \times C \times FT \times PA \times S_{der} \times n \times t / BW}$$

For this exposure estimate, the terms are defined with following values for the calculation considering a worst-case scenario:

F_1	percentage weight fraction of substance in product	***2%*** (0.02) [AISE/HERA 2002]
C	product concentration in mg/ml:	***10 mg/ml*** [AISE/HERA 2002]
FT	film thickness, assumed	***0.01 cm*** [TGD, 1996, 2003]
PA	percutaneous absorption	***1%*** (0.01) over 24 hours *[Assumption: based on Schaefer et al., 1996]

* The basis for the 1% percutaneous absorption used throughout the assessment is (1) general belief that ionic substances are expected to have very low absorption, and (2) the Schaefer et al, 1996 publication on principles of percutaneous absorption indicates "low" absorption.

S_{der}	surface area of exposed skin	***1980 cm²*** [TGD, 1996, 2003]
n	product use frequency (tasks per day)	***3*** [AISE/HERA 2002]
t	task duration	**10 min (0.007 day)** [AISE/HERA 2002]
BW	body weight	***60 kg***

[TGD, 1996, 2003]

Exp_{sys} = [(0.02) x (10 mg/ml) x (0.01 cm) x (0.01) x (1980 cm²) x 3 x 0.007 day] x 1000 µg/mg / 60 kg =

0.014 µg/kg/day

B. Laundry pre-treatment. Consumers typically spot-treat stains by hand with the help of either a detergent paste (i.e. water/laundry powder = 1:1) or a laundry liquid that is applied directly on the garment. In this exposure scenario, only the skin surface of both hands (~ 840 cm^2) is exposed and the treatment time is typically less than 10 minutes [AISE/HERA, 2002 unpublished data].

The exposure calculation is conducted by using the algorithm described above for hand-washing laundry. The following assumptions are considered to represent a conservative reflection of this scenario.

F_1	percentage weight fraction of substance in product	***2% (0.02)*** [AISE/HERA 2002]
C	product concentration in mg/ml:	***1000 mg/ml*** [AISE/HERA 2002]
FT	film thickness, assumed	***0.01 cm*** [TGD, 1996, 2003]
PA	percutaneous absorption	***1%*** (0.01) over 24 hours [Assumption: based on Schaefer et al., 1996]
S_{der}	surface area of exposed skin	***840cm²*** [TGD, 1996, 2003]
n	product use frequency (tasks per day)	***0.5*** [AISE/HERA 2002]
t	task duration	**10 min (0.007 day)** [AISE/HERA 2002]
BW	body weight	***60 kg*** [TGD, 1996, 2003]

Exp_{sys}= [(0.02) x (1000 mg/ml) x (0.01 cm) x (0.01) x (840cm²) x 0.5 x 0.007 day] x 1000 µg/mg./ 60kg =

0.10 µg/kg/day

This exposure estimate can be regarded to be very conservative in many respects. To note are the assumptions related to neat product use and the surface area of exposed skin. Typically, consumers pre-wet the laundry before applying the detergent for pre-treatment or conduct the pre-treatment under running tap water. Both practices lead to a significant dilution that is not reflected in this exposure estimate. It should also be considered that only a fraction of the two hands' surface skin

would actually be exposed. The assumption that both hands will be fully immersed leads to a likely overestimate of the true exposure.

C. Hand dishwashing. The determination of hydrotrope exposure from hand dishwashing using a hydrotrope containing product can be estimated using the following algorithm:

$$\mathbf{Exp_{sys} = F_1 \times C \times FT \times PA \times S_{der} \times n \times t / BW}$$

For a reasonable worst-case scenario, the following assumptions have been made:

F_1	percentage weight fraction of substance in product	***3%*** (0.036) [AISE/HERA 2002]
C	product concentration in mg/ml:	***1 mg/ml*** [AISE/HERA 2002]
FT	film thickness, assumed	***0.01 cm*** [TGD, 1996, 2003]
PA	percutaneous absorption	***1%*** (0.01) over 24 hours [Assumption: based on Schaefer et al., 1996]
S_{der}	surface area of exposed skin	***1980 cm^2*** [TGD, 1996, 2003]
n	product use frequency (tasks per day)	***3*** [AISE/HERA 2002]
t	task duration	**45 min (0.03 day)** [AISE/HERA 2002]
BW	body weight	***60 kg*** [TGD, 1996, 2003]

$$\mathbf{Exp_{sys}} = [(0.03) \times (1\ mg/ml) \times (0.01\ cm) \times (0.01) \times (1980\ cm^2) \times 3 \times (0.03\ day)] \times 1000\ \mu g/mg / 60\ kg =$$

$$\mathbf{0.009\ \mu g/kg/day}$$

D. Hard surface cleaning. For this scenario it is assumed that the solution of the hard surface cleaning product containing hydrotrope comes into direct contact with the skin of the hands. The dermal exposure to hydrotrope can be estimated using an algorithm similar to that used for hand dishwashing (See scenario C).

The assumptions below are considered representative of a reasonable worst case:

F_1	percentage weight fraction of substance in product	6***% (0.06)*** [AISE/HERA 2002]
C	product concentration in mg/ml:	***12 mg/ml*** [AISE/HERA 2002]
FT	film thickness, assumed	***0.01 cm*** [TGD, 1996, 2003]
PA	percutaneous absorption	***1%*** (0.01) over 24 hours

		[Assumption: based on Schaefer et al., 1996]
S_{der}	surface area of exposed skin	***1980 cm²*** [TGD, 1996, 2003]
n	product use frequency (tasks per day)	***1*** [AISE/HERA 2002]
t	task duration	**10 min (0.007 day)** [AISE/HERA 2002]
BW	body weight	***60 kg*** [TGD, 1996, 2003]

Exp_{sys} = [(0.06) x (12 mg/ml) x (0.01 cm) x (0.01) x (1980 cm²) x 1 x (0.007 day)] x 1000 µg/mg / 60 kg=

0.017 µg/kg/day

E. Other direct skin contact scenarios. Other scenarios for potential direct dermal exposures may include activities such as hand washing with fabric conditioners or toilet cleaners. These are not considered here because the short contact time and the small skin surface area involved or the low frequency (once weekly) combined with a short duration (< 1 minute). Exposure resulting from such activities is considered to be negligible.

5.1.3.2 Indirect skin contact

Wearing clothes. Residues of components of laundry detergents may remain on textiles after washing and can transfer from the textile to the skin. There are no data available showing how much hydrotrope is deposited on the fabric following a wash process. This value has, however, been determined for LAS, an anionic surfactant that is widely used in laundry detergents. Rodriguez et al (1994) determined that after a typical washing process with a laundry detergent containing linear alkylbenzene sulphonate (LAS), 2.5 g LAS per kilogram wash resided on the fabric. LAS is present in laundry detergents at levels higher than hydrotropes (18% LAS versus 2% hydrotrope) [Rodriguez, C., et al. (1994)]. It is assumed that these data on LAS represent a worst-case assumption for the remaining amounts of hydrotrope on fabric.

The following algorithm was recommended in the HERA guidance document to estimate the dermal exposure to detergent residues in the fabric:

$$Exp_{sys} = F_1 \times C` \times S_{der} \times n \times F_2 \times F_3 \times F_4 / BW$$

For the hydrotrope 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 (hydrotrope) load*:	***2.5 x 10^{-2}*** mg/cm^2 [Rodriguez et al., 1994]
S_{der}	surface area of exposed skin	***17600 cm²***

		[TGD, 1996, 2003]
n	product use frequency (tasks per day)	***Not used, = 1***
F_2	percent weight fraction transferred to skin	***1% (0.01)*** [Vermeire et al, 1993]
F_3	percent weight fraction remaining on skin	***100% (1)*** (worst case)
F_4	percent weight fraction absorbed via skin	***1% (0.01)*** [Assumption: based on Schaefer et al., 1996]
BW	body weight	***60 kg*** [TGD, 1996, 2003]

* C' was determined by multiplying the experimental value of the amount of LAS deposited on fabric after a typical wash (2.5 g/kg [Rodriguez et al., 1994]) times an estimated value of the fabric density (FD = 10 mg/cm^2 [Internal P&G data]).

$$\mathbf{Exp_{sys\ (indirect\ skin\ contact)}} = [(2.5 \times 10^{-2}\ mg/cm^2) \times (17{,}600\ cm^2) \times (0.01) \times (0.01)] \times 1000\ \mu g/mg / 60kg =$$

0.73 µg/kg/day

5.1.3.3 Exposure by inhalation

A. Aerosols. The use of surface cleaning sprays can result in aerosol formation. Hydrotrope may be present in these products at a maximum concentration of 2%. The HERA guidance document specifies the algorithm to be used for calculation of consumers' worst-case exposure to hydrotrope-containing aerosols generated by the spray cleaner:

$$\mathbf{Exp_{sys} = F_1 \times C` \times Q_{inh} \times t \times n \times F_7 \times F_8 / BW}$$

F_1	percentage weight fraction of substance in product	***2% (0.02)*** [AISE/HERA 2002]
C`	product concentration in air:	***0.35 mg/m^3 **** [P&G, internal data]
Q_{inh}	ventilation rate	***0.8 m^3/h*** [TGD, 1996, 2003]
t	duration of exposure	***10 min (0.17h)*** [AISE/HERA 2002]
n	product use frequency (tasks per day)	***1*** [AISE/HERA 2002]
F_7	weight fraction of respirable particles	***100% (1)*** [worst case]
F_8	weight fraction absorbed or bioavailable	***75% (0.75)*** [TGD, 1996, 2003]
BW	body weight	***60 kg*** [TGD, 1996, 2003]

* This value was obtained by experimental measurements of the concentration of aerosol particles smaller than 6.4 microns in size which are generated upon spraying with typical surface cleaning spray products. It is assumed that these particles are fully respirable and bio-available.

$$\mathbf{Exp_{sys\ (inhal.\ of\ aerosol)}} = [(0.02) \times (0.35\ mg/m^3) \times (0.8\ m^3/hr) \times (0.17\ h) \times (0.75)] \times 1000\ \mu g/mg / 60\ kg =$$

$$\mathbf{0.012\ \mu g\ /kg/day}$$

B. Inhalation of detergent dust during washing processes

Some studies (Van de Plassche-b et al., 1999) determined an average release of about 0.27 µg dust per cup of product used for machine laundering. Given the composition of powder laundry detergents, containing up to 0.66% hydrotropes, 0.002 µg/use of the detergent dust can be expected to be hydrotropes (AISE unpublished data). In the worst case assumptions that all of the dust is inhaled during machine loading and that this task is done 3 times daily, the exposure to hydrotropes of an adult with an average body weight of 60 kg is estimated to be:

$$\mathbf{Exp_{sys} = F_1 \times n / BW}$$

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

F_1	percentage weight fraction of substance in dust	***0.27 x 0.66% = 0.002 µg*** [Van de Plassche et al., 1999 & AISE/HERA 2002]
n	product use frequency (tasks per day)	***3*** [AISE/HERA 2002]
BW	body weight	***60 kg*** [TGD, 1996, 2003]

$$\mathbf{Exp_{sys\ (inhalation\ of\ detergent\ dust)}} = [0.002\ (\mu g/use) \times 3] / 60\ kg =$$

$$\mathbf{0.0001\ \mu g\ /kg/day}$$

This amount does not contribute significantly to the total exposure of hydrotropes. Similarly, lint formation during drying of fabrics in tumble-dryers which vent indoors is considered not to contribute significantly to inhalation exposure of hydrotropes, since washed fabrics do not contain any relevant amount of hydrotropes (see above).

5.1.3.4 Oral exposures

A Indirect exposure via the environment

The presence of hydrotropes in the environment following down-the-drain disposal can potentially lead to indirect exposure through the intake of drinking water and food. EUSES modelling (see

Chapter 4, Table 7) provides a Regional PEC in surface water of approximately 6 µg/L dissolved hydrotropes (Table 7). Assuming 2 liters of daily water consumption (TGD, 2003), 100% bioavailability of hydrotropes in humans (worst case) as 60 kg of body weight, the daily human exposure to hydrotropes from drinking water can be estimated as:

$$\mathbf{Exp_{sys\ (oral\ via\ drinking\ water)} = [6\ (}\mu g/L) \times 2\ (L)] / 60(kg) = \mathbf{0.2\ \mu g/kg\ bw/day}$$

The estimated drinking water exposure should be regarded as highly conservative as it assumes that all drinking water contains hydrotropes and does not account for any removal in drinking water treatment plants. Exposure from food consumption is considered to be negligible. The local PEC in soil (Table 8) is an extremely small 7.29E-12 mg/kg and bioaccumulation potential which would affect food exposure from, for example, fish consumption is described as very low, <1 L/kg (Section 4.1.7).

B. Indirect exposure via automatic dishwashing residues

Oral exposure to hydrotropes can originate from residues present on eating utensils and crockery cleaned in an automatic dishwasher that used a rinse aid. The daily exposure to hydrotropes from eating with utensils and dishware that have been cleaned in an automatic dishwasher that used a rinse aid can be estimated according to the following algorithm from the HERA guidance document:

$$\mathbf{Exp_{sys\ (oral\ from\ dish\ washing\ residues)} = F1 \times C` \times Ta' \times Sa \times F'' \times F9 / BW}$$

For this exposure estimate, the terms are defined with following values for the calculation considering a worst-case scenario:

F_1	percentage weight fraction of substance in product	***11.9%*** (0.119) [AISE/HERA 2002]
C`	concentration of product in dish wash solution:	***0.33 mg/mL*** [see Note 1 below]
Ta'	amount of water left on dishes after rinsing	***5.5 x 10^{-5} ml/cm^2*** [see Note 2 below]
Sa	area of dishes in daily contact with food	***5400cm^2*** [O. J. France, 1990]
F"	percentage (%)transferred from article and ingested	***100%*** [conservative assumption]
n	product use frequency, in *number of events per day*	***1*** [AISE/HERA 2002]
F9	percentage (%)absorbed or bioavailability	***100%*** = 1 [conservative assumption]
BW	body weight	***60 kg*** [TGD, 1996, 2003]

Note 1: C' the product concentration (in mg/ml) in the dishwash solution which can remain on the surface of the article was determined dividing the amount of product per task over the wash water volume. The worst case assumption for product use is a maximum amount of 6 mL (or 6000 mg) dishwashing rinse aid (AISE/HERA 2002 unpublished data). According to manufacturers, the average wash water volume used by current automatic dishwashers in Europe is about 18 liters (18 000 ml). The resulting estimated value is 0.33 mg/ml.

Note 2: Ta' amount of water left on dishes after washing and rinsing. The dish surface (including dishes, utensils, glassware, pans etc.) in contact with food and used by one individual each day is the equivalent of 5400 cm2. The amount of wash water left on non-rinsed dishware was estimated to amount 3 ml for this surface of 5400 cm2, i.e. 0.00055 ml/cm2. With a factor 10 for rinsing, the amount of water left on dinnerware is 0.000055 ml/cm2 (O.J.France, 1990).

$\mathbf{Exp_{sys\ (oral\ autodish\ deposition)}}$ = [(0.119) x (0.33 mg/mL) x (5.5 x10^{-5} ml/cm^2) x (5400 cm^2)] x 1000 µg/mg / 60 kg =

0.19 µg /kg/day

C. Indirect exposure via hand dishwashing residues

Oral exposure to hydrotropes can originate from residues present on eating utensils and crockery washed with hand dishwashing detergents. The daily exposure to hydrotropes from eating with utensils and dishware that have been washed with hand dishwashing detergents can be estimated according to the following algorithm from the HERA guidance document:

$$\mathbf{Exp_{sys\ (oral\ from\ dish\ washing\ residues)} = F1 \times C` \times Ta' \times Sa / BW}$$

For this exposure estimate, the terms are defined with following values for the calculation considering a worst-case scenario:

F_1	percentage weight fraction of substance in product	3***.0% (0.03)*** [AISE/HERA 2002]
C`	concentration of product in dish wash solution:	***1 mg/cm^3*** [AISE/HERA 2002]
Ta'	amount of water left on dishes after rinsing	***5.5 x 10^{-5} ml/cm^2*** [O.J. France, 1990; Schmitz (1973)]
Sa	area of dishes in daily contact with food	***5400cm^2*** [O. J. France, 1990]
BW	body weight	***60 kg*** [TGD, 1996, 2003]

$\mathbf{Exp_{sys\ (oral\ dish\ deposition)}}$ = [(0.03) x (1 mg/cm^3) x (5.5 x 10^{-5} ml/cm^2) x (5400 cm^2)] x 1000 µg/mg / 60 kg =

0.15 µg /kg/day

5.1.3.5 Aggregate Exposure

The overall body burden of consumers to hydrotropes through the use of hydrotrope-containing house hold laundry and cleaning products by combining all scenarios and all exposure routes is calculated to be:

$$Exp_{sys} = 1.42 \text{ µg/kg bw/day}$$

Considering the contribution of the different routes of exposure, the exposure via the skin represents the major route of exposure (*ca*. 77% of the total systemic exposure), and the oral route being less prominent (*ca*. 22% of the total systemic exposure). Exposure to hydrotropes by inhalation is of minor (*ca*. 1%) importance in the use of household laundry and cleaning products.

The aggregate exposure estimate is an unrealistic, worst-case estimate of the body burden of hydrotropes. It combines several scenarios, each using highly conservative or worst-case assumptions and it is virtually impossible that each of these conservative input parameters will apply concurrently in all cases for this overall exposure estimate. For example, both the 0.19 µg/kg/day (from automatic dishwashing residue on dishes) and the 0.15 µg/kg/day (from hand dishwashing residue on dishes) are included in the 1.42 µg/kg/day aggregate.

5.1.3.6 Accidental or intentional overexposure

Accidental or intentional overexposure to hydrotropes can occur through splashing, spilling or ingestion of household detergent products.

There are no reports of fatal cases or serious injuries arising from accidental ingestion of hydrotropes via household detergent products, which may contain levels of up to 11.9% hydrotrope. The German Federal Institute for Health Protection of Consumers and Veterinary Medicine [BgVV (1999)] has published a report on the products involved in poisoning cases. No fatal case of poisoning with detergents was reported in this report. Detergent products were not listed as dangerous.

Equally, in the UK, the Department of Trade and Industry (DTI) produces an annual report of the home accident surveillance system (HASS). The data in this report 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.

Hydrotropes in concentrated form have a potential for irritation of skin and eyes (see section 5.2.1.3). Inadvertent skin or eye contact of consumers with household cleaning and laundry products containing hydrotropes involves only formulated products. Therefore the potential for skin or eye irritation should be assessed taking into account formulated product instead of neat hydrotrope.

5.2 Hazard assessment

5.2.1 Summary of the available toxicological data

5.2.1.1 Toxicokinetics

No ADME (adsorption, distribution, metabolism and elimination) studies for hydrotropes were identified.

5.2.1.2 Acute toxicity

Acute toxicity for oral exposures (9 studies), dermal exposures (2 studies) and inhalation exposures (3 studies) are reported. Roughly one half of the studies are reported in considerable detail with regard to methods and results and the other half are brief data summaries. Table 11 provides the available acute toxicity results for toluene, xylene and cumene sulfonates and their various salts. Clinical signs observed in some of the acute oral toxicity studies included decreased activity, weakness, prostration, increased salivation and anogenital staining. No clinical effects were reported following inhalation and dermal exposures. [Note that results from studies reporting chemical purity information are designated "a.i." based on % active ingredient]

Table 11: Acute Mammalian Toxicity

Compound	CAS No.	Acute Toxicity Endpoints	Method	Reference*
Toluene sulfonate, Na	12068-03-0	Oral rat LD_{50} 6500 mg/kg	Not specified	50 [4]
Toluene sulfonate, K	16106-44-8	Oral rat LD_{50} 4400 mg/kg	Not specified	50 [4]
Toluene sulfonate, Na	12068-03-0	Inhalation rat LC_{50} >557 mg/L	US CPSC CFR1500.40	50, 53 [4]
Xylene sulfonate, Na	1300-72-7	Oral rat LD50 >5000 mg/kg	Not specified	50, 53 [4]
Xylene sulfonate, Na	1300-72-7	Oral rat LD_{50} 7200 mg/kg	Not Specified	3, 16 [2]
Xylene sulfonate, Na	1300-72-7	Oral rat LD_{50} 16,200 mg/kg	Not Specified	4 [2]
Xylene sulfonate, Na	1300-72-7	Oral rat LD_{50} >5000-16,200 mg/kg	Not Specified	50 [4]
Xylene sulfonate, NH_4	26447-10-9	Oral rat LD_{50} >2100 mg/kg	Not Specified	52 [4]
Xylene sulfonate, Ca	28088-63-3	Oral rat LD_{50} 3346 mg/kg	USEPA 798.1175	24 [1]
Xylene sulfonate, Ca	28088-63-3	Dermal rabbit LD_{50} >2000 mg/kg	USEPA 798.1100	22 [1]
Xylene sulfonate, NH_4	26447-10-9	Inhalation rabbit LC_{50} >6.41 mg/L	Not Specified	52 [4]
Cumene sulfonate, Na	28348-53-0	Oral rat LD_{50} >7000 mg/kg	OECD 401	7, 10 [4] & 11 [2]
Cumene sulfonate, Na	28348-53-0	Dermal rabbit $L_{50}D$ >2000 mg/kg	Not Specified	50 [4]
Cumene sulfonate, Na	28348-53-0	Inhalation rat LC_{50} >770 mg/L	US CPSC CFR1500.40	50, 53 [4]

USCPSC = U.S. Consumer Product Safety Commission

CFR = Code of Federal Register (U.S.)
* Reference numbers refer to the OECD HPV Dossier references
** value in brackets [ ] indicates Klimisch score

Conclusion

The acute oral LD_{50} in rats ranges from 3346 mg/kg to 16,200 mg/kg, the dermal LD_{50} in rabbits is >2000 mg/kg and the inhalation LC_{50} in rats is >557 mg/L and in rabbits >6.41 mg/L. Hydrotropes demonstrate a low order of acute oral, dermal and inhalation toxicity. The results are consistent across the toluene, xylene and cumene sulfonates and their various salts.

5.2.1.3 Skin and eye irritation

Irritation for skin exposure (7 studies) and eye exposure (8 studies) are reported. A number of the results are reported with limited study detail as part of summary reports; however, several studies include considerable detail with regard to methods and results. Tables 12 and 13 provide the

available rabbit skin and eye irritation results, respectively, for toluene, xylene and cumene sulfonates and their various salts.

Table 12: Skin Irritation

Compound	CAS No.	Irritation Endpoints	Method	Reference*
Toluene + xylene sulfonates, Na [50:50]	12068-03-0 + 1300-72-7	Slight irritation at 40% solution	Not specified	50 [4]
Xylene sulfonate,Na	1300-72-7	Slight irritation at 40% solution	Not specified	5 [2] 50, 52 [4]
Xylene sulfonate, NH_4	26447-10-9	Slight irritation at 40% solution	Not specified	52 [4]
Xylene sulfonate, Ca	28088-63-3	Not irritating at 31% solution	USEPA 81-5 & USEPA TSCA 798	52 [4] 36 [1]
Cumene sulfonate, Na	28348-53-0	Not irritating at 60% solution	OECD 404	14 [2]
Cumene sulfonate, Na	28348-53-0	Not irritating at 60% solution	Not specified	7, 10 [4]
Cumene sulfonate, Na	28348-53-0	Mild to moderate irritation	Not specified	50 [4]

TSCA = Toxic Substances Control Act (U.S.)
* Reference numbers refer to the OECD HPV Dossier references
****** value in brackets [ ] indicates Klimisch score

Table 13: Eye Irritation

Compound	CAS No.	Irritation Endpoints	Method	Reference*
Toluene sulfonate, Na	12068-03-0	Moderate irritation at 20%solution	Not specified	50 [4]
Toluene sulfonate, K	16106-44-8	Irritation at 20% solution	Not specified	50 [4]
Xylene sulfonate, Na	1300-72-7	Slight irritation at 40% solution	Not specified	50, 52, 53 [4]
Xylene sulfonate, NH_4	26447-10-9	Slight irritation at 40% solution	Not specified	52 [4]
Xylene sulfonate, Ca	28088-63-3	Slight irritation at 31% solution	USEPA798.4500	37 [1]
Cumene sulfonate, Na	28348-53-0	Mild irritation,at 60% solution,	OECD 405	13 [2]
Cumene sulfonate, Na	28348-53-0	Not irritating at 60% solution	Not specified	7, 10 [4]
Cumene sulfonate, Na	28348-53-0	Irritating depending on diluted or not, and rinsed or not at 10% solution	Not specified	50 [4]

TSCA = Toxic Substances Control Act (U.S.)

* Reference numbers refer to the OECD HPV Dossier references
****** value in brackets [ ] indicates Klimisch score

Conclusion

Skin and eye irritation results are generally consistent across the hydrotropes. Skin irritation is negligible to slight and eye irritation is slight to moderate.

5.2.1.4 Sensitisation

Studies in Humans

There was no evidence of skin sensitization in a human repeat insult patch test of 0.5% aqueous sodium cumene sulfonate in a diluted granular laundry detergent product (50). Only a brief study result summary is available; the reliability rating is 4.

The Information Network of Departments of Dermatology (IVDK) in Germany was contacted for information on hydrotropes. In the IVDK literature database, no records for these substances or structurally similar substances were found. No suspected cases were reported and no reports on positive findings (sensitization) were found in a database covering more than 130,000 tested individuals.

Studies in Animals
A guideline study with guinea pigs reports no evidence of skin sensitization following dermal, semiocclusive exposure to a 42.8% solution (deionized water) of sodium toluene sulfonate (58). The protocol follows the Buehler Test and the reliability rating of this GLP study is 1.

Conclusion

There is no indication of skin sensitization of the hydrotropes category based on the available animal and human data. The chemical structure activity of these chemicals do not predict any concerns for contact sensitization.

5.2.1.5 Repeated dose toxicity

Oral and dermal subchronic repeated dose toxicity studies conducted in rats and mice are available for hydrotropes including the xylene and cumene sulfonates. Complete study reports are available in most cases. The results are summarized in Table 14.

5.2.1.5.1 Dermal route

Two subchronic dermal toxicity studies in both rats and mice were conducted using technical grade sodium xylenesulfonate in water (in 17-day) and ethanol (in 90-day) vehicles (51). All four studies are detailed in a 1998 U.S. National Institutes of Health report and have been assigned a reliability rating of 2. Five doses and a vehicle only were applied 5 days per week to clipped skin.

17-day study
In the 17-day study, 5 animals per sex were exposed to doses ranging from 10-800 mg active ingredient (a.i.)/kg body weight (bw) for male rats, 13-1030 for female rats, 20-1600 for male mice and 26-2000 for female mice. Rats were 5-6 weeks old and mice were 6-7 weeks old at study initiation. Endpoints in the 17-day study were mortality, body and organ weight, clinical signs and histopathology of skin from site of application, skin from an untreated site, and gross lesions.

No deaths or other treatment related effects were observed in the 17-day study for either species. The highest doses were 2000 mg a.i./kg bw for mice and 1030 mg a.i./kg bw for rats. The relative liver weights of male and female rats at the two highest doses were significantly greater than those of the control groups but the absolute weights were similar. The biological significance of the differences in relative liver weights was unclear. Similar observations, and conclusions, were reported in the mouse study for males at the highest dose and for females at the mid-dose levels.

90-day study
In the 90-day study, 10 animals per sex were exposed to doses ranging from 6-500 mg a.i./kg bw for male rats, 10-800 for female rats, 17-1300 for male mice, and 20-1620 for female mice. Rats were 5-6 weeks old and mice were 6-7 weeks old at study initiation. Endpoints in the 90-day study were the same as in the 17-day study but also included hematology, clinical biochemistry and

complete histopathology at necropsy on control mice and rats as well as on mice from the 400 mg/mL group.

No deaths or other treatment related effects were observed in the 90-day study for rats. The highest dose was 800 mg a.i./kg bw. The absolute and relative liver weights of males at the mid and upper doses were significantly less than those of the controls. There were no treatment-related histopathologic alterations in the livers, thus the biological significance of the decreased liver weights was unclear.

No treatment related effects were observed in the 90-day study for female mice at the highest dose which was 1620 mg a.i./kg bw. There was, however, a gain in mean body weight in male mice at the highest dose of 1300 mg a.i./kg bw. This change, though statistically significant (105% of the controls), was not considered by the investigators to be toxicologically significant. There were no clinical findings related to sodium xylenesulfonate administration. There was some epidermal hyperplasia (reported as "typically minimal in severity" multifocal increase in the thickness of the epidermis) observed in male and female mice at the highest doses. However, the results of the 2-year study (51) conducted by the same investigators (reported below, 5.2.1.7) showed no evidence that these lesions progressed to skin neoplasms. The No Observed Adverse Effect Level (NOAEL) for local effects, based on epidermal hyperplasia at the site of application, was 440 mg a.i./kg bw for male mice and 530 mg a.i./kg bw for female mice.

5.2.1.5.2 Oral route

Three subchronic 90-day feeding studies in rats were conducted; two with sodium xylene sulfonate (2 and 54) and the other with sodium cumene sulfonate (18).

In the first study (2), 15 Wistar rats per sex per dose level were exposed to purified sodium xylene sulfonate at 0, 0.2, 1.0 and 5.0% in the diet. Mean administered doses were 0, 140, 710 and 3800 mg/kg bw for males and 0, 160, 820 and 4400 mg/kg bw for females. The purity of the test substance was at least 93% (3), therefore, the doses based on active ingredient (a.i.) are 130, 660 and 3534 mg a.i./kg bw for males and 149, 763 and 4092 mg a.i./kg bw for females. Endpoints were those specified in OECD 408 with the exception of clinical signs, functional observations, ophthalmoscopy, cholesterol, sodium and potassium as part of clinical chemistry and platelets and blood clotting potential as part of hematology. No treatment related effects other than some sporadic clinical chemistry and haematology changes were observed in males at up to the highest dose (3534 mg a.i./kg bw). A loss of relative spleen weight in females, along with some clinical chemistry and haematology changes, was observed at the highest dose (4092 mg a.i./kg bw). The NOAEL is 1% in the diet (763 mg a.i./kg bw).

In the second study (54), five male and five female rats and mice were exposed per dose level to sodium xylene sulfonate as 0, 0.125%, 0.25%, 0.5%, 1% and 2% in the diet. A nuclear magnetic resonance spectrum was run on the test material to determine purity. The conclusion of this analysis was that the major component of the test material was xylene sulfonate; although an exact percent purity was not stated in the report. These dietary levels equate to 0, 152, 305, 610, 1220 and 2439 mg/kg bw daily doses for male mice, 0, 154, 308, 617, 1234 and 2467 mg/kg bw for female mice, 0, 89, 179, 357, 715 and 1429 mg/kg bw for male rats, and 0, 98, 195, 390, 781 and 1561 for female rats. There were no significant dose-related treatment effects on food consumption, body weight or body weight gain in any group for either species. There were also no treatment-related gross or microscopic lesions noted at necropsy in either rats or mice. The NOELs are therefore 2439 mg/kg bw/day for male mice, 2467 for female mice, 1429 for male rats and 1561 for female rats.

This 90-day study (54) was preceded by a two-week range-finding study in both mice and rats (55). The dose concentrations in this study were 1, 2, and 4%. Palatability was an issue in mice and even more pronounced in rats. Animals were observed scratching the food out of their dishes beginning about day 5. Some refused the food until they became thin and even died.

Subsequent to the 90-day study, a second two-week study (56) was conducted to determine reproducibility of the lack of toxicity noted in the subchronic study in light of the mortailities reported in the first two-week range-finding study. The results of this study reproduced the lack of toxicity seen in the 90-day study with regard to clinical or histological signs of toxicity. The dose concentrations in this study were 1, 2, and 4%. Again, palatability appeared to be an issue, especially in the 4% group. Animals were again observed scratching their feed from the feeders during the last eight days of the test. Body weight gains versus control animals were significantly lower at this high dose, but there was no dose-response relationship between test material concentration and body weight gain. Low-dose males and females gained 84% and 79% of controls, mid-dose males and females gained 96% and 91% of controls, and the high-dose males and females gained 38% and 40% of controls. Because of the food spillage issues, an accurate measurement of food consumption was not possible.

These studies (54, 55, 56) were sponsored by the U.S. National Institutes of Health (NTP, National Toxicology Program) as a range-finding study for a 2 year chronic study. However, the NTP did not pursue a 2-year oral toxicity study, but instead opted to conduct 2-year dermal studies with rats and mice as reported in the previous section.

In the third study (18), 20 CD rats per sex per dose level were exposed to sodium cumene sulfonate at 0, 0.005, 0.05 and 0.5% in the diet. Mean administered doses were 0, 2.6, 26 and 270 mg/kg bw for males and 0, 3.6, 36 and 375 mg/kg bw for females. Taking into account the content of active ingredient, 42.3%, these doses equate to 1.1, 11 and 114 mg a.i./kg bw and 1.5, 15 ad 159 mg a.i./kg bw, respectively. Endpoints were mortality, body and organ weight, food consumption, haematology, and histopathology. No treatment related effects were observed in males at up to the highest dose (114 mg a.i./kg bw). The only effect observed was an 11.7% decrease in body weight gain in females at the highest dose (159 mg a.i./kg bw). The study report stated that this decrease in body weight gain was within the established ranges for animals of this species and age and was therefore not considered an adverse effect by the authors. The feed efficiency of the high dose females was statistically higher than the controls. The decrease in body weight gain of the high dose females was not associated with any histopathologic or other effects. In light of the palatability issues seen in the previously discussed study, this slight decrease in body weight gain may be explained as a palatability effect Also, the intervals between the dose levels in this study are large (factor of 10), while OECD 408 prefers 2-4 fold intervals and prefers an additional group if the factors are > 6-10. A NOAEL for sodium cumene sulfonate is therefore >114 mg a.i./kg bw for males and >159 mg a.i./kg bw in females if the slight decrease in body weight gain is not considered toxicologically significant.

Table 14: Repeat Dose Toxicity

Compound	CAS No.	Species	Route of Exposure	Study Duration	NOAEL mg/kg bw	LOAEL mg/kg bw	Doses mg/kg bw	Reference ŦŦ
Xylene sulfonate,Na	1300-72-7	Rat	Dermal	17-day	No effects at high dose (1030)	N/A	♂ 10, 30, 90, 260, 800 a.i. ♀ 13, 40, 120, 330, 1030 a.i.	51 [2]
Xylene sulfonate, Na	1300-72-7	Mouse	Dermal	17-day	No effects at high dose (2000)	N/A	♂ 20, 60, 190, 540, 1600 a.i. ♀ 26, 80, 220, 680, 2000 a.i.	51 [2]
Xylene sulfonate, Na	1300-72-7	Rat	Dermal	90-day	No effects at high dose (800)	N/A	♂ 6, 20, 60, 170, 500 a.i. ♀ 10, 30, 90, 260, 800 a.i.	51 [2]
Xylene sulfonate, Na	1300-72-7	Mouse	Dermal	90-day	540 for ♀ 440 for ♂	1620 for ♀ 1300 for ♂ epidermal hyperplasia	♂ 17, 50, 140, 440, 1300 a.i. ♀ 20, 60, 170, 540, 1620 a.i.	51 [2]
Xylene sulfonate, Na	1300-72-7	Mouse	Dermal	2-years	No systemic effects at high dose (727)	N/A	182, 364, 727 a.i.	51 [2]
Xylene sulfonate, Na	1300-72-7	Rat	Dermal	2-years	No systemic effects at high dose (240)	N/A	60, 150, 240 a.i.	51 [2]
Xylene sulfonate, Na	1300-72-7	Rat	Oral feed	28-day	No effects 3% of diet	N/A	1% and 3% of diet	3 [4]
Xylene sulfonate, Na	1300-72-7	Rat	Oral feed	90-day	763for ♀ No effects at high dose (3534) for ♂	4092 for ♀ relative spleen wt loss	♂ 130, 660, 3534 a.i. ♀ 149, 763, 4092 a.i.	2 [2]
Xylene sulfonate, Na	1300-72-7	Rat	Oral feed	90-day	No effects at high dose (1429 for ♂ 1561 for ♀)	N/A	♂ 89, 179, 357, 715, 1429 a.i. ♀ 98, 195, 390, 781, 1561 a.i.	54 [2]
Xylene sulfonate, Na	1300-72-7	Mouse	Oral feed	90-day	No effects at high dose (2439 for ♂ 2467 for ♀	N/A	♂ 152, 305, 610, 1220, 2439 a.i. ♀ 154, 308, 617, 1234, 2467 a.i.	54 [2]
Cumene sulfonate, Na	28348-53-0	Rat	Oral feed	91-day	No systemic effects at high dose (159)	N/A	♂ 1.1, 11, 114 a.i. ♀ 1.5, 15, 159 a.i.	18 [2]

ŦŦ Reference numbers refer to the OECD HPV Dossier references
****** value in brackets [ ] indicates Klimisch score

Conclusion

The repeated dose toxicity of hydrotropes has been assessed using oral and dermal studies in rats and mice. Test durations ranged from 17 days up to 2 years and exposure doses ranged from 6 up to 4092 mg a.i./kg bw/day. LOAELs ranged from 1300 mg a.i./kg bw/day in dermal studies to 4092 mg a.i./kg bw/day in oral studies. The corresponding NOAELs are 440 mg a.i./kg bw/day in dermal studies based on local hyperplasia (no systemic toxicity was observed up to the highest dose level), and 763 mg a.i./kg bw/day in oral studies based on systemic toxicity.

5.2.1.6 Genetic toxicity

Hydrotropes have been assessed for mutagenic potential in a variety of *in vitro* and *in vivo* assays. Specifically Ames assay, mouse lymphoma, sister chromatid exchange, and chromosome aberration assays with sodium xylene sulfonate and an Ames assay with calcium xylene sulfonate, and mouse micronucleus cytogenetic assays with calcium xylene sulfonate and sodium cumene sulfonate, have been reported. All studies include full reports; reliability ratings are 1.

5.2.1.6.1 *In vitro*

Ames Assays

The mutagenic potential of sodium xylene sulfonate (51), calcium xylene sulfonate (21) and sodium cumene sulfonate (8), at 65%, 31% and 40% active ingredient, respectively, were evaluated in the bacterial reverse mutation (Ames) assay using S*almonella typhimurium* strains TA 98, 100, 1535, 1537 and 1538. There was no evidence of mutagenicity observed for any of the three compounds with and without metabolic activation. The negative results for sodium xylene sulfonate are corroborated by an Albright & Wilson study reported in the IUCLID (3).

Mouse Lymphoma Test

Technical grade (65% a.i.) sodium xylene sulfonate was tested for mutagenicity potential in F344/N rats and B6C3F1 mice using a dermal exposure and L5178Y mouse lymphoma cells (51). There were two independent tests with duplicate cultures per treatment. The exposure period was 4 hours and the expression period was 2 days. There was no mutagenic activity with or without metabolic activation.

Sister Chromatid Exchange Test

Technical grade (65% a.i.) sodium xylene sulfonate was tested at 500 – 5000 µg/mL using Chinese hamster ovary cells (51). There were two independent tests with an exposure period of 25.5 hours. The results indicated clastogenic activity (cell cycle delay) without metabolic activation at 2513 – 5000 µg/mL which was addressed by lengthening incubation time to 32.5 hours to ensure a sufficient number of scorable (second-division metaphase) cells. No clastogenic activity was recorded with metabolic activation.

Chromosome Aberration Test

Technical grade (65% a.i.) sodium xylene sulfonate was tested for mutagenicity potential in F344/N rats and B6C3F1 mice using a dermal exposure and Chinese hamster ovary cells (51). Test concentrations were 2513, 3750 and 5000 µg/mL. Exposure with S9 activation was 2 hours (+ 10 hr incubation) and 18 hours without S9 activation. There was no mutagenic activity with and without metabolic activation.

5.2.1.6.2 *In vivo*

Mouse micronucleus

Three mouse micronucleus cytogenetic assays were reported; one with calcium xylene sulfonate (35) and the other two with sodium cumene sulfonate (9, 12). The first study (35) used a single intra-peritoneal (i.p.) administration at 0, 145, 290 and 580 mg a.i./kg bw given to 6-8 week old mice (5 per sex per dose). The second study (12) used a single oral dose administration at 0 and 4467 mg a.i./kg bw given to 24-30 gram mice (5 per sex per dose). The third study (9) used total oral doses of 0, 400, 2000 and 4000 mg a.i./kg bw delivered gavage in two equal applications 24 hours apart to male and female mice. No mutagenic effects were detected in any treatment group for either compound.

Conclusion

No indication of genotoxicity potential for hydrotropes is evident in any of the studies conducted.

5.2.1.7 Carcinogenicity

Chronic toxicity/carcinogenicity studies are reported for both rats and mice dermally exposed for 2 years to sodium xylene sulfonate. Both studies are supported by full reports; reliability ratings are 1.

Fifty male and 50 female rats (F344/N) and mice (B6C3F1) received dermal application (5 days per week to clipped skin) of technical grade sodium xylene sulfonate (65% a.i.) in 2-year carcinogenicity studies (51). Dosing was done using a 50% ethanol vehicle. Doses in the rat study were 0, 60, 120 and 240 mg a.i./kg bw and 0, 182, 364 and 727 mg a.i./kg bw in the mouse study. Observations were as per OECD 453 Guideline with the exception of clinical signs recorded monthly, and no observations of food consumption (feeding was *ad libitum*), blood parameters, urinalysis and organ weights were undertaken. Stability of the test compound in ethanol was confirmed. Body weight gain was not affected by the exposures in either species. No treatment related effects were observed with the exception of epidermal hyperplasia at the application site which was more prevalent in the mouse. There was no evidence of carcinogenic activity.

Conclusion

Hydrotropes demonstrated no evidence of a carcinogenic response based upon 2-year dermal exposure studies.

5.2.1.8 Reproductive toxicity

No multi-generation reproduction toxicity studies are reported for hydrotropes. The 91-day oral rat feeding study with sodium cumene sulfonate (18), the 90-day feeding study with sodium xylene sulfonate (2) and the dermal studies with sodium xylene sulfonate (51) included examination of sex organs. No treatment related effects were reported.

5.2.1.9 Developmental toxicity

Developmental toxicity in rats, including fertility, was evaluated for calcium xylene sulfonate (32). Female rats (Crl:CD) were mated with untreated males (1/1) from the same strain. Calcium xylene sulfonate (31% a.i.) was administered via gavage to 30 female rats (~87 days old) per dose at 0, 150, 1500 and 3000 mg/kg bw in water vehicle at a dosing volume of 10 ml/kg during days 6 to 15

of gestation. EPA TSCA Guideline 1985 was followed. Clinical symptoms were noted daily from day 6 to 20. Body weight/food consumption was recorded on day 0, 6, 9, 12, 16 and 20. All females were macroscopically examined on day 20 (or on day of death). The uteri were removed, weighed and examined for number of *corpora lutea*, number of implantation sites and number and location of fetuses and resorptions. Fetuses were inspected on total number, sex, weight and external, visceral (one-half) and skeletal (one-half) defects. Stability of the test compound in water vehicle was confirmed. The reliability rating of this study is 2.

Only one animal died during the study (mid-dose). No treatment related effects were observed. An increase in food intake observed at the highest dose was considered to be within ranges of biological variation for this species. The NOAEL for maternal toxicity and for reproductive toxicity is the highest dose, 3000 mg/kg bw; corresponds to 936 mg a.i./kg bw.

Conclusion

Hydrotropes were not observed to be developmental toxicants. The NOAEL for maternal toxicity and for developmental toxicity is the highest dose, 3000 mg/kg bw; corresponds to 936 mg a.i./kg bw. There were no indications of fertility effects in the numerous 90-day studies.

5.2.2 Identification of critical endpoints

5.2.2.1 Overview on hazard identification

Where comparative data are available (i.e., acute oral, dermal and inhalation, eye and skin irritation, repeated dose and genotoxicity) toxicological studies across the range of hydrotropes including the toluene, xylene and cumene sulfonates and their various salts demonstrate consistent results and a relatively low hazard potential for these compounds.

Acute oral LD_{50} values for rats range from 3346 – 16,200 mg test material/kg bw. Acute dermal LD_{50} values were >2000 mg/kg bw and the LC_{50} following inhalation exposure was >557 mg/L.

In a series of studies in rabbits, skin irritation was negligible to slight at test concentrations of 31% to 60%, and eye irritation was slight to moderate at test concentrations of 20% to 96%. Rinsing reduced the degree of eye irritation.

Hydrotropes do not appear to be contact sensitizers based on a human repeat insult patch test of 0.5% aqueous sodium cumene sulfonate. A guideline study with guinea pigs reports no evidence of skin sensitization following dermal, semiocclusive exposure to a 42.8% solution (deionized water) of sodium toluene sulfonate.

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In repeated dose exposure to hydrotropes via oral and dermal routes, no significant toxicity was observed in 9 of 11 studies. The NOAELs in the 9 studies ranged from 159 - 2467 mg a.i./kg bw. One dermal study (mouse) reported a LOAEL of 1300 mg a.i./kg bw and a NOAEL of 440 mg a.i./kg bw for local effects. Effects observed were epidermal hyperplasia at the site of application. The only systemic effect observed was a body weight gain in males, but this change was not considered to be biologically significant. One oral study reported a LOAEL of 4092 mg a.i./kg bw and a NOAEL of 763 mg a.i./kg bw. Effects observed were a decrease in spleen weight in females. No adverse effects were reported for males. The most appropriate NOAEL for systemic toxicity from mammalian toxicity studies was therefore determined to be 763 mg a.i./kg bw/day based on a reduction in spleen weight in female rats. The most appropriate NOAEL for local effects was determined to be 440 mg a.i./kg/bw based on epidermal hyperplasia at the site of application

(dermal exposure) in male mice. The results of a 2-year dermal study conducted by the same investigators showed no evidence that these lesions progressed to skin neoplasms.

No evidence was found of either genotoxicity in *in vivo* and *in vitro* assays or of carcinogenicity in 2-year dermal exposures of rats and mice.

No developmental effects or maternal toxicity was observed in a developmental toxicity study where female rats were gavaged with up to 936 mg a.i./kg bw of calcium xylene sulfonate. No multiple generation reproduction studies were reported. There were no indications of fertility effects in the numerous 90-day studies.

The results are consistent across the toluene, xylene and cumene sulfonates and their various salts where comparative data are available (i.e., acute oral and dermal, eye and skin irritation, and repeated dose and genotoxicity tests).

5.2.2.2 Adverse effects related to accidental exposure

The oral toxicity is greater than 3000 mg/kg bw and the dermal toxicity is greater than 2000 mg/kg bw for hydrotropes at the concentration of about 50%. Hydrotropes are present in detergent formulations at 11.9% as a maximum.

Skin irritation of hydrotropes is negligible to slight at test concentrations of 40% to 60%, and eye irritation was slight to moderate at test concentrations of 20% to 96%. Rinsing reduced the degree of eye irritation.

5.2.3 Determination of NOAEL or quantitative evaluation of data

Repeated dose toxicity
The repeated dose toxicity of hydrotropes has been assessed in numerous oral and dermal studies in both rats and mice. Test durations ranged from 17 days up to 2 years and exposure doses ranged from 6 up to 4092 mg a.i./kg bw/day.

- The most appropriate overall dermal exposure NOAEL was determined to be 440 mg a.i./kg bw. This value comes from the 90-day study where local epidermal hyperplasia was observed in male mice exposed at 1300 mg a.i./kg bw. Female mice in the same study responded comparably. No adverse systemic effects were reported for either male or female rats and mice exposed for 2 years at up to 727 mg a.i./kg bw.
- The most appropriate overall oral exposure NOAEL was determined to be 763 mg a.i./kg bw. This value comes from the 90-day study where a relative spleen weight loss was observed in female rats exposed to 4092 mg a.i./kg bw. Males were not affected at the highest dose (3534). The results of this study is generally consistent with that of the other three 90-day oral studies.

These two NOAELs, 440 mg a.i./kg bw for local effects following dermal exposure, and 763 mg a.i./kg bw for systemic effects following oral exposure, are of approximately the same magnitude.

Carcinogenicity
The dermal long-term studies performed did not indicate any potential for carcinogenicity of hydrotropes and showed no treatment related effects at doses up to 240 mg a.i. /kg bw for the rats and 727 mg a.i./kg bw for the mouse with the exception of epidermal hyperplasia at the application site which was more prevalent in the mouse.

Reproductive toxicity
No multi-generation reproduction toxicity studies are reported for hydrotropes. The 91-day oral rat feeding study with sodium cumene sulfonate (18), the 90-day feeding study with sodium xylene sulfonate (2) and the dermal studies with sodium xylene sulfonate (51) included examination of sex organs. No treatment related effects were reported.

Developmental toxicity and teratogenicity
Developmental toxicity in rats, including fertility, was evaluated and there was no maternal toxicity or evidence of developmental toxicity/teratogenicity at the highest dose. The NOAEL is therefore >3000 mg/kg bw which corresponds to 936 mg a.i./kg bw.

5.3 Risk assessment

5.3.1 Margin of exposure calculations

The Margin of Exposure (MOE) is the ratio of the No Observed Adverse Effect Level (NOAEL) or an appropriate substitute to the estimated or actual level of human exposure to a substance. The NOAEL for local effects is 440 mg a.i./kg bw following dermal exposure and for systemic effects is 763 mg a.i./kg bw following oral exposure as described in Section 5.2.3. The MOEs for each of the individual exposure scenarios and for the aggregate exposure scenario are calculated below.

The consumer exposure estimates derived in Section 5.1.3 were all based on conservative assumptions to obtain an internal dose. The direct and indirect skin contact exposure scenarios assumed 1% percutaneous absorption. Because local epidermal hyperplasia was observed at the site of application following dermal exposure to hydrotropes and because such exposure would have been to 100% of the amount applied to the skin (that is, the external dose), the exposure levels used in the following MOE calculations are adjusted up by a factor of 100 (i.e., replacing the 1% percutaneous absorption assumption with a 100% external dose) for direct and indirect skin contact,

5.3.1.1 Exposure scenario: direct skin contact

A. Hand-wash laundry. The local effects NOEL of 440 mg/kg bw/day was divided by the estimated external exposure dose of 1.4 µg/kg bw/day which was estimated for the dermal exposure to hydrotropes from hand-washed laundry. **Note that for all exposure scenarios the NOEL is in mg/kg and the dose is in µg/kg, meaning there is a 1000X conversion factor implicit in each of the calculations**

$$MOE_{direct\ skin\ \ hand\text{-}washed\ laundry} = 440/1.4\ [\mu g/kg\ bw/day] = 314{,}290$$

B. Laundry Pre-treatment. The MOE was calculated by dividing the local effects NOEL of 440 mg/kg bw/day by the estimated external exposure from pre-treatment of clothes of 10 µg/kg bw/day.

$$MOE_{direct\ skin\ pre\text{-}treatement} = 440/10\ [\mu g/kg\ bw/day] = 44{,}000$$

C. Hand dishwashing. The MOE was calculated by dividing the local effects NOEL of 440 mg/kg bw/day by the estimated external exposure from hand dishwashing of 0.9 µg/kg bw/day

$$MOE_{direct\ skin\ hand\ dishwashing} = 440/0.9\ [\mu g/kg\ bw/day] = 488{,}890$$

D. Hard surface cleaning. The MOE was calculated by dividing the local effects NOEL of 440 mg/kg bw/day by the estimated external exposure from hard surface cleaning of 1.7 µg/kg bw/day

$$MOE_{direct\ skin\ hard\ surface\ cleaning} = 440/1.7\ [\mu g/kg\ bw/day] = 258{,}820$$

5.3.1.2. Exposure scenario: Indirect skin exposure

Wearing clothes. The MOE was calculatd by dividing the local effects NOEL of 44 mg/kg bw/day by the estimated external exposure from hydrotropes residues on washed fabric of 73 µg/kg bw/day.

$$MOE_{indirect\ skin\ wearing\ clothes} = 440/73\ [\mu g/kg\ bw/day] = 6{,}030$$

5.3.1.3. Exposure scenario: inhalation

A. Aerosols. For calculation of the MOE, the systemic effects NOEL of 763 mg/kg bw/day was divided by the daily systemic dose of 0.012 µg/kg, estimated for the inhalation of hydrotrope-containing aerosols in spray cleaning applications.

$$MOE_{aerosol\ inhalation} = 763/0.012\ [\mu g/kg\ bw/day] = 63{,}583{,}333$$

B. Detergent Dust. For calculation of the MOE, the systemic effects NOEL of 763 mg/kg bw/day was divided by the daily systemic dose of 0.0001 µg/kg, estimated for the inhalation of hydrotrope-containing laundry powder detergent dust.

$$\mathbf{MOE}_{\text{dust inhalation}} = 763/0.0001\ [\mu g/kg\ bw/day] = 7{,}630{,}000{,}000$$

5.3.1.4. Exposure scenario: oral route

A. Indirect exposure via the environment. For calculation of the MOE, the systemic effects NOEL of 763 mg/kg bw/day was divided by the daily systemic dose of 0.2 µg/kg estimated for the uptake of hydrotropes from drinking water and food.

$$\mathbf{MOE}_{\text{oral route food and water}} = 763/\ 0.2\ [\mu g/kg\ bw/day] = 3{,}815{,}000$$

B. Indirect exposure via dinnerware cleaned via automatic dishwasher. The MOE was calculated by dividing the systemic effects NOEL of 763 mg/kg bw/day by the estimated oral exposure from hydrotrope residues left on eating utensils and dinnerware of 0.19 µg/kg bw/day.

$$\mathbf{MOE}_{\text{oral route dinnerware from dishwasher}} = 763/0.19\ [\mu g/kg\ bw/day] = 4{,}015{,}789$$

C. Indirect exposure via dinnerware cleaned via hand dishwashing. The MOE was calculated by dividing the systemic effects NOEL of 763 mg/kg bw/day by the estimated oral exposure from hydrotrope residues left on eating utensils and dinnerware of 0.15 µg/kg bw/day.

$$\mathbf{MOE}_{\text{oral route dinnerware from hand washing}} = 763/0.15\ [\mu g/kg\ bw/day] = 5,\ 086{,}666$$

5.3.1.5 Aggregate exposure

The consumer exposure calculated by summation of the all routes of exposure, including direct and indirect skin contact of neat or diluted hydrotrope-containing products, inhalation of hydrotrope-containing aerosols from spray cleaner applications and from the oral route via the environment (in food and drinking water) and residues on eating utensils and crockery, results in an estimated total systemic hydrotrope exposure of 1.42 µg/kg bw/day. As discussed previously (see 5.1.3.5), the calculated aggregate exposure is based on a combination of scenarios, and is considered to be highly unrealistic and an extreme worst case for the total consumer exposure.

In addition, an aggregate exposure can be calculated for the external dose on the skin by summation of the direct and indirect skin contact routes of exposure. This extreme worst case estimate is 87 µg/kg bw/day.

Separate aggregate exposure MOEs can be calculated for each scenario. The MOE for systemic effects is calculated by dividing the systemic effects NOEL of 763 mg/kg bw/day by the total internal exposure: The MOE for local effects is calculated by dividing the local effects NOEL of 440 mg/kg bw/day by the total external exposure. As before, because the NOELs are expressed in mg/kg

bw/day and the exposures are expressed in µg/kg bw/day there is a 1000X conversion factor implicit in each of the calculations.

MOE $_{\text{aggregate for total internal exposure}}$ = 763 mg/kg.bw/day /1.42 [µg/kg bw/day] = 537,324

MOE $_{\text{aggregate for total external exposure}}$ = 440 mg/kg.bw/day /87 [µg/kg bw/day] = 5,057

5.3.1.6. Accidental and intentional overexposure

Accidental ingestion of a few milligrams of hydrotropes as a consequence of accidental ingestion of laundry and cleaning products is not expected to result in any significant adverse health effects given the low acute toxicity profile of laundry and cleaning products in general, and hydrotropes in particular. This view is supported not only by available toxicological information from animal studies, but also by the fact that national poison control centers, such as for example those in Germany and UK, have not reported any case of lethal poisoning with detergents containing hydrotropes.

Accidental eye contact and accidental or intentional skin contact with undiluted laundry or cleaning products containing hydrotropes at a concentration up to 11.9 % might potentially cause irritation. However if the material is rinsed off immediately after skin or eye contact, the effects are reversible shortly after the accidental exposure. Nevertheless, in case of accidental eye contact, immediate rinsing with plenty of water is recommended. In animal experiments such immediate action has been shown to minimize irritation effects.

Skin or eye contact with hydrotrope-containing solutions under typical usage conditions (e.g., in hand-washed laundry or hand dishwashing) is not expected to cause significant irritation.

5.3.2 Risk characterization

5.3.2.1 Systemic toxicity

Scenarios relevant to the consumer exposure to hydrotropes have been identified and assessed using the margin of exposure or equivalent assessments. The Margin of Exposure for the combined estimated systemic dose is >500,000.

This is a 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 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 NOAEL (which is a systemic NOAEL given the absence of oral toxicokinetic data). The critical adverse effect identified associated to the NOAEL was a decrease in relative spleen weight. Other than that, the toxicological data show that hydrotropes are not genotoxic in vitro or in vivo, did not induce tumors in rodents after two years daily dosing, and failed to induce developmental, teratogenic or fertility effects (based on sex organ effects) at the highest doses tested. Based on the above, the presence of hydrotropes in consumer products does not raise any safety concerns associated to systemic toxicity.

5.3.2.2 Local effects

Scenarios relevant to the consumer exposure to hydrotropes have been identified and assessed using the margin of exposure or equivalent assessments. The Margin of Exposure for the combined estimated external dose is >5,000. This is a large Margin of Exposure, especially considering the adverse effect was epidermal hyperplasia at the site of application following repeated exposure.

Hydrotropes can be classified as a negligible-to-slight irritant to skin and a slight-to-moderate irritant to eyes. The irritation potential of aqueous solutions of hydrotropes depends on concentration, and the irritation is lessened with rinsing. hydrotropes are not considered to be skin sensitizers.

Contact of hand wash solutions containing hydrotropes with the skin is not a cause of concern given that hydrotropes are not a contact sensitizer and that the concentrations of hydrotropes in such solutions are 1% (10 mg/mL per section 5.1.3.1) . As reported in section 5.2.1.3 of this assessment, aqueous solutions of hydrotropes at concentrations up to 40% failed to show more than a slight irritation on rabbit skin after 24 hours of occlusive application.

Accidental contact of hand wash solutions containing hydrotropes (at 1% concentration) 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. Eye irritation was reduced upon rinsing with water.

In the course of laundry pre-treatment, skin contact with concentrated powder paste or neat liquid detergent (in the worst case containing up to 2% hydrotropes) 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 at most) and the initial high hydrotropes concentration is usually diluted out rapidly in the course of the pre-treatment task. Failing to rinse hands in water after contact with the laundry pre-treatment paste or liquid may result in transient skin irritation in 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 lack of adverse effects in the acute inhalation studies at quite high levels, and because there is not expected to be much exposure to hydrotropes from spray or granular products (see Sections 5.1.3.3 A and B). Granular products (e.g., powdered laundry detergents) are deliberately formulated for low dust.

Hydrotropes are present in household liquid detergent and cleaning products at concentrations that range from 0.66% to 11.9%. Accidental spillage of neat product into the eye is to be avoided as can be expected to result in likely irritation. Immediate rinsing of the eyes with water for several minutes should follow accidental spillage of neat product. The experience from many years of marketing of household liquid detergent and cleaning products containing hydrotropes is that accidental eye spillage results at worst in transient irritation, which heals after a few days with no irreversible effects to the eye.

5.3.2.3 Acute effects

Occasional ingestion of a few milligrams of hydrotropes 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 hydrotropes. This view is reinforced by the fact that poison control centers, such as for example those in Germany and UK, have not reported any case of lethal poisoning with detergents containing hydrotropes**.**

5.3.3 Summary and conclusions

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

The consumer aggregate systemic 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 1.42 µg/kg bw/day. The consumer aggregate external exposure from direct and indirect skin contact is 87 µg/kg bw/day using worst case assumptions.

The toxicological data demonstrate that hydrotropes have a low order of acute toxicity by all relevant routes (LC50s range from 100s to 1000s mg/kg), are not genotoxic *in vitro* or *in vivo*, show no evidence of a carcinogenic response in 2-year dermal exposure studies, and failed to induce developmental, teratogenic or fertility (sex organ) effects. The critical adverse systemic effect identified after repeat long term dosing of hydrotropes to animals is epidermal hyperplasia at the site of application from dermal exposure and a decrease in the relative spleen weight from oral exposure. For risk assessment purposes, a NOAEL of 440 mg a.i./kg bw is determined to be a representative and protective value based on dermal repeated dose studies, and likewise a NOAEL of 763 mg a.i./kg bw for oral repeated dose exposures.

Comparison of the aggregate consumer internal exposure to hydrotropes with the systemic toxicity NOAEL results in an estimated Margin of Exposure (MOE) of >500,000. This is a very large MOE, large enough to account for the inherent uncertainty and variability of the hazard database and inter- and intra-species extrapolations (which are usually conventionally estimated at a factor of 100). Comparision of the aggregate consumer external exposure with the epidermal hyperplasia NOAEL results in an estimated MOE of >5,000. This too is a large Margin of Exposure considering the adverse effect was epidermal hyperplasia at the site of exposure following repeated exposure.

Hydrotrope can be classified as a negligible-to-slight irritant to skin and a slight-to-moderate irritant to eyes. The irritation potential of aqueous solutions of hydrotropes depends on concentration, and the irritation is lessened with rinsing. Hydrotropes are not considered to be skin sensitizers.

In view of the 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 hydrotropes in household laundry and cleaning products raises no safety concerns for the consumers.

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7. Contributors to this report

This Risk Assessment has been developed by experts of Stepan, Huntsman, Sasol and Procter & Gamble in cooperation with Daniel M. Woltering, Virginia, USA.

Additional input was provided by the experts of the HERA Human Health and Environmental Task Force.

HERA for Hydrotropes - Appendix 1

Hydrotropes SCSb2 EUSES 2.02 Output – March 2005

Section/parameter	Value		Unit	Stat
STUDY				
STUDY IDENTIFICATION				
Study name	Hydrotropes			S
Study description	HERA			S
Author	Caritas			S
Institute	AISE			S
Address				D
Zip code				D
City				D
Country				D
Telephone				D
Telefax				D
Email				D
Calculations checksum	358D5E2F			S
DEFAULTS				
DEFAULT IDENTIFICATION				
General name	Standard Euses 2.0			D
Description	According to TGDs			D
CHARACTERISTICS OF COMPARTMENTS				
GENERAL				
Density of solid phase		2.5	[kg.l-1]	D
Density of water phase		1	[kg.l-1]	D
Density of air phase		1.30E-03	[kg.l-1]	D
Environmental temperature		12	[oC]	D
Standard temperature for Vp and Sol		25	[oC]	D

Constant of Junge equation	0.01	[Pa.m]	D
Surface area of aerosol particles	0.01	[m2.m-3]	D
Gas constant (8.314)	8.314	[Pa.m3.mol-1.K-1]	D
SUSPENDED MATTER			
Volume fraction solids in suspended matter	0.1	[m3.m-3]	D
Volume fraction water in suspended matter	0.9	[m3.m-3]	D
Weight fraction of organic carbon in suspended matter	0.1	[kg.kg-1]	D
Bulk density of suspended matter	1.15E+03	[kgwwt.m-3]	O
Conversion factor wet-dry suspened matter	4.6	[kgwwt.kgdwt-1]	O
SEDIMENT			
Volume fraction solids in sediment	0.2	[m3.m-3]	D
Volume fraction water in sediment	0.8	[m3.m-3]	D
Weight fraction of organic carbon in sediment	0.05	[kg.kg-1]	D
SOIL			
Volume fraction solids in soil	0.6	[m3.m-3]	D
Volume fraction water in soil	0.2	[m3.m-3]	D
Volume fraction air in soil	0.2	[m3.m-3]	D
Weight fraction of organic carbon in soil	0.02	[kg.kg-1]	D
Weight fraction of organic matter in soil	0.034	[kg.kg-1]	O
Bulk density of soil	1.70E+03	[kgwwt.m-3]	O
Conversion factor wet-dry soil	1.13	[kgwwt.kgdwt-1]	O
STP SLUDGE			
Fraction of organic carbon in raw sewage sludge	0.3	[kg.kg-1]	D
Fraction of organic carbon in settled sewage sludge	0.3	[kg.kg-1]	D
Fraction of organic carbon in activated sewage sludge	0.37	[kg.kg-1]	D
Fraction of organic carbon in effluent sewage sludge	0.37	[kg.kg-1]	D
DEGRADATION AND TRANSFORMATION RATES			
Rate constant for abiotic degradation in STP	0	[d-1]	D
Rate constant for abiotic degradation in bulk sediment	0	[d-1] (12[oC])	D
Rate constant for anaerobic biodegradation in sediment	0	[d-1] (12[oC])	D
Fraction of sediment compartment that is aerated	0.1	[m3.m-3]	D

Concentration of OH-radicals in atmosphere		5.00E+05	[molec.cm-3]	D
Rate constant for abiotic degradation in bulk soil		0	[d-1] (12[oC])	D
RELEASE ESTIMATION				
Fraction of EU production volume for region		10	[%]	S
Fraction of EU tonnage for region (private use)		10	[%]	D
Fraction connected to sewer systems		80	[%]	D
SEWAGE TREATMENT				
GENERAL				
Number of inhabitants feeding one STP		1.00E+04	[eq]	D
Sewage flow		200	[l.eq-1.d-1]	D
Effluent discharge rate of local STP		2.00E+06	[l.d-1]	O
Temperature dependency correction	No			D
Temperature of air above aeration tank		15	[oC]	D
Temperature of water in aeration tank		15	[oC]	D
Height of air column above STP		10	[m]	D
Number of inhabitants of region		2.00E+07	[eq]	D
Number of inhabitants of continental system		3.50E+08	[eq]	O
Windspeed in the system		3	[m.s-1]	D
RAW SEWAGE				
Mass of O2 binding material per person per day		54	[g.eq-1.d-1]	D
Dry weight solids produced per person per day		0.09	[kg.eq-1.d-1]	D
Density solids in raw sewage		1.5	[kg.l-1]	D
Fraction of organic carbon in raw sewage sludge		0.3	[kg.kg-1]	D
PRIMARY SETTLER				
Depth of primary settler		4	[m]	D
Hydraulic retention time of primary settler		2	[hr]	D
Density suspended and settled solids in primary settler		1.5	[kg.l-1]	D
Fraction of organic carbon in settled sewage sludge		0.3	[kg.kg-1]	D
ACTIVATED SLUDGE TANK				
Depth of aeration tank		3	[m]	D
Density solids of activated sludge		1.3	[kg.l-1]	D
Concentration solids of activated sludge		4	[kg.m-3]	D

Steady state O2 concentration in activated sludge		2.00E-03	[kg.m-3]	D
Mode of aeration	Surface			D
Aeration rate of bubble aeration		1.31E-05	[m3.s-1.eq-1]	D
Fraction of organic carbon in activated sewage sludge		0.37	[kg.kg-1]	D
Sludge loading rate		0.15	[kg.kg-1.d-1]	D
Hydraulic retention time in aerator (9-box STP)		6.9	[hr]	O
Hydraulic retention time in aerator (6-box STP)		10.8	[hr]	O
Sludge retention time of aeration tank		9.2	[d]	O
SOLIDS-LIQUIDS SEPARATOR				
Depth of solids-liquid separator		3	[m]	D
Density suspended and settled solids in solids-liquid separator		1.3	[kg.l-1]	D
Concentration solids in effluent		30	[mg.l-1]	D
Hydraulic retention time of solids-liquid separator		6	[hr]	D
Fraction of organic carbon in effluent sewage sludge		0.37	[kg.kg-1]	D
LOCAL DISTRIBUTION				
AIR AND SURFACE WATER				
Concentration in air at source strength 1 [kg.d-1]		2.78E-04	[mg.m-3]	D
Standard deposition flux of aerosol-bound compounds		0.01	[mg.m-2.d-1]	D
Standard deposition flux of gaseous compounds		5.00E-04	[mg.m-2.d-1]	O
Suspended solids concentration in STP effluent water		15	[mg.l-1]	D
Dilution factor (rivers)		10	[-]	D
Flow rate of the river		1.80E+04	[m3.d-1]	D
Calculate dilution from river flow rate	No			D
Dilution factor (coastal areas)		100	[-]	D
SOIL				
Mixing depth of grassland soil		0.1	[m]	D
Dry sludge application rate on agricultural soil		5.00E+03	[kg.ha-1.yr-1]	D
Dry sludge application rate on grassland		1000	[kg.ha-1.yr-1]	D
Averaging time soil (for terrestrial ecosystem)		30	[d]	D
Averaging time agricultural soil		180	[d]	D
Averaging time grassland		180	[d]	D
PMTC, air side of air-soil interface		1.05E-03	[m.s-1]	O
Soil-air PMTC (air-soil interface)		5.56E-06	[m.s-1]	D
Soil-water film PMTC (air-soil interface)		5.56E-10	[m.s-1]	D

Mixing depth agricultural soil	0.2	[m]	D
Fraction of rain water infiltrating soil	0.25	[-]	D
Average annual precipitation	700	[mm.yr-1]	D
REGIONAL AND CONTINENTAL DISTRIBUTION CONFIGURATION			
Fraction of direct regional emissions to sea water	1	[%]	D
Fraction of direct continental emissions to sea water	0	[%]	D
Fraction of regional STP effluent to sea water	0	[%]	D
Fraction of continental STP effluent to sea water	0	[%]	D
Fraction of flow from continental rivers to regional rivers	0.034	[-]	D
Fraction of flow from continental rivers to regional sea	0	[-]	D
Fraction of flow from continental rivers to continental sea	0.966	[-]	O
Number of inhabitants of region	2.00E+07	[eq]	D
Number of inhabitants in the EU	3.70E+08	[eq]	D
Number of inhabitants of continental system	3.50E+08	[eq]	O
AREAS			
REGIONAL			
Area (land+rivers) of regional system	4.00E+04	[km2]	D
Area fraction of fresh water, region (excl. sea)	0.03	[-]	D
Area fraction of natural soil, region (excl. sea)	0.27	[-]	D
Area fraction of agricultural soil, region (excl. sea)	0.6	[-]	D
Area fraction of industrial/urban soil, region (excl. sea)	0.1	[-]	D
Length of regional sea water	40	[km]	D
Width of regional sea water	10	[km]	D
Area of regional sea water	400	[km2]	O
Area (land+rivers+sea) of regional system	4.04E+04	[km2]	O
Area fraction of fresh water, region (total)	0.0297	[-]	O
Area fraction of sea water, region (total)	9.90E-03	[-]	O
Area fraction of natural soil, region (total)	0.267	[-]	O
Area fraction of agricultural soil, region (total)	0.594	[-]	O
Area fraction of industrial/urban soil, region (total)	0.099	[-]	O
CONTINENTAL			
Total area of EU (continent+region, incl. sea)	7.04E+06	[km2]	D
Area (land+rivers+sea) of continental system	7.00E+06	[km2]	O

Area (land+rivers) of continental system	3.50E+06	[km2]	O
Area fraction of fresh water, continent (excl. sea)	0.03	[-]	D
Area fraction of natural soil, continent (excl. sea)	0.27	[-]	D
Area fraction of agricultural soil, continent (excl. sea)	0.6	[-]	D
Area fraction of industrial/urban soil, continent (excl. sea)	0.1	[-]	D
Area fraction of fresh water, continent (total)	0.015	[-]	O
Area fraction of sea water, continent (total)	0.5	[-]	D
Area fraction of natural soil, continent (total)	0.135	[-]	O
Area fraction of agricultural soil, continent (total)	0.3	[-]	O
Area fraction of industrial/urban soil, continent (total)	0.05	[-]	O
MODERATE			
Area of moderate system (incl.continent,region)	8.50E+07	[km2]	D
Area of moderate system (excl.continent, region)	7.80E+07	[km2]	O
Area fraction of water, moderate system	0.5	[-]	D
ARCTIC			
Area of arctic system	4.25E+07	[km2]	D
Area fraction of water, arctic system	0.6	[-]	D
TROPIC			
Area of tropic system	1.28E+08	[km2]	D
Area fraction of water, tropic system	0.7	[-]	D
TEMPERATURE			
Environmental temperature, regional scale	12	[oC]	D
Environmental temperature, continental scale	12	[oC]	D
Environmental temperature, moderate scale	12	[oC]	D
Environmental temperature, arctic scale	-10	[oC]	D
Environmental temperature, tropic scale	25	[oC]	D
Enthalpy of vaporisation	50	[kJ.mol-1]	D
Enthalpy of solution	10	[kJ.mol-1]	D
MASS TRANSFER			
Air-film PMTC (air-water interface)	3.86E-03	[m.s-1]	O
Water-film PMTC (air-water interface)	4.66E-06	[m.s-1]	O
PMTC, air side of air-soil interface	1.05E-03	[m.s-1]	O

PMTC, soil side of air-soil interface	3.06E-08	[m.s-1]	O
Soil-air PMTC (air-soil interface)	5.56E-06	[m.s-1]	D
Soil-water film PMTC (air-soil interface)	5.56E-10	[m.s-1]	D
Water-film PMTC (sediment-water interface)	2.78E-06	[m.s-1]	D
Pore water PMTC (sediment-water interface)	2.78E-08	[m.s-1]	D
AIR			
GENERAL			
Atmospheric mixing height	1000	[m]	D
Windspeed in the system	3	[m.s-1]	D
Aerosol deposition velocity	1.00E-03	[m.s-1]	D
Aerosol collection efficiency	2.00E+05	[-]	D
RAIN			
Average precipitation, regional system	700	[mm.yr-1]	D
Average precipitation, continental system	700	[mm.yr-1]	D
Average precipitation, moderate system	700	[mm.yr-1]	D
Average precipitation, arctic system	250	[mm.yr-1]	D
Average precipitation, tropic system	1.30E+03	[mm.yr-1]	D
RESIDENCE TIMES			
Residence time of air, regional	0.687	[d]	O
Residence time of air, continental	9.05	[d]	O
Residence time of air, moderate	30.2	[d]	O
Residence time of air, arctic	22.3	[d]	O
Residence time of air, tropic	38.6	[d]	O
WATER			
DEPTH			
Water depth of fresh water, regional system	3	[m]	D
Water depth of sea water, regional system	10	[m]	D
Water depth of fresh water, continental system	3	[m]	D
Water depth of sea water, continental system	200	[m]	D
Water depth, moderate system	1000	[m]	D
Water depth, arctic system	1000	[m]	D
Water depth, tropic system	1000	[m]	D

SUSPENDED SOLIDS			
Suspended solids conc. fresh water, regional	15	[mg.l-1]	D
Suspended solids conc. sea water, regional	5	[mg.l-1]	D
Suspended solids conc. fresh water, continental	15	[mg.l-1]	D
Suspended solids conc. sea water, continental	5	[mg.l-1]	D
Suspended solids conc. sea water, moderate	5	[mg.l-1]	D
Suspended solids conc. sea water, arctic	5	[mg.l-1]	D
Suspended solids conc. sea water, tropic	5	[mg.l-1]	D
Concentration solids in effluent, regional	30	[mg.l-1]	D
Concentration solids in effluent, continental	30	[mg.l-1]	D
Concentration biota	1	[mgwwt.l-1]	D
RESIDENCE TIMES			
Residence time of fresh water, regional	43.3	[d]	O
Residence time of sea water, regional	4.64	[d]	O
Residence time of fresh water, continental	172	[d]	O
Residence time of sea water, continental	2.10E+03	[d]	O
Residence time of water, moderate	3.03E+03	[d]	O
Residence time of water, arctic	5.84E+03	[d]	O
Residence time of water, tropic	1.09E+04	[d]	O
SEDIMENT			
DEPTH			
Sediment mixing depth	0.03	[m]	D
SUSPENDED SOLIDS			
(Biogenic) prod. susp. solids in fresh water, reg	10	[g.m-2.yr-1]	D
(Biogenic) prod. susp. solids in sea water, reg	10	[g.m-2.yr-1]	D
(Biogenic) prod. susp. solids in fresh water, cont	10	[g.m-2.yr-1]	D
(Biogenic) prod. susp. solids in sea water, cont	5	[g.m-2.yr-1]	D
(Biogenic) prod. susp. solids in water, moderate	1	[g.m-2.yr-1]	D
(Biogenic) prod. susp. solids in water, arctic	1	[g.m-2.yr-1]	D
(Biogenic) prod. susp. solids in water, tropic	1	[g.m-2.yr-1]	D
SEDIMENTATION RATES			
Settling velocity of suspended solids	2.5	[m.d-1]	D
Net sedimentation rate, fresh water, regional	2.8	[mm.yr-1]	O

Net sedimentation rate, sea water, regional		1.53	[mm.yr-1]	O
Net sedimentation rate, fresh water, continental		2.75	[mm.yr-1]	O
Net sedimentation rate, sea water, continental		6.69E-03	[mm.yr-1]	O
Net sedimentation rate, moderate		2.80E-03	[mm.yr-1]	O
Net sedimentation rate, arctic		2.00E-03	[mm.yr-1]	O
Net sedimentation rate, tropic		2.00E-03	[mm.yr-1]	O
SOIL				
GENERAL				
Fraction of rain water infiltrating soil		0.25	[-]	D
Fraction of rain water running off soil		0.25	[-]	D
DEPTH				
Chemical-dependent soil depth	No			D
Mixing depth natural soil		0.05	[m]	D
Mixing depth agricultural soil		0.2	[m]	D
Mixing depth industrial/urban soil		0.05	[m]	D
Mixing depth of soil, moderate system		0.05	[m]	D
Mixing depth of soil, arctic system		0.05	[m]	D
Mixing depth of soil, tropic system		0.05	[m]	D
EROSION				
Soil erosion rate, regional system		0.03	[mm.yr-1]	D
Soil erosion rate, continental system		0.03	[mm.yr-1]	D
Soil erosion rate, moderate system		0.03	[mm.yr-1]	D
Soil erosion rate, arctic system		0.03	[mm.yr-1]	D
Soil erosion rate, tropic system		0.03	[mm.yr-1]	D
CHARACTERISTICS OF PLANTS, WORMS AND CATTLE				
PLANTS				
Volume fraction of water in plant tissue		0.65	[m3.m-3]	D
Volume fraction of lipids in plant tissue		0.01	[m3.m-3]	D
Volume fraction of air in plant tissue		0.3	[m3.m-3]	D
Correction for differences between plant lipids and octanol		0.95	[-]	D
Bulk density of plant tissue (wet weight)		0.7	[kg.l-1]	D
Rate constant for metabolism in plants		0	[d-1]	D
Rate constant for photolysis in plants		0	[d-1]	D

Leaf surface area	5	[m2]	D
Conductance	1.00E-03	[m.s-1]	D
Shoot volume	2	[l]	D
Rate constant for dilution by growth	0.035	[d-1]	D
Transpiration stream	1	[l.d-1]	D

WORMS

Volume fraction of water inside a worm	0.84	[m3.m-3]	D
Volume fraction of lipids inside a worm	0.012	[m3.m-3]	D
Density of earthworms	1	[kgwwt.l-1]	D
Fraction of gut loading in worm	0.1	[kg.kg-1]	D

CATTLE

Daily intake for cattle of grass (dryweight)	16.9	[kg.d-1]	D
Conversion factor grass from dryweight to wetweight	4	[kg.kg-1]	D
Daily intake of soil (dryweight)	0.41	[kg.d-1]	D
Daily inhalation rate for cattle	122	[m3.d-1]	D
Daily intake of drinking water for cattle	55	[l.d-1]	D

CHARACTERISTICS OF HUMANS

Daily intake of drinking water	2	[l.d-1]	D
Daily intake of fish	0.115	[kg.d-1]	D
Daily intake of leaf crops (incl. fruit and cereals)	1.2	[kg.d-1]	D
Daily intake of root crops	0.384	[kg.d-1]	D
Daily intake of meat	0.301	[kg.d-1]	D
Daily intake of dairy products	0.561	[kg.d-1]	D
Inhalation rate for humans (consumers, environment)	0.833333	[m3.hr-1]	D
Inhalation rate for humans (worker exposure)	1.5	[m3.hr-1]	D
Bodyweight of the human considered	70	[kg]	D
Correction factor for duration and frequency of exposure	2.8	[-]	D

SUBSTANCE

SUBSTANCE IDENTIFICATION

General name	Hydrotropes			S
Description				D
CAS-No				D
EC-notification no.				D

EINECS no.				D
PHYSICO-CHEMICAL PROPERTIES				
Molecular weight		226	[g.mol-1]	S
Melting point		375	[oC]	S
Boiling point	??		[oC]	D
Vapour pressure at test temperature	??		[Pa]	D
Temperature at which vapour pressure was measured		25	[oC]	D
Vapour pressure at 25 [oC]		1.20E-14	[Pa]	S
Octanol-water partition coefficient		-2.7	[log10]	S
Water solubility at test temperature	??		[mg.l-1]	D
Temperature at which solubility was measured		25	[oC]	D
Water solubility at 25 [oC]		5.53E+05	[mg.l-1]	S
PARTITION COEFFICIENTS AND BIOCONCENTRATION FACTORS				
SOLIDS-WATER				
Chemical class for Koc-QSAR	Predominantly hydrophobics			S
Organic carbon-water partition coefficient		8.19E-03	[l.kg-1]	O
Solids-water partition coefficient in soil		1.64E-04	[l.kg-1]	O
Solids-water partition coefficient in sediment		4.10E-04	[l.kg-1]	O
Solids-water partition coefficient suspended matter		8.19E-04	[l.kg-1]	O
Solids-water partition coefficient in raw sewage sludge		2.46E-03	[l.kg-1]	O
Solids-water partition coefficient in settled sewage sludge		2.46E-03	[l.kg-1]	O
Solids-water partition coefficient in activated sewage sludge		3.03E-03	[l.kg-1]	O
Solids-water partition coefficient in effluent sewage sludge		3.03E-03	[l.kg-1]	O
Soil-water partition coefficient		0.2	[m3.m-3]	O
Suspended matter-water partition coefficient		0.9	[m3.m-3]	O
Sediment-water partition coefficient		0.8	[m3.m-3]	O
AIR-WATER				
Sub-cooled liquid vapour pressure		6.84E-11	[Pa]	O
Fraction of chemical associated with aerosol particles		1	[-]	O
Henry's law constant		4.90E-18	[Pa.m3.mol-1]	O
Air-water partitioning coefficient		2.07E-21	[m3.m-3]	O
BIOCONCENTRATION FACTORS				
PREDATOR EXPOSURE				

Bioconcentration factor for earthworms		0.84	[l.kgwwt-1]	O
HUMAN AND PREDATOR EXPOSURE				
Bioconcentration factor for fish		1.41	[l.kgwwt-1]	O
QSAR valid for calculation of BCF-Fish	Yes			O
Biomagnification factor in fish		1	[-]	O
Biomagnification factor in predator		1	[-]	O
HUMAN EXPOSURE				
Partition coefficient between leaves and air		3.14E+20	[m3.m-3]	O
Partition coefficient between plant tissue and water		0.65	[m3.m-3]	O
Transpiration-stream concentration factor		2.10E-04	[-]	O
Bioaccumulation factor for meat		7.94E-07	[d.kg-1]	O
Bioaccumulation factor for milk		7.94E-06	[d.kg-1]	O
Purification factor for surface water		1	[-]	O
BIOTA-WATER				
FOR REGIONAL/CONTINENTAL DISTRIBUTION				
Bioconcentration factor for aquatic biota		1.41	[l.kgwwt-1]	O
DEGRADATION AND TRANSFORMATION RATES				
CHARACTARIZATION				
Characterization of biodegradability	Readily biodegradable			S
STP				
Degradation calculation method in STP	First order, standard OECD/EU tests			D
Rate constant for biodegradation in STP		24	[d-1]	O
Total rate constant for degradation in STP		24	[d-1]	O
Maximum growth rate of specific microorganisms		2	[d-1]	D
Half saturation concentration		0.5	[g.m-3]	D
WATER/SEDIMENT				
WATER				
Rate constant for hydrolysis in surface water		6.93E-07	[d-1] (12[oC])	O
Rate constant for photolysis in surface water		6.93E-07	[d-1]	O
Rate constant for biodegradation in surface water		0.0462	[d-1] (12[oC])	O
Total rate constant for degradation in bulk surface water		0.0462	[d-1] (12[oC])	O

SEDIMENT				
Rate constant for biodegradation in aerated sediment		0.0231	[d-1] (12[oC])	O
Total rate constant for degradation in bulk sediment		2.31E-03	[d-1] (12[oC])	O
AIR				
Specific degradation rate constant with OH-radicals		0	[cm3.molec-1.s-1]	D
Rate constant for degradation in air		0	[d-1]	O
SOIL				
Rate constant for biodegradation in bulk soil		0.0231	[d-1] (12[oC])	O
Total rate constant for degradation in bulk soil		0.0231	[d-1] (12[oC])	O
REMOVAL RATE CONSTANTS SOIL				
Total rate constant for degradation in bulk soil		0.0231	[d-1] (12[oC])	O
Rate constant for volatilisation from agricultural soil		4.68E-18	[d-1]	O
Rate constant for volatilisation from grassland soil		9.36E-18	[d-1]	O
Rate constant for leaching from agricultural soil		0.012	[d-1]	O
Rate constant for leaching from grassland soil		0.0239	[d-1]	O
Total rate constant for removal from agricultural top soil		0.0351	[d-1]	O
Total rate constant for removal from grassland top soil		0.047	[d-1]	O
RELEASE ESTIMATION				
CHARACTERIZATION AND TONNAGE				
High Production Volume Chemical	Yes			S
Production volume of chemical in EU		1.70E+04	[tonnes.yr-1]	S
Fraction of EU production volume for region		10	[%]	S
Regional production volume of substance		1.70E+03	[tonnes.yr-1]	O
Continental production volume of substance		1.53E+04	[tonnes.yr-1]	O
Volume of chemical imported to EU		0	[tonnes.yr-1]	D
Volume of chemical exported from EU		0	[tonnes.yr-1]	D
Tonnage of substance in Europe		1.70E+04	[tonnes.yr-1]	O
USE PATTERNS				
PRODUCTION STEPS				
OTHER LIFE CYCLE STEPS				

EMISSION INPUT DATA

Usage/production title				D

USE PATTERN

Industry category	5 Personal / domestic use			S
Use category	9 Cleaning/washing agents and additives			S
Extra details on use category	Unknown type			D
Extra details on use category	No extra details necessary			D

PRIVATE USE

Use specific emission scenario	Yes			S
Emission scenario	Emission fractions, fraction-main-source			S

TONNAGE

Fraction of tonnage for application		1	[-]	O
Fraction of chemical in formulation		1	[-]	D
Tonnage of formulated product		1.70E+03	[tonnes.yr-1]	O
Relevant tonnage for application		1.70E+04	[tonnes.yr-1]	O
Regional tonnage of substance		1.70E+03	[tonnes.yr-1]	O
Tonnage of formulated product		1.70E+03	[tonnes.yr-1]	O
Regional tonnage of substance (private use step)		1.70E+03	[tonnes.yr-1]	O
Continental tonnage of substance (private use step)		1.53E+04	[tonnes.yr-1]	O
Total of fractions for all applications		1	[-]	O

INTERMEDIATE RESULTS

USE PATTERN 1

RELEASE FRACTIONS AND EMISSION DAYS

PRIVATE USE

Emission scenario	Emission fractions, fraction-main-source			S
Emission tables	A4.1 (specific uses), B4.# (specific uses)			S
Number of inhabitants feeding one STP		1.00E+04	[eq]	D
Number of inhabitants of region		2.00E+07	[eq]	D

RELEASE FRACTIONS

Fraction of tonnage released to air		0	[-]	O
Fraction of tonnage released to waste water		1	[-]	O
Fraction of tonnage released to surfacewater		0	[-]	O

Fraction of tonnage released to industrial soil		0	[-]	O
Fraction of tonnage released to agricultural soil		0	[-]	O
Emission fractions determined by special scenario	Yes			O
EMISSION DAYS				
Fraction of the main local source		5.00E-04	[-]	O
Number of emission days per year		365	[-]	O
Emission day determined by special scenario	No			O
REGIONAL AND CONTINENTAL RELEASES				
PRIVATE USE				
REGIONAL				
Regional release to air		0	[kg.d-1]	O
Regional release to waste water		4.66E+03	[kg.d-1]	O
Regional release to surface water		0	[kg.d-1]	O
Regional release to industrial soil		0	[kg.d-1]	O
Regional release to agricultural soil		0	[kg.d-1]	O
CONTINENTAL				
Continental release to air		0	[kg.d-1]	O
Continental release to waste water		4.19E+04	[kg.d-1]	O
Continental release to surface water		0	[kg.d-1]	O
Continental release to industrial soil		0	[kg.d-1]	O
Continental release to agricultural soil		0	[kg.d-1]	O
REGIONAL AND CONTINENTAL TOTAL EMISSIONS				
Total regional emission to air		0	[kg.d-1]	O
Total regional emission to wastewater		3.73E+03	[kg.d-1]	O
Total regional emission to surface water		932	[kg.d-1]	O
Total regional emission to industrial soil		0	[kg.d-1]	O
Total regional emission to agricultural soil		0	[kg.d-1]	O
Total continental emission to air		0	[kg.d-1]	O
Total continental emission to wastewater		3.35E+04	[kg.d-1]	O
Total continental emission to surface water		8.38E+03	[kg.d-1]	O
Total continental emission to industrial soil		0	[kg.d-1]	O
Total continental emission to agricultural soil		0	[kg.d-1]	O

LOCAL				
[PRIVATE USE]				
Local emission to air during episode		0	[kg.d-1]	O
Emission to air calculated by special scenario	No			O
Local emission to wastewater during episode		2.33	[kg.d-1]	O
Emission to water calculated by special scenario	No			O
Show this step in further calculations	Yes			O
Intermittent release	No			D
DISTRIBUTION				
SEWAGE TREATMENT				
CONTINENTAL				
Fraction of emission directed to air		-2.11E-14	[%]	O
Fraction of emission directed to water		12.7	[%]	O
Fraction of emission directed to sludge		7.74E-05	[%]	O
Fraction of the emission degraded		87.3	[%]	O
Total of fractions		100	[%]	O
Indirect emission to air		-7.07E-12	[kg.d-1]	O
Indirect emission to surface water		4.24E+03	[kg.d-1]	O
Indirect emission to agricultural soil		0.026	[kg.d-1]	O
REGIONAL				
Fraction of emission directed to air		-3.45E-13	[%]	O
Fraction of emission directed to water		12.7	[%]	O
Fraction of emission directed to sludge		7.74E-05	[%]	O
Fraction of the emission degraded		87.3	[%]	O
Total of fractions		100	[%]	O
Indirect emission to air		-1.29E-11	[kg.d-1]	O
Indirect emission to surface water		472	[kg.d-1]	O
Indirect emission to agricultural soil		2.88E-03	[kg.d-1]	O
LOCAL				
[PRIVATE USE]				
INPUT AND CONFIGURATION [PRIVATE USE]				
INPUT				
Use or bypass STP (local fresh water assessment)	Use STP			D
Use or bypass STP (local marine assessment)	Bypass STP			D

Local emission to wastewater during episode		2.33	[kg.d-1]	O
Concentration in untreated wastewater		1.16	[mg.l-1]	O
Local emission entering the STP		2.33	[kg.d-1]	O
CONFIGURATION				
Type of local STP	With primary settler (9-box)			D
Number of inhabitants feeding this STP		1.00E+04	[eq]	O
Effluent discharge rate of this STP		2.00E+06	[l.d-1]	O
Calculate dilution from river flow rate	No			O
Flow rate of the river		1.80E+04	[m3.d-1]	O
Dilution factor (rivers)		10	[-]	O
Dilution factor (coastal areas)		100	[-]	O
OUTPUT [PRIVATE USE]				
Fraction of emission directed to air by STP		2.14E-18	[%]	O
Fraction of emission directed to water by STP		12.7	[%]	O
Fraction of emission directed to sludge by STP		7.74E-05	[%]	O
Fraction of the emission degraded in STP		87.3	[%]	O
Total of fractions		100	[%]	O
Local indirect emission to air from STP during episode		4.98E-20	[kg.d-1]	O
Concentration in untreated wastewater		1.16	[mg.l-1]	O
Concentration of chemical (total) in the STP-effluent		0.147	[mg.l-1]	O
Concentration in effluent exceeds solubility	No			O
Concentration in dry sewage sludge		2.28E-03	[mg.kg-1]	O
PEC for micro-organisms in the STP		0.147	[mg.l-1]	O
REGIONAL, CONTINENTAL AND GLOBAL DISTRIBUTION				
PECS				
REGIONAL				
Regional PEC in surface water (total)		5.78E-03	[mg.l-1]	O
Regional PEC in sea water (total)		4.68E-04	[mg.l-1]	O
Regional PEC in surface water (dissolved)		5.78E-03	[mg.l-1]	O
Qualitative assessment might be needed (TGD Part II, 5.6)	No			O
Regional PEC in sea water (dissolved)		4.68E-04	[mg.l-1]	O
Qualitative assessment might be needed (TGD Part II, 5.6)	No			O
Regional PEC in air (total)		-6.04E-28	[mg.m-3]	O
Regional PEC in agricultural soil (total)		7.51E-09	[mg.kgwwt-1]	O

Regional PEC in pore water of agricultural soils	6.38E-08	[mg.l-1]	O
Regional PEC in natural soil (total)	-3.15E-17	[mg.kgwwt-1]	O
Regional PEC in industrial soil (total)	-3.15E-17	[mg.kgwwt-1]	O
Regional PEC in sediment (total)	3.83E-03	[mg.kgwwt-1]	O
Regional PEC in sea water sediment (total)	3.15E-04	[mg.kgwwt-1]	O
CONTINENTAL			
Continental PEC in surface water (total)	7.70E-04	[mg.l-1]	O
Continental PEC in sea water (total)	5.40E-08	[mg.l-1]	O
Continental PEC in surface water (dissolved)	7.70E-04	[mg.l-1]	O
Continental PEC in sea water (dissolved)	5.40E-08	[mg.l-1]	O
Continental PEC in air (total)	-1.71E-30	[mg.m-3]	O
Continental PEC in agricultural soil (total)	7.72E-10	[mg.kgwwt-1]	O
Continental PEC in pore water of agricultural soils	6.56E-09	[mg.l-1]	O
Continental PEC in natural soil (total)	-9.26E-20	[mg.kgwwt-1]	O
Continental PEC in industrial soil (total)	-1.05E-19	[mg.kgwwt-1]	O
Continental PEC in sediment (total)	5.11E-04	[mg.kgwwt-1]	O
Continental PEC in sea water sediment (total)	3.64E-08	[mg.kgwwt-1]	O
GLOBAL: MODERATE			
Moderate PEC in water (total)	9.88E-12	[mg.l-1]	O
Moderate PEC in water (dissolved)	9.88E-12	[mg.l-1]	O
Moderate PEC in air (total)	-2.24E-34	[mg.m-3]	O
Moderate PEC in soil (total)	-5.16E-24	[mg.kgwwt-1]	O
Moderate PEC in sediment (total)	6.66E-12	[mg.kgwwt-1]	O
GLOBAL: ARCTIC			
Arctic PEC in water (total)	1.66E-13	[mg.l-1]	O
Arctic PEC in water (dissolved)	1.66E-13	[mg.l-1]	O
Arctic PEC in air (total)	6.85E-38	[mg.m-3]	O
Arctic PEC in soil (total)	-3.21E-26	[mg.kgwwt-1]	O
Arctic PEC in sediment (total)	1.14E-13	[mg.kgwwt-1]	O
GLOBAL: TROPIC			
Tropic PEC in water (total)	7.91E-15	[mg.l-1]	O
Tropic PEC in water (dissolved)	7.91E-15	[mg.l-1]	O
Tropic PEC in air (total)	2.76E-37	[mg.m-3]	O

Tropic PEC in soil (total)	-3.95E-27	[mg.kgwwt-1]	O
Tropic PEC in sediment (total)	5.16E-15	[mg.kgwwt-1]	O
STEADY-STATE FRACTIONS			
REGIONAL			
Steady-state mass fraction in regional fresh water	6.81	[%]	O
Steady-state mass fraction in regional sea water	0.612	[%]	O
Steady-state mass fraction in regional air	-7.99E-24	[%]	O
Steady-state mass fraction in regional agricultural soil	2.01E-05	[%]	O
Steady-state mass fraction in regional natural soil	-9.47E-15	[%]	O
Steady-state mass fraction in regional industrial soil	-3.51E-15	[%]	O
Steady-state mass fraction in regional fresh water sediment	0.052	[%]	O
Steady-state mass fraction in regional sea water sediment	1.42E-03	[%]	O
CONTINENTAL			
Steady-state mass fraction in continental fresh water	79.4	[%]	O
Steady-state mass fraction in continental sea water	12.4	[%]	O
Steady-state mass fraction in continental air	-3.91E-24	[%]	O
Steady-state mass fraction in continental agricultural soil	1.81E-04	[%]	O
Steady-state mass fraction in continental natural soil	-2.44E-15	[%]	O
Steady-state mass fraction in continental industrial soil	-1.02E-15	[%]	O
Steady-state mass fraction in continental fresh water sediment	0.606	[%]	O
Steady-state mass fraction in continental sea water sediment	1.44E-03	[%]	O
	99.8830611		
GLOBAL: MODERATE			
Steady-state mass fraction in moderate water	0.126	[%]	O
Steady-state mass fraction in moderate air	-5.71E-27	[%]	O
Steady-state mass fraction in moderate soil	-5.60E-18	[%]	O
Steady-state mass fraction in moderate sediment	2.93E-06	[%]	O
GLOBAL: ARCTIC			
Steady-state mass fraction in arctic water	1.38E-03	[%]	O
Steady-state mass fraction in arctic air	9.53E-31	[%]	O
Steady-state mass fraction in arctic soil	-1.52E-20	[%]	O
Steady-state mass fraction in arctic sediment	3.28E-08	[%]	O
GLOBAL: TROPIC			

Steady-state mass fraction in tropic water	2.31E-04	[%]	O
Steady-state mass fraction in tropic air	1.15E-29	[%]	O
Steady-state mass fraction in tropic soil	-4.20E-21	[%]	O
Steady-state mass fraction in tropic sediment	5.20E-09	[%]	O

STEADY-STATE MASSES

REGIONAL

Steady-state mass in regional fresh water	2.08E+04	[kg]	O
Steady-state mass in regional sea water	1.87E+03	[kg]	O
Steady-state mass in regional air	-2.44E-20	[kg]	O
Steady-state mass in regional agricultural soil	0.0613	[kg]	O
Steady-state mass in regional natural soil	-2.89E-11	[kg]	O
Steady-state mass in regional industrial soil	-1.07E-11	[kg]	O
Steady-state mass in regional fresh water sediment	159	[kg]	O
Steady-state mass in regional sea water sediment	4.35	[kg]	O

CONTINENTAL

Steady-state mass in continental fresh water	2.43E+05	[kg]	O
Steady-state mass in continental sea water	3.78E+04	[kg]	O
Steady-state mass in continental air	-1.20E-20	[kg]	O
Steady-state mass in continental agricultural soil	0.552	[kg]	O
Steady-state mass in continental natural soil	-7.44E-12	[kg]	O
Steady-state mass in continental industrial soil	-3.11E-12	[kg]	O
Steady-state mass in continental fresh water sediment	1.85E+03	[kg]	O
Steady-state mass in continental sea water sediment	4.4	[kg]	O

GLOBAL: MODERATE

Steady-state mass in moderate water	385	[kg]	O
Steady-state mass in moderate air	-1.74E-23	[kg]	O
Steady-state mass in moderate soil	-1.71E-14	[kg]	O
Steady-state mass in moderate sediment	8.96E-03	[kg]	O

GLOBAL: ARCTIC

Steady-state mass in arctic water	4.23	[kg]	O
Steady-state mass in arctic air	2.91E-27	[kg]	O
Steady-state mass in arctic soil	-4.65E-17	[kg]	O
Steady-state mass in arctic sediment	1.00E-04	[kg]	O

GLOBAL: TROPIC				
Steady-state mass in tropic water		0.706	[kg]	O
Steady-state mass in tropic air		3.52E-26	[kg]	O
Steady-state mass in tropic soil		-1.28E-17	[kg]	O
Steady-state mass in tropic sediment		1.59E-05	[kg]	O
LOCAL				
[PRIVATE USE]				
LOCAL CONCENTRATIONS AND DEPOSITIONS [PRIVATE USE]				
Concentration in air during emission episode		1.38E-23	[mg.m-3]	O
Annual average concentration in air, 100 m from point source		1.38E-23	[mg.m-3]	O
Total deposition flux during emission episode		4.98E-22	[mg.m-2.d-1]	O
Annual average total deposition flux		4.98E-22	[mg.m-2.d-1]	O
Concentration in surface water during emission episode (dissolved)		0.0147	[mg.l-1]	O
Annual average concentration in surface water (dissolved)		0.0147	[mg.l-1]	O
Concentration in sea water during emission episode (dissolved)		0.0116	[mg.l-1]	O
Annual average concentration in sea water (dissolved)		0.0116	[mg.l-1]	O
Concentration in agric. soil averaged over 30 days		2.07E-06	[mg.kgwwt-1]	O
Concentration in agric. soil averaged over 180 days		5.30E-07	[mg.kgwwt-1]	O
Concentration in grassland averaged over 180 days		1.58E-07	[mg.kgwwt-1]	O
Fraction of steady-state (agricultural soil)		1	[-]	O
Fraction of steady-state (grassland soil)		1	[-]	O
LOCAL PECS [PRIVATE USE]				
Annual average local PEC in air (total)		1.38E-23	[mg.m-3]	O
Local PEC in surface water during emission episode (dissolved)		0.0205	[mg.l-1]	O
Qualitative assessment might be needed (TGD Part II, 5.6)	No			O
Annual average local PEC in surface water (dissolved)		0.0205	[mg.l-1]	O
Local PEC in fresh-water sediment during emission episode		0.0161	[mg.kgwwt-1]	O
Local PEC in sea water during emission episode (dissolved)		0.0121	[mg.l-1]	O
Qualitative assessment might be needed (TGD Part II, 5.6)	No			O
Annual average local PEC in sea water (dissolved)		0.0121	[mg.l-1]	O
Local PEC in marine sediment during emission episode		9.48E-03	[mg.kgwwt-1]	O
Local PEC in agric. soil (total) averaged over 30 days		2.07E-06	[mg.kgwwt-1]	O
Local PEC in agric. soil (total) averaged over 180 days		5.30E-07	[mg.kgwwt-1]	O
Local PEC in grassland (total) averaged over 180 days		1.58E-07	[mg.kgwwt-1]	O

Local PEC in pore water of agricultural soil	4.50E-06	[mg.l-1]	O
Local PEC in pore water of grassland	1.34E-06	[mg.l-1]	O
Local PEC in groundwater under agricultural soil	4.50E-06	[mg.l-1]	O
EXPOSURE			
SECONDARY POISONING			
SECONDARY POISONING [PRIVATE USE]			
Concentration in fish for secondary poisoning (fresh water)	0.0186	[mg.kgwwt-1]	O
Concentration in fish for secondary poisoning (marine)	8.88E-03	[mg.kgwwt-1]	O
Concentration in fish-eating marine top-predators	2.31E-03	[mg.kgwwt-1]	O
Concentration in earthworms from agricultural soil	1.75E-06	[mg.kg-1]	O
HUMANS EXPOSED TO OR VIA THE ENVIRONMENT			
REGIONAL			
CONCENTRATIONS IN FISH, PLANTS AND DRINKING WATER			
Regional concentration in wet fish	8.16E-03	[mg.kg-1]	O
Regional concentration in root tissue of plant	5.92E-08	[mg.kg-1]	O
Regional concentration in leaves of plant	2.73E-10	[mg.kg-1]	O
Regional concentration in grass (wet weight)	2.73E-10	[mg.kg-1]	O
Fraction of total uptake by crops from pore water	1	[-]	O
Fraction of total uptake by crops from air	-1.33E-20	[-]	O
Fraction of total uptake by grass from pore water	1	[-]	O
Fraction of total uptake by grass from air	-1.33E-20	[-]	O
Regional concentration in drinking water	5.78E-03	[mg.l-1]	O
CONCENTRATIONS IN MEAT AND MILK			
Regional concentration in meat (wet weight)	2.52E-07	[mg.kg-1]	O
Regional concentration in milk (wet weight)	2.52E-06	[mg.kg-1]	O
Fraction of total intake by cattle through grass	5.81E-08	[-]	O
Fraction of total intake by cattle through drinking water	1	[-]	O
Fraction of total intake by cattle through air	-2.32E-25	[-]	O
Fraction of total intake by cattle through soil	1.10E-08	[-]	O
DAILY HUMAN DOSES			
Daily dose through intake of drinking water	1.65E-04	[mg.kg-1.d-1]	O
Fraction of total dose through intake of drinking water	0.925	[-]	O
Daily dose through intake of fish	1.34E-05	[mg.kg-1.d-1]	O

Fraction of total dose through intake of fish	0.0751	[-]	O
Daily dose through intake of leaf crops	4.68E-12	[mg.kg-1.d-1]	O
Fraction of total dose through intake of leaf crops	2.62E-08	[-]	O
Daily dose through intake of root crops	3.25E-10	[mg.kg-1.d-1]	O
Fraction of total dose through intake of root crops	1.82E-06	[-]	O
Daily dose through intake of meat	1.09E-09	[mg.kg-1.d-1]	O
Fraction of total dose through intake of meat	6.08E-06	[-]	O
Daily dose through intake of milk	2.02E-08	[mg.kg-1.d-1]	O
Fraction of total dose through intake of milk	1.13E-04	[-]	O
Daily dose through intake of air	-1.73E-28	[mg.kg-1.d-1]	O
Fraction of total dose through intake of air	-9.67E-25	[-]	O
Regional total daily intake for humans	1.79E-04	[mg.kg-1.d-1]	O

LOCAL

[PRIVATE USE]

CONCENTRATIONS IN FISH, PLANTS AND DRINKING WATER [PRIVATE USE]

Local concentration in wet fish	0.029	[mg.kg-1]	O
Local concentration in root tissue of plant	4.18E-06	[mg.kg-1]	O
Local concentration in leaves of plant	1.93E-08	[mg.kg-1]	O
Local concentration in grass (wet weight)	5.76E-09	[mg.kg-1]	O
Fraction of total uptake by crops from pore water	1	[-]	O
Fraction of total uptake by crops from air	4.33E-18	[-]	O
Fraction of total uptake by grass from pore water	1	[-]	O
Fraction of total uptake by grass from air	1.45E-17	[-]	O
Local concentration in drinking water	0.0205	[mg.l-1]	O
Annual average local PEC in air (total)	1.38E-23	[mg.m-3]	O

CONCENTRATIONS IN MEAT AND MILK [PRIVATE USE]

Local concentration in meat (wet weight)	8.96E-07	[mg.kg-1]	O
Local concentration in milk (wet weight)	8.96E-06	[mg.kg-1]	O
Fraction of total intake by cattle through grass	3.45E-07	[-]	O
Fraction of total intake by cattle through drinking water	1	[-]	O
Fraction of total intake by cattle through air	1.50E-21	[-]	O
Fraction of total intake by cattle through soil	6.52E-08	[-]	O

DAILY HUMAN DOSES [PRIVATE USE]

Daily dose through intake of drinking water		5.86E-04	[mg.kg-1.d-1]	O
Fraction of total dose through intake of drinking water		0.925	[-]	O
Daily dose through intake of fish		4.76E-05	[mg.kg-1.d-1]	O
Fraction of total dose through intake of fish		0.0751	[-]	O
Daily dose through intake of leaf crops		3.31E-10	[mg.kg-1.d-1]	O
Fraction of total dose through intake of leaf crops		5.22E-07	[-]	O
Daily dose through intake of root crops		2.29E-08	[mg.kg-1.d-1]	O
Fraction of total dose through intake of root crops		3.62E-05	[-]	O
Daily dose through intake of meat		3.85E-09	[mg.kg-1.d-1]	O
Fraction of total dose through intake of meat		6.08E-06	[-]	O
Daily dose through intake of milk		7.18E-08	[mg.kg-1.d-1]	O
Fraction of total dose through intake of milk		1.13E-04	[-]	O
Daily dose through intake of air		3.95E-24	[mg.kg-1.d-1]	O
Fraction of total dose through intake of air		6.23E-21	[-]	O
Local total daily intake for humans		6.34E-04	[mg.kg-1.d-1]	O

EFFECTS
INPUT OF EFFECTS DATA
MICRO-ORGANISMS

	Respiration inhibition, EU Annex V C.11, OECD			
Test system	209			D
EC50 for micro-organisms in a STP	??		[mg.l-1]	D
EC10 for micro-organisms in a STP		1.60E+04	[mg.l-1]	S
NOEC for micro-organisms in a STP	??		[mg.l-1]	D

AQUATIC ORGANISMS
FRESH WATER
L(E)C50 SHORT-TERM TESTS

LC50 for fish		400	[mg.l-1]	S
L(E)C50 for Daphnia		318	[mg.l-1]	S
EC50 for algae		230	[mg.l-1]	S
LC50 for additional taxonomic group	??		[mg.l-1]	D
Aquatic species	other			D

NOEC LONG-TERM TESTS

NOEC for fish	??		[mg.l-1]	D
NOEC for Daphnia		30	[mg.l-1]	S

NOEC for algae		31	[mg.l-1]	S
NOEC for additional taxonomic group	??		[mg.l-1]	D
NOEC for additional taxonomic group	??		[mg.l-1]	D
NOEC for additional taxonomic group	??		[mg.l-1]	D
NOEC for additional taxonomic group	??		[mg.l-1]	D
MARINE				
L(E)C50 SHORT-TERM TESTS				
LC50 for fish (marine)	??		[mg.l-1]	D
L(E)C50 for crustaceans (marine)	??		[mg.l-1]	D
EC50 for algae (marine)	??		[mg.l-1]	D
LC50 for additional taxonomic group (marine)	??		[mg.l-1]	D
Marine species	other			D
LC50 for additional taxonomic group (marine)	??		[mg.l-1]	D
Marine species	other			D
NOEC LONG-TERM TESTS				
NOEC for fish (marine)	??		[mg.l-1]	D
NOEC for crustaceans (marine)	??		[mg.l-1]	D
NOEC for algae (marine)	??		[mg.l-1]	D
NOEC for additional taxonomic group (marine)	??		[mg.l-1]	D
NOEC for additional taxonomic group (marine)	??		[mg.l-1]	D
FRESH WATER SEDIMENT				
L(E)C50 SHORT-TERM TESTS				
LC50 for fresh-water sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
EC10/NOEC LONG-TERM TESTS				
EC10 for fresh-water sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
EC10 for fresh-water sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
EC10 for fresh-water sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
NOEC for fresh-water sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D

NOEC for fresh-water sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
NOEC for fresh-water sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D

MARINE SEDIMENT

L(E)C50 SHORT-TERM TESTS

LC50 for marine sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D

EC10/NOEC LONG-TERM TESTS

EC10 for marine sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
EC10 for marine sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
EC10 for marine sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
NOEC for marine sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
NOEC for marine sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D
NOEC for marine sediment organism	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested sediment		0.05	[kg.kg-1]	D

TERRESTRIAL ORGANISMS

L(E)C50 SHORT-TERM TESTS

LC50 for plants	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested soil		0.02	[kg.kg-1]	D
LC50 for earthworms	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested soil		0.02	[kg.kg-1]	D
EC50 for microorganisms	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested soil		0.02	[kg.kg-1]	D
LC50 for other terrestrial species	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested soil		0.02	[kg.kg-1]	D

NOEC LONG-TERM TESTS

NOEC for plants	??		[mg.kgwwt-1]	D

Weight fraction of organic carbon in tested soil		0.02	[kg.kg-1]	D
NOEC for earthworms	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested soil		0.02	[kg.kg-1]	D
NOEC for microorganisms	??		[mg.kgwwt-1]	D
Weight fraction of organic carbon in tested soil		0.02	[kg.kg-1]	D
NOEC for additional taxonomic group	??		[mg.kgwwt-1]	D
Terrestrial species	other			D
Weight fraction of organic carbon in tested soil		0.02	[kg.kg-1]	D
NOEC for additional taxonomic group	??		[mg.kgwwt-1]	D
Terrestrial species	other			D
Weight fraction of organic carbon in tested soil		0.02	[kg.kg-1]	D
BIRDS				
LC50 in avian dietary study (5 days)	??		[mg.kg-1]	D
NOEC via food (birds)	??		[mg.kg-1]	D
NOAEL (birds)	??		[mg.kg-1.d-1]	D
Conversion factor NOAEL to NOEC (birds)		8	[kg.d.kg-1]	D
MAMMALS				
REPEATED DOSE				
ORAL				
Oral NOAEL (repdose)	??		[mg.kg-1.d-1]	D
Oral LOAEL (repdose)	??		[mg.kg-1.d-1]	D
Oral CED (repdose)	??		[mg.kg-1.d-1]	D
Species for conversion of NOAEL to NOEC	Rattus norvegicus (<=6 weeks)			D
Conversion factor NOAEL to NOEC		10	[kg.d.kg-1]	O
NOEC via food (repdose)	??		[mg.kg-1]	D
LOEC via food (repdose)	??		[mg.kg-1]	D
CED via food (repdose)	??		[mg.kgfood-1]	D
INHALATORY				
Inhalatory NOAEL (repdose)	??		[mg.m-3]	D
Inhalatory LOAEL (repdose)	??		[mg.m-3]	D
Inhalatory CED (repdose)	??		[mg.m-3]	D
Correction factor for allometric scaling		1	[-]	D
DERMAL				

Dermal NOAEL (repdose)	??		[mg.kg-1.d-1]	D
Dermal LOAEL (repdose)	??		[mg.kg-1.d-1]	D
Dermal CED (repdose)	??		[mg.kg-1.d-1]	D
FERTILITY				
ORAL				
Oral NOAEL (fert)	??		[mg.kg-1.d-1]	D
Oral LOAEL (fert)	??		[mg.kg-1.d-1]	D
Oral CED (fert)	??		[mg.kg-1.d-1]	D
Species for conversion of NOAEL to NOEC	Rattus norvegicus (<=6 weeks)			D
Conversion factor NOAEL to NOEC		10	[kg.d.kg-1]	O
NOEC via food (fert)	??		[mg.kg-1]	D
LOEC via food (fert)	??		[mg.kg-1]	D
CED via food (fert)	??		[mg.kgfood-1]	D
INHALATORY				
Inhalatory NOAEL (fert)	??		[mg.m-3]	D
Inhalatory LOAEL (fert)	??		[mg.m-3]	D
Inhalatory CED (fert)	??		[mg.m-3]	D
Correction factor for allometric scaling		1	[-]	D
DERMAL				
Dermal NOAEL (fert)	??		[mg.kg-1.d-1]	D
Dermal LOAEL (fert)	??		[mg.kg-1.d-1]	D
Dermal CED (fert)	??		[mg.kg-1.d-1]	D
MATERNAL-TOX				
ORAL				
Oral NOAEL (mattox)	??		[mg.kg-1.d-1]	D
Oral LOAEL (mattox)	??		[mg.kg-1.d-1]	D
Oral CED (mattox)	??		[mg.kg-1.d-1]	D
Species for conversion of NOAEL to NOEC	Rattus norvegicus (<=6 weeks)			D
Conversion factor NOAEL to NOEC		10	[kg.d.kg-1]	O
NOEC via food (mattox)	??		[mg.kg-1]	D
LOEC via food (mattox)	??		[mg.kg-1]	D
CED via food (mattox)	??		[mg.kgfood-1]	D

INHALATORY				
Inhalatory NOAEL (mattox)	??		[mg.m-3]	D
Inhalatory LOAEL (mattox)	??		[mg.m-3]	D
Inhalatory CED (mattox)	??		[mg.m-3]	D
Correction factor for allometric scaling		1	[-]	D
DERMAL				
Dermal NOAEL (mattox)	??		[mg.kg-1.d-1]	D
Dermal LOAEL (mattox)	??		[mg.kg-1.d-1]	D
Dermal CED (mattox)	??		[mg.kg-1.d-1]	D
DEVELOPMENT-TOX				
ORAL				
Oral NOAEL (devtox)	??		[mg.kg-1.d-1]	D
Oral LOAEL (devtox)	??		[mg.kg-1.d-1]	D
Oral CED (devtox)	??		[mg.kg-1.d-1]	D
Species for conversion of NOAEL to NOEC	Rattus norvegicus (<=6 weeks)			D
Conversion factor NOAEL to NOEC		10	[kg.d.kg-1]	O
NOEC via food (devtox)	??		[mg.kg-1]	D
LOEC via food (devtox)	??		[mg.kg-1]	D
CED via food (devtox)	??		[mg.kgfood-1]	D
INHALATORY				
Inhalatory NOAEL (devtox)	??		[mg.m-3]	D
Inhalatory LOAEL (devtox)	??		[mg.m-3]	D
Inhalatory CED (devtox)	??		[mg.m-3]	D
Correction factor for allometric scaling		1	[-]	D
DERMAL				
Dermal NOAEL (devtox)	??		[mg.kg-1.d-1]	D
Dermal LOAEL (devtox)	??		[mg.kg-1.d-1]	D
Dermal CED (devtox)	??		[mg.kg-1.d-1]	D
CARC (THRESHOLD)				
ORAL				
Oral NOAEL (carc)	??		[mg.kg-1.d-1]	D
Oral LOAEL (carc)	??		[mg.kg-1.d-1]	D

Oral CED (carc)	??		[mg.kg-1.d-1]	D
Species for conversion of NOAEL to NOEC	Rattus norvegicus (<=6 weeks)			D
Conversion factor NOAEL to NOEC		10	[kg.d.kg-1]	O
NOEC via food (carc)	??		[mg.kg-1]	D
LOEC via food (carc)	??		[mg.kg-1]	D
CED via food (carc)	??		[mg.kgfood-1]	D
INHALATORY				
Inhalatory NOAEL (carc)	??		[mg.m-3]	D
Inhalatory LOAEL (carc)	??		[mg.m-3]	D
Inhalatory CED (carc)	??		[mg.m-3]	D
Correction factor for allometric scaling		1	[-]	D
DERMAL				
Dermal NOAEL (carc)	??		[mg.kg-1.d-1]	D
Dermal LOAEL (carc)	??		[mg.kg-1.d-1]	D
Dermal CED (carc)	??		[mg.kg-1.d-1]	D
CARC (NON-THRESHOLD)				
ORAL				
Oral T25 for non-threshold effects	??		[mg.kg-1.d-1]	D
Oral CED for non-threshold effects	??		[mg.kg-1.d-1]	D
Species for conversion of NOAEL to NOEC	Rattus norvegicus (<=6 weeks)			D
Conversion factor NOAEL to NOEC		10	[kg.d.kg-1]	O
T25 via food for non-threshold effects	??		[mg.kgfood-1]	D
CED via food for non-threshold effects	??		[mg.kgfood-1]	D
INHALATORY				
Inhalatory T25 for non-threshold effects	??		[mg.m-3]	D
Inhalatory CED for non-threshold effects	??		[mg.m-3]	D
Correction factor for allometric scaling		1	[-]	D
DERMAL				
Dermal T25 for non-threshold effects	??		[mg.kg-1.d-1]	D
Dermal CED for non-threshold effects	??		[mg.kg-1.d-1]	D
ACUTE				

Oral LD50	??		[mg.kg-1]	D
Oral Discriminatory Dose	??		[mg.kg-1]	D
Inhalatory LC50	??		[mg.m-3]	D
Dermal LD50	??		[mg.kg-1]	D
PREDATOR				
Duration of (sub-)chronic oral test	28 days			D
NOEC via food for secondary poisoning	??		[mg.kg-1]	O
Source for NOEC-via-food data	No data available, enter manually			S
BIO-AVAILIBILITY				
Bioavailability for oral uptake (oral to inhalation)		0.5	[-]	D
Bioavailability for oral uptake (oral to dermal)		1	[-]	D
Bioavailability for oral uptake (route to oral)		1	[-]	D
Bioavailability for inhalation (route from inhalation)		1	[-]	D
Bioavailability for inhalation (route to inhalation)		1	[-]	D
Bioavailability for dermal uptake (route from dermal)		1	[-]	O
Bioavailability for dermal uptake (route to dermal)		1	[-]	O
HUMANS				
REPEATED DOSE				
ORAL				
Oral NOAEL (repdose)	??		[mg.kg-1.d-1]	D
Oral LOAEL (repdose)	??		[mg.kg-1.d-1]	D
INHALATORY				
Inhalatory NOAEL (repdose)	??		[mg.m-3]	D
Inhalatory LOAEL (repdose)	??		[mg.m-3]	D
DERMAL				
Dermal NOAEL (repdose)	??		[mg.kg-1.d-1]	D
Dermal LOAEL (repdose)	??		[mg.kg-1.d-1]	D
Dermal NOEC in a medium (repdose)	??		[mg.cm-3]	D
Dermal LOEC in a medium (repdose)	??		[mg.cm-3]	D
FERTILITY				
ORAL				

Oral NOAEL (fert)	??	[mg.kg-1.d-1]	D
Oral LOAEL (fert)	??	[mg.kg-1.d-1]	D
INHALATORY			
Inhalatory NOAEL (fert)	??	[mg.m-3]	D
Inhalatory LOAEL (fert)	??	[mg.m-3]	D
DERMAL			
Dermal NOAEL (fert)	??	[mg.kg-1.d-1]	D
Dermal LOAEL (fert)	??	[mg.kg-1.d-1]	D
Dermal NOEC in a medium (fert)	??	[mg.cm-3]	D
Dermal LOEC in a medium (fert)	??	[mg.cm-3]	D
MATERNAL-TOX			
ORAL			
Oral NOAEL (mattox)	??	[mg.kg-1.d-1]	D
Oral LOAEL (mattox)	??	[mg.kg-1.d-1]	D
INHALATORY			
Inhalatory NOAEL (mattox)	??	[mg.m-3]	D
Inhalatory LOAEL (mattox)	??	[mg.m-3]	D
DERMAL			
Dermal NOAEL (mattox)	??	[mg.kg-1.d-1]	D
Dermal LOAEL (mattox)	??	[mg.kg-1.d-1]	D
Dermal NOEC in a medium (mattox)	??	[mg.cm-3]	D
Dermal LOEC in a medium (mattox)	??	[mg.cm-3]	D
DEVELOPMENT-TOX			
ORAL			
Oral NOAEL (devtox)	??	[mg.kg-1.d-1]	D
Oral LOAEL (devtox)	??	[mg.kg-1.d-1]	D
INHALATORY			
Inhalatory NOAEL (devtox)	??	[mg.m-3]	D
Inhalatory LOAEL (devtox)	??	[mg.m-3]	D

DERMAL			
Dermal NOAEL (devtox)	??	[mg.kg-1.d-1]	D
Dermal LOAEL (devtox)	??	[mg.kg-1.d-1]	D
Dermal NOEC in a medium (devtox)	??	[mg.cm-3]	D
Dermal LOEC in a medium (devtox)	??	[mg.cm-3]	D
CARC (THRESHOLD)			
ORAL			
Oral NOAEL (carc)	??	[mg.kg-1.d-1]	D
Oral LOAEL (carc)	??	[mg.kg-1.d-1]	D
INHALATORY			
Inhalatory NOAEL (carc)	??	[mg.m-3]	D
Inhalatory LOAEL (carc)	??	[mg.m-3]	D
DERMAL			
Dermal NOAEL (carc)	??	[mg.kg-1.d-1]	D
Dermal LOAEL (carc)	??	[mg.kg-1.d-1]	D
Dermal NOEC in a medium (carc)	??	[mg.cm-3]	D
Dermal LOEC in a medium (carc)	??	[mg.cm-3]	D
CURRENT CLASSIFICATION			
Corrosive (C, R34 or R35)	No		D
Irritating to skin (Xi, R38)	No		D
Irritating to eyes (Xi, R36)	No		D
Risk of serious damage to eyes (Xi, R41)	No		D
Irritating to respiratory system (Xi, R37)	No		D
May cause sensitisation by inhalation (Xn, R42)	No		D
May cause sensitisation by skin contact (Xi, R43)	No		D
May cause cancer (T, R45)	No		D
May cause cancer by inhalation (T, R49)	No		D
Possible risk of irreversible effects (Xn, R40)	No		D
ENVIRONMENTAL EFFECTS ASSESSMENT			
ENVIRONMENTAL PNECS			
FRESH WATER			
Same taxonomic group for LC50 and NOEC	Yes		O

Toxicological data used for extrapolation to PNEC Aqua		31	[mg.l-1]	S
Assessment factor applied in extrapolation to PNEC Aqua		50	[-]	O
PNEC for aquatic organisms		0.62	[mg.l-1]	O
INTERMITTENT RELEASES				
Toxicological data used for extrapolation to PNEC Aqua		230	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC Aqua		100	[-]	O
PNEC for aquatic organisms, intermittent releases		2.3	[mg.l-1]	O
STATISTICAL				
PNEC for aquatic organisms with statistical method	??		[mg.l-1]	D
MARINE				
Same taxonomic group for marine LC50 and NOEC	Yes			O
Toxicological data used for extrapolation to PNEC Marine		30	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC Marine		500	[-]	O
PNEC for marine organisms		0.06	[mg.l-1]	O
STATISTICAL				
PNEC for marine organisms with statistical method	??		[mg.l-1]	D
FRESH WATER SEDIMENT				
Toxicological data used for extrapolation to PNEC sediment (fresh)	??		[mg.kgwwt-1]	O
Assessment factor applied in extrapolation to PNEC sediment (fresh)	??		[-]	O
PNEC for fresh-water sediment organisms (from toxicological data)	??		[mg.kgwwt-1]	O
PNEC for fresh-water sediment organisms (equilibrium partitioning)		0.485	[mg.kgwwt-1]	O
Equilibrium partitioning used for PNEC in fresh-water sediment?	Yes			O
PNEC for fresh-water sediment-dwelling organisms		0.485	[mg.kgwwt-1]	O
MARINE SEDIMENT				
Toxicological data used for extrapolation to PNEC sediment (marine)	??		[mg.kgwwt-1]	O
Assessment factor applied in extrapolation to PNEC sediment (marine)	??		[-]	O
PNEC for marine sediment organisms (from toxicological data)	??		[mg.kgwwt-1]	O
PNEC for marine sediment organisms (equilibrium partitioning)		0.047	[mg.kgwwt-1]	O
Equilibrium partitioning used for PNEC in marine sediment?	Yes			O
PNEC for marine sediment organisms		0.047	[mg.kgwwt-1]	O

TERRESTRIAL				
Same taxonomic group for LC50 and NOEC	No			O
Toxicological data used for extrapolation to PNEC Terr	??		[mg.kgwwt-1]	O
Assessment factor applied in extrapolation to PNEC Terr	??		[-]	O
PNEC for terrestrial organisms (from toxicological data)	??		[mg.kgwwt-1]	O
PNEC for terrestrial organisms (equilibrium partitioning)		0.073	[mg.kgwwt-1]	O
Equilibrium partitioning used for PNEC in soil?	Yes			O
PNEC for terrestrial organisms		0.073	[mg.kgwwt-1]	O
STATISTICAL				
PNEC for terrestrial organisms with statistical method	??		[mg.kgwwt-1]	D
SECONDARY POISONING				
Toxicological data used for extrapolation to PNEC oral	??		[mg.kg-1]	O
Assessment factor applied in extrapolation to PNEC oral	??		[-]	O
PNEC for secondary poisoning of birds and mammals	??		[mg.kg-1]	O
STP				
Toxicological data used for extrapolation to PNEC micro		1.60E+04	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC micro		10	[-]	O
PNEC for micro-organisms in a STP		1.60E+03	[mg.l-1]	O
RISK CHARACTERIZATION				
REFERENCE MOS				
HUMANS EXPOSED TO OR VIA THE ENVIRONMENT				
REPEATED DOSE				
ORAL				
Assessment factor for allometric scaling		1	[-]	D
Assessment factor for remaining interspecies differences		1	[-]	D
Assessment factor for intraspecies differences		1	[-]	D
Assessment factor for differences in exposure duration		1	[-]	D
Assessment factor for differences in exposure route		1	[-]	D
Assessment factor for dose-response relationship		1	[-]	D
Reference-MOS, human environmental, oral (repdose)		1	[-]	O
INHALATORY				
Assessment factor for allometric scaling		1	[-]	D

Assessment factor for remaining interspecies differences	1	[-]	D
Assessment factor for intraspecies differences	1	[-]	D
Assessment factor for differences in exposure duration	1	[-]	D
Assessment factor for differences in exposure route	1	[-]	D
Assessment factor for dose-response relationship	1	[-]	D
Reference-MOS, human environmental, inhalatory (repdose)	1	[-]	O

FERTILITY

ORAL

Assessment factor for allometric scaling	1	[-]	D
Assessment factor for remaining interspecies differences	1	[-]	D
Assessment factor for intraspecies differences	1	[-]	D
Assessment factor for differences in exposure duration	1	[-]	D
Assessment factor for differences in exposure route	1	[-]	D
Assessment factor for dose-response relationship	1	[-]	D
Reference-MOS, human environmental, oral (fert)	1	[-]	O

INHALATORY

Assessment factor for allometric scaling	1	[-]	D
Assessment factor for remaining interspecies differences	1	[-]	D
Assessment factor for intraspecies differences	1	[-]	D
Assessment factor for differences in exposure duration	1	[-]	D
Assessment factor for differences in exposure route	1	[-]	D
Assessment factor for dose-response relationship	1	[-]	D
Reference-MOS, human environmental, inhalatory (fert)	1	[-]	O

MATERNAL-TOX

ORAL

Assessment factor for allometric scaling	1	[-]	D
Assessment factor for remaining interspecies differences	1	[-]	D
Assessment factor for intraspecies differences	1	[-]	D
Assessment factor for differences in exposure duration	1	[-]	D
Assessment factor for differences in exposure route	1	[-]	D
Assessment factor for dose-response relationship	1	[-]	D
Reference-MOS, human environmental, oral (mattox)	1	[-]	O

INHALATORY

Assessment factor for allometric scaling	1	[-]	D
Assessment factor for remaining interspecies differences	1	[-]	D
Assessment factor for intraspecies differences	1	[-]	D
Assessment factor for differences in exposure duration	1	[-]	D
Assessment factor for differences in exposure route	1	[-]	D
Assessment factor for dose-response relationship	1	[-]	D
Reference-MOS, human environmental, inhalatory (mattox)	1	[-]	O

DEVELOPMENT-TOX

ORAL

Assessment factor for allometric scaling	1	[-]	D
Assessment factor for remaining interspecies differences	1	[-]	D
Assessment factor for intraspecies differences	1	[-]	D
Assessment factor for differences in exposure duration	1	[-]	D
Assessment factor for differences in exposure route	1	[-]	D
Assessment factor for dose-response relationship	1	[-]	D
Reference-MOS, human environmental, oral (devtox)	1	[-]	O

INHALATORY

Assessment factor for allometric scaling	1	[-]	D
Assessment factor for remaining interspecies differences	1	[-]	D
Assessment factor for intraspecies differences	1	[-]	D
Assessment factor for differences in exposure duration	1	[-]	D
Assessment factor for differences in exposure route	1	[-]	D
Assessment factor for dose-response relationship	1	[-]	D
Reference-MOS, human environmental, inhalatory (devtox)	1	[-]	O

CARC (THRESHOLD)

ORAL

Assessment factor for allometric scaling	1	[-]	D
Assessment factor for remaining interspecies differences	1	[-]	D
Assessment factor for intraspecies differences	1	[-]	D
Assessment factor for differences in exposure duration	1	[-]	D
Assessment factor for differences in exposure route	1	[-]	D
Assessment factor for dose-response relationship	1	[-]	D
Reference-MOS, human environmental, oral (carc)	1	[-]	O

INHALATORY				
Assessment factor for allometric scaling		1	[-]	D
Assessment factor for remaining interspecies differences		1	[-]	D
Assessment factor for intraspecies differences		1	[-]	D
Assessment factor for differences in exposure duration		1	[-]	D
Assessment factor for differences in exposure route		1	[-]	D
Assessment factor for dose-response relationship		1	[-]	D
Reference-MOS, human environmental, inhalatory (carc)		1	[-]	O
CARC (NON-THRESHOLD)				
ORAL				
Assessment factor for allometric scaling		1	[-]	D
Assessment factor for remaining interspecies differences		1	[-]	D
Assessment factor for differences in exposure route		1	[-]	D
Assessment factor for dose-response relationship		1	[-]	D
Assessment factor for extrapolation to a low-risk level		2.50E+05	[-]	D
Reference-MOE, human environmental, oral (non-threshold)		2.50E+05	[-]	O
INHALATORY				
Assessment factor for allometric scaling		1	[-]	D
Assessment factor for remaining interspecies differences		1	[-]	D
Assessment factor for differences in exposure route		1	[-]	D
Assessment factor for dose-response relationship		1	[-]	D
Assessment factor for extrapolation to a low-risk level		2.50E+05	[-]	D
Reference-MOE, human environmental, inhalatory (non-threshold)		2.50E+05	[-]	O
HUMAN EQUIV. DOSE				
INHALATORY				
Assessment factor for allometric scaling		1	[-]	D
Assessment factor for differences in exposure route		1	[-]	D
Assessment factor humans via environment, inhalatory, non-threshold		1	[-]	O
Human equivalent dose humans via environment, inhalatory, non-threshold	??		[mg.m-3]	O
TOTAL EXPOSURE				
Assessment factor for allometric scaling		1	[-]	D
Assessment factor for differences in exposure route		1	[-]	D
Assessment factor humans via environment, total, non-threshold		1	[-]	O

Human equivalent dose humans via environment, total, non-threshold	??		[mg.kg-1.d-1]	O
ENVIRONMENTAL EXPOSURE				
LOCAL				
RISK CHARACTERIZATION OF [PRIVATE USE]				
WATER				
RCR for the local fresh-water compartment		0.0331	[-]	O
Intermittent release	No			D
RCR for the local marine compartment		0.202	[-]	O
RCR for the local fresh-water compartment, statistical method	??		[-]	O
RCR for the local marine compartment, statistical method	??		[-]	O
SEDIMENT				
RCR for the local fresh-water sediment compartment		0.0331	[-]	O
Extra factor 10 applied to PEC/PNEC	No			O
RCR for the local marine sediment compartment		0.202	[-]	O
Extra factor 10 applied to PEC/PNEC	No			O
SOIL				
RCR for the local soil compartment		2.84E-05	[-]	O
Extra factor 10 applied to PEC/PNEC	No			O
RCR for the local soil compartment, statistical method	??		[-]	O
STP				
RCR for the sewage treatment plant		9.21E-05	[-]	O
PREDATORS				
RCR for fish-eating birds and mammals (fresh-water)	??		[-]	O
RCR for fish-eating birds and mammals (marine)	??		[-]	O
RCR for top predators (marine)	??		[-]	O
RCR for worm-eating birds and mammals	??		[-]	O
REGIONAL				
WATER				
RCR for the regional fresh-water compartment		9.32E-03	[-]	O
RCR for the regional marine compartment		7.80E-03	[-]	O
RCR for the regional fresh-water compartment, statistical method	??		[-]	O

RCR for the regional marine compartment, statistical method	??		[-]	O
SEDIMENT				
RCR for the regional fresh-water sediment compartment		7.90E-03	[-]	O
Extra factor 10 applied to PEC/PNEC	No			O
RCR for the regional marine sediment compartment		6.72E-03	[-]	O
Extra factor 10 applied to PEC/PNEC	No			O
SOIL				
RCR for the regional soil compartment		1.03E-07	[-]	O
Extra factor 10 applied to PEC/PNEC	No			O
RCR for the regional soil compartment, statistical method	??		[-]	O
HUMANS EXPOSED TO OR VIA THE ENVIRONMENTAL				
LOCAL				
RISK CHARACTERIZATION OF [PRIVATE USE]				
REPEATED DOSE				
INHALATORY				
MOS, local, inhalatory (repdose)	??		[-]	O
Ratio MOS/Ref-MOS, local, inhalatory (repdose)	??		[-]	O
TOTAL EXPOSURE				
MOS, local, total exposure (repdose)	??		[-]	O
Ratio MOS/Ref-MOS, local, total exposure (repdose)	??		[-]	O
FERTILITY				
INHALATORY				
MOS, local, inhalatory (fert)	??		[-]	O
Ratio MOS/Ref-MOS, local, inhalatory (fert)	??		[-]	O
TOTAL EXPOSURE				
MOS, local, total exposure (fert)	??		[-]	O
Ratio MOS/Ref-MOS, local, total exposure (fert)	??		[-]	O
MATERNAL-TOX				
INHALATORY				
MOS, local, inhalatory (mattox)	??		[-]	O

Ratio MOS/Ref-MOS, local, inhalatory (mattox)	??	[-]	O
TOTAL EXPOSURE			
MOS, local, total exposure (mattox)	??	[-]	O
Ratio MOS/Ref-MOS, local, total exposure (mattox)	??	[-]	O
DEVELOPMENT-TOX			
INHALATORY			
MOS, local, inhalatory (devtox)	??	[-]	O
Ratio MOS/Ref-MOS, local, inhalatory (devtox)	??	[-]	O
TOTAL EXPOSURE			
MOS, local, total exposure (devtox)	??	[-]	O
Ratio MOS/Ref-MOS, local, total exposure (devtox)	??	[-]	O
CARC (THRESHOLD)			
INHALATORY			
MOS, local, inhalatory (carc)	??	[-]	O
Ratio MOS/Ref-MOS, local, inhalatory (carc)	??	[-]	O
TOTAL EXPOSURE			
MOS, local, total exposure (carc)	??	[-]	O
Ratio MOS/Ref-MOS, local, total exposure (carc)	??	[-]	O
CARC (NON-THRESHOLD)			
INHALATORY			
MOE, local, inhalatory (non-threshold)	??	[-]	O
Ratio MOE/Ref-MOE, local, inhalatory (non-threshold)	??	[-]	O
TOTAL EXPOSURE			
MOE, local, total exposure (non-threshold)	??	[-]	O
Ratio MOE/Ref-MOE, local, total exposure (non-threshold)	??	[-]	O
LIFETIME CANCER RISK			
Lifetime cancer risk, local, exposure via air	??	[-]	O
Lifetime cancer risk, local, total exposure	??	[-]	O

REGIONAL			
REPEATED DOSE			
INHALATORY			
MOS, regional, inhalatory (repdose)	??	[-]	O
Ratio MOS/Ref-MOS, regional, inhalatory (repdose)	??	[-]	O
TOTAL EXPOSURE			
MOS, regional, total exposure (repdose)	??	[-]	O
Ratio MOS/Ref-MOS, regional, total exposure (repdose)	??	[-]	O
FERTILITY			
INHALATORY			
MOS, regional, inhalatory (fert)	??	[-]	O
Ratio MOS/Ref-MOS, regional, inhalatory (fert)	??	[-]	O
TOTAL EXPOSURE			
MOS, regional, total exposure (fert)	??	[-]	O
Ratio MOS/Ref-MOS, regional, total exposure (fert)	??	[-]	O
MATERNAL-TOX			
INHALATORY			
MOS, regional, inhalatory (mattox)	??	[-]	O
Ratio MOS/Ref-MOS, regional, inhalatory (mattox)	??	[-]	O
TOTAL EXPOSURE			
MOS, regional, total exposure (mattox)	??	[-]	O
Ratio MOS/Ref-MOS, regional, total exposure (mattox)	??	[-]	O
DEVELOPMENT-TOX			
INHALATORY			
MOS, regional, inhalatory (devtox)	??	[-]	O
Ratio MOS/Ref-MOS, regional, inhalatory (devtox)	??	[-]	O
TOTAL EXPOSURE			
MOS, regional, total exposure (devtox)	??	[-]	O
Ratio MOS/Ref-MOS, regional, total exposure (devtox)	??	[-]	O

CARC (THRESHOLD)			
INHALATORY			
MOS, regional, inhalatory (carc)	??	[-]	O
Ratio MOS/Ref-MOS, regional, inhalatory (carc)	??	[-]	O
TOTAL EXPOSURE			
MOS, regional, total exposure (carc)	??	[-]	O
Ratio MOS/Ref-MOS, regional, total exposure (carc)	??	[-]	O
CARC (NON-THRESHOLD)			
INHALATORY			
MOE, regional, inhalatory (non-threshold)	??	[-]	O
Ratio MOE/Ref-MOE, regional, inhalatory (non-threshold)	??	[-]	O
TOTAL EXPOSURE			
MOE, regional, total exposure (non-threshold)	??	[-]	O
Ratio MOE/Ref-MOE, regional, total exposure (non-threshold)	??	[-]	O
LIFETIME CANCER RISK			
Lifetime cancer risk, regional, exposure via air	??	[-]	O
Lifetime cancer risk, regional, total exposure	??	[-]	O