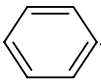
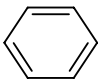
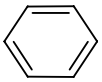
SIDS INITIAL ASSESSMENT PROFILE

CAS Nos. **and** **Chemical names**	(**1300-72-7** and 827-21-4) Xylenesulfonic acid, sodium salt (**12068-03-0**) Toluenesulfonic acid, sodium salt (**26447-10-9**) Xylenesulfonic acid, ammonium salt (**28348-53-0** and **32073-22-6**) Cumenesulfonic acid, sodium salt (**37475-88-0**) Cumenesulfonic acid, ammonium salt (28088-63-3) Xylenesulfonic acid, calcium salt (30346-73-7) Xylenesulfonic acid, potassium salt (16106-44-8) Toluenesulfonic acid, potassium salt **The 6 compounds in** bold **are sponsored HPV chemicals; the remaining 4 compounds are supporting/supported chemicals in the category.**
Category Name	**Hydrotropes**
Structural Formulas	 -CH_3 -SO_3Na toluene sulfonic acid, sodium salt  -$(CH_3)_2$ -SO_3Na xylene sulfonic acid, sodium salt  -$CH.(CH_3)_2$ -SO_3Na cumene sulfonic acid, sodium salt The category also includes isomeric forms (ortho, meta, and/or para) of the respective sulfonic acid salts (sodium, ammonium, calcium and potassium).

SUMMARY CONCLUSIONS OF THE SIAR

Category Identification/ Justification

Hydrotropes are supported as a category because of the close consistency of the compounds, their commercial uses, fate, and health and environmental effects. The 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 formulas in water. They function to stabilize solutions, modify viscosity and cloud-point, limit low temperature phase separation and reduce foam formation. Manufactured products are used as aqueous solutions (30-60% active substance) or as granular

solids containing 90-95% active substance.

The hydrotropes category may be initially considered as three sub-groups: the methyl, dimethyl and methylethyl benzene sulfonates, (or the toluene, xylene and cumene sulfonates). Although the counter ion will also determine the physical and chemical behavior of the compounds, the chemical reactivity and classification for this purpose is not expected to be affected by the difference in counter ion (i.e., Na^+, NH_4^+, Ca^{++}, or K^+). Note that two of the compounds (xylene and cumene sulfonic acid, sodium salts) 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 led 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.

In general, the presence of one or two methyl groups or a methylethyl group on the benzene ring is not expected 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 watery solutions may differ somewhat for the hydrotropes. However, the decisive factor in determining water solubility of these compounds will be ionic character, not the number and identity of the alkyl substituents on the benzene ring.

It was therefore concluded that the three sub-groups are expected to be generally comparable and predictable in their chemical behavior (as such or in solution) and that members from one sub-group may be useful for read across to other sub-groups and to the hydrotropes category as a whole.

Human Health

Toxicological studies have been conducted with numerous members of the hydrotropes category. Data on all SIDS-endpoints are available and indicate a relatively low toxicity for these compounds.

No studies on absorption, distribution, metabolism and elimination for the hydrotropes category were identified. However, based on the physico-chemical properties such as molecular weight, water solubility and octanol-water partition coefficient, and the available toxicological studies, it can be concluded that significant absorption occurs following oral administration while absorption following dermal application is limited.

Across the hydrotropes category, toxicity results are consistent across the toluene, xylene and cumene sulfonates and their various salts. The acute oral LD50 in rats ranges from 1044 mg a.i./kg bw (calcium xylene sulfonate) to 6500 mg a.i./kg bw (sodium xylene sulfonate), , the dermal LD50 in rabbits is >624 mg a.i./kg bw (calcium xylene sulfonate), and the inhalation LC50 in rats is >557 mg/L (557 g/m^3 sodium toluene sulfonate) and in rabbits >6.41 mg/L (6.41 g/m^3 ammonium xylene sulfonate). The inhalation studies are from secondary sources. Clinical signs observed in acute oral toxicity studies included decreased activity, weakness, prostration, increased salivation, diarrhea, ptosis and anogenital staining. Necropsy findings reported in these same studies included slight pulmonary inflammation, gastrointestinal inflammation and hemorrhage, mild liver changes, congestion of liver, kidneys, adrenal glands an gastrointestinal tract, and redness of stomach mucosa in animals that died. Observations were within normal limits with a report of slight to moderate congestion of adrenal glands in animals that survived. Clinical signs observed in acute dermal exposure included erythema with additional desquamation. At necropsy findings reported were focal or multifocal red discoloration and desquamation of the treated skin.

A series of rabbit skin and eye irritation studies are reported for members of the hydrotropes category. Sodium xylene sulfonate is not a skin irritant. Calcium xylene sulfonate and sodium cumene sulfonate are not skin irritants and both caused slight but reversible eye irritation. There is no indication of skin sensitization for the hydrotropes category based on the available animal (GLP Buehler study). No reliable human data are available for sensitization.

Thirteen oral and dermal repeat dose toxicity studies (subchronic and chronic) conducted in rats or mice are available

for the hydrotropes category. Test durations ranged from 17 days up to 2 years and exposure doses ranged from 6 to 2000 mg a.i. /kg bw/day sodium xylene sulphonate by the dermal route and from 1.1 up to 4092 mg a.i./kg bw/day sodium xylene sulphonate by the oral route. No significant systemic toxicity was observed in any of the dermal studies. Local effects were reported in one of six dermal studies. In that study the LOAEL was 1300 mg a.i./kg bw/day of sodium xylene sulphonate and the adverse effect was epidermal hyperplasia at the site of application in both male and female mice.. The corresponding NOAEL was 440 mg a.i./kg bw/day.. In the same study, the mean body weight gain of the high dose males was significantly greater (105%) than that of the control group. This change was not considered to be biologically significant by the authors (US National Institute of Health).

One of the eight oral repeat dose studies reported a 17% (statistically significant) decrease in relative spleen weight in female rats exposed 90 days to sodium xylene sulfonate. No adverse effects were reported in males. The LOAEL for this study was 4092 mg a.i./kg bw/day and the NOAEL was 763 mg a.i./kg bw/day. A 12% (statistically significant) reduction in body weight gain of female rats was reported in an older (1968) 91-day oral study with sodium cumene sulfonate at the dose level of 159 mg a.i./kg bw/day. No effects were observed in male rats. The study report stated that the decrease in body weight gain for females was within the established ranges for animals of this species and age and was therefore not considered an adverse effect by the authors. The decrease in body weight gain wasnot associated with any other effects. Two more recent (1980) and well reported 90 day studies with rats and mice exposed to sodium xylene sulfonate did not report a reduction in body weight gain at much higher doses, and consequently the effect in the sodium cumene sulfonate study is considered questionable. 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 relative spleen weight in female rats.

The hydrotropes category has been assessed for mutagenic potential in a variety of *in vivo* and *in vitro* assays. Specifically mouse micronucleus cytogenetic assays with calcium xylene sulfonate and sodium cumene sulfonate, Ames assay with calcium xylene sulphonate, sodium cumene sulphonate and sodium xylene sulphonate and mouse lymphoma, sister chromatid exchange, and chromosome aberration assays with sodium xylene sulfonate. No positive results were seen *in vitro* or *in vivo* in any of the studies. Thus the available data indicate that the chemicals in the hydrotropes category do not have a genotoxic potential.

Chronic toxicity/carcinogenicity data exist for the hydrotropes category for both rats and mice dermally exposed for 2 years. There was no evidence of a carcinogenic potential for the hydrotropes category in these dermal exposure studies. It is noted that there is limited dermal absorption of hydrotropes.

No reproductive toxicity studies are reported for the hydrotropes category. However, the 91-day oral rat feeding study with sodium cumene sulfonate, the 90-day feeding study with sodium xylene sulfonate and the 90-day and 2-year dermal studies with sodium xylene sulfonate included examination of sex organs such as the prostate, testes and ovaries. There is no evidence from these repeat dose studies to suggest that these chemicals would have an adverse effect on reproductive organs.

Calcium xylene sulfonate has been evaluated for the potential to cause developmental toxicity in rats. Calcium xylene sulfonate (31% a.i.) was administered via gavage to female rats (30 per dose) at 0, 150, 1500 or 3000 mg/kg bw in water on days 6 to 15 of gestation. This study followed the US EPA TSCA Guideline 1985. 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. There was no evidence of developmental toxicity in rats. The NOAEL for maternal and foetal toxicity was the highest dose tested at 3000 mg/kg bw/day (corresponding to 936 mg a.i./kg bw/day).

Environment

Hydrotropes are solid at ambient temperatures. Melting point experiments were carried out with calcium xylene sulfonate and sodium toluene sulfonate. Calcium xylene sulfonate decomposed in a melting point experiment at a temperature between 100°C and 375°C. No clear melting point was observed up to 300°C with sodium toluene sulfonate. Modelled estimates across the range of hydrotropes for melting points are in excess of 200°C and boiling points are in excess of 450°C. Hydrotropes are water soluble (>1000 mg/L) and have low volatility with a vapour

pressure of <2.0 x10^{-5} Pa for sodium xylene sulfonate at 25°C (vapour pressure was measured at 240-250°C and extrapolated to 25°C). A measured octanol-water partition coefficient (logKow) value of -2.7 exists for calcium xylene sulfonate, which correlates with modeled logKow estimations ranging between -2.4 and -1.5 for the sodium xylene, toluene and cumene sulfonates. Fugacity modelling across the range of hydrotropes predicts a 99+% residence in the water compartment following environmental release.
Biodegradation constitutes the primary elimination mechanism from the environment. Studies across the hydrotropes category demonstrate rapid and complete biodegradation under aerobic conditions and the hydrotropes are considered to be readily biodegradable according to OECD criteria. No data are available on anaerobic degradation. There is photodegradation potential for hydrotropes based upon modelled atmospheric oxidation half-lives of 40 hours for the cumene sulfonates, 41 hours for the xylene sulfonates, and 105 hours for the toluene sulfonates. Hydrotropes are not subject to hydrolysis. Commercial products containing hydrotropes are often aqueous solutions and they are stable. Removal of hydrotropes from secondary activated sludge sewage treatment processes is greater than 94%, as observed in a modified SCAS study with calcium xylene sulfonate. Bacterial toxicity studies indicate that the hydrotropes category is not expected to negatively impact sewage treatment microorganisms. Fish bioconcentration studies conducted at two exposure concentrations with sodium xylene sulfonate and sodium toluene sulfonate reported BCF values of <2.3. Model predictions using the measured and estimated log Kow values of -2.7 to -1.5 also indicate low bioaccumulation potential. The highest estimated Bioconcentration Factor [BCF] was approximately 3. Monitoring data are not available for the hydrotropes category.

Reliable ecotoxicity data are available on all SIDS-endpoints for selected members of the category. The data cover fish, invertebrates and algae for xylene sulfonate (sodium, ammonium and calcium salts) and cumene sulfonate (sodium salt). While the toluene benzene derivative is not represented in the available data set, results are consistent for the chemicals tested, providing confidence in the ability to read-across for other category members. Based on hazard data, aquatic toxicity is considered to be uniformly low across the hydrotropes category.

Fish acute LC_{50} values are >400 mg/L in six studies. *Daphnia* acute EC_{50} values are >318 mg/L in five studies. The acute LC_{50} to the marine invertebrate *Artemia* is >400 mg/L in one study. Freshwater green algae are considered the most sensitive species with EC_{50} values ranging between 230-236 mg a.i./L and No Observed Effect Concentrations (NOECs) ranging between 31-75 mg a.i./L. The 48-hr EC10 for the bacteria *Pseudomonas putida* exposed in a Bringmann-Kuehn-Test is reported as >16,000 mg/L sodium cumene sulfonate. A daphnid 21-day chronic toxicity NOEC value of approximately 30 mg/L has been reported for sodium cumene sulfonate, however the data is sourced from secondary literature with limited reliability.

The suggested aquatic Predicted No Effect Concentration (PNEC) is 2.3 mg/L calculated as the lowest EC_{50} for three species (algae, fish, daphnia) divided by an assessment factor of 100. The lowest EC_{50} is 230 mg/L (based on algal toxicity for sodium xylene sulfonate), this divided by 100 equals 2.3 mg/L. A PNEC of 2.3mg/L is consistent with what would be predicted using the chronic daphnia NOEC divided by 10, or using the 96-hour algal NOEC as a chronic endpoint divided by 10.

Exposure

Current hydrotrope volumes (production + importation) based on 100% active material are approximately 29,000 metric tonnes in the U.S., 1,100 metric tonnes (40% concentration) in Australia, and 19,000 metric tonnes in Europe. Hydrotropes are used at active concentrations between 0.1 and 15% in consumer cleaning and personal care products. They function as coupling agents in liquid and powder laundry detergents, hand dishwashing liquid detergents, machine dishwashing rinse aids, hard surface cleaners, body washes, shampoos, hair conditioners, liquid face and hand soaps, toilet treatments, solvent hand cleaners, carpet cleaners and optical brightener products. In Australia, a relatively small volume (about 55 tonnes per year) is used in liquid sulphur textile dyes present at 7.5 – 50%, acidic recirculation cleaning products present at 10-25%, wetting agent for tanning industry present at 10%, enzymatic recirculation cleaner for dairy and food processing applications at 4%, coolant system conditioner at 6.9%, car wash detergents at 1.3–6.3%, cleaners and degreasers at 0.1–6.3%, vinyl, plastic rubber restorer at 0.2% and floor stripper at 2.7–9 %. There are no industrial process intermediate uses of the hydrotropes.

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous and particulate material. The potential for human exposure to hydrotropes by inhalation is minimized by its low volatility and because most of the production, formulation and industrial end use of products are in aqueous solutions. Inhalation exposure to the solid form is likely to be minimal as dust generation is low. Dermal exposure is possible. Engineering controls (e.g., closed system operations, exhaust ventilation, dust collection) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for the hydrotropes category. No workplace air monitoring data are available.

Hydrotropes are used in consumer/professional cleaning and personal care products, which may be used "as is", or diluted prior to or during use. Dermal contact will occur with these products. There is some potential for incidental or accidental ingestion of, inhalation of, and/or eye contact with products during handling and use. Exposure to hydrotropes in formulated consumer products is mitigated by following use and precaution instructions on product labels. Human exposure will be mitigated by the fact that residues from many of these products are washed or rinsed off.

Environmental releases from production facilities and from down-the-drain discharges following product use may lead to potential environmental exposures in surface waters and indirect human exposures via drinking water and/or fish consumption. Environmental exposure will be mitigated by the fact that hydrotropes, which reside predominantly in the water compartment, are readily biodegraded and are removed to a large degree during wastewater treatment and have low potential for bioaccumulation.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemicals in this category are of low priority for further work because of their low hazard profile.

Environment: The chemicals in this category are of low priority for further work because of their low hazard profile.