SIDS INITIAL ASSESSMENT PROFILE

CAS No.	68515-32-2, 68855-24-3, 84961-70-6, 85117-41-5, 151911-58-9, 129813-62-3, 68515-34-4, and 94094-93-6
Category Name	Linear Alkylbenzene (LAB) Alkylate Bottoms Category
Structural Formula	[See Figure 1 of SIAR]

SUMMARY CONCLUSIONS OF THE SIAR

Category/Analogue Rationale

The linear alkylbenzene (LAB) alkylate bottoms are best described as a category of Class 2 substances. Class 2 substances are generally ones that may have variable compositions or be composed of a complex combination of different molecules. Therefore, they cannot be represented by unique chemical structures or molecular formulae. This Class 2 category is process based, and represents co-products of the LAB manufacturing process. Analysis of LAB alkylate bottoms samples from all member companies shows that the mixtures are predominantly comprised of di- and trialkylbenzenes, alkyl tetralins/indanes and diphenylalkanes, with lesser amounts of other constituents (e.g. LAB) and only trace amounts of other component classes. The analytical characterization demonstrates that composition is relatively consistent across production processes as well as among all LAB alkylate bottoms category members. No single product represents the extremes of the ranges determined. This includes the light and heavy ends, which are produced by distillation of whole bottoms into two subfractions, and which fit in the range of values found for the whole bottoms.

The LAB alkylate bottoms products manufactured and tested are 100% LAB alkylate bottoms, with no additives. GC-MS analyses of LAB alkylate bottoms samples indicate that PAH compounds of concern are not detected.

Based on the similarity of the chemical structural compositions and physico-chemical properties, a predictable pattern in environmental fate properties, environmental effects and mammalian toxicity is anticipated for the chemicals in this category. Therefore, they can be grouped and evaluated together.

Data are available for various preparations of LAB alkylate bottoms and for analogues (discussed below) that are used as supporting evidence and to fill data gaps.

C10-C14 dialkylbenzenes comprise the largest single component of LAB alkylate bottoms. A C10-C14 dialkylbenzene (CAS No. 85117-31-3) is used as an analogue for LAB alkylate bottoms for the biodegradation endpoint.

Data for benzene, C10-C13 alkyl derivatives (LAB, CAS No. 67774-74-7) and benzene, C10-C16 alkyl derivatives (C10-14 LAB, CAS No. 68648-87-3) are used to fill data gaps for LAB alkylate bottoms, e.g. acute inhalation toxicity and *in vivo* genotoxicity. LAB has been previously assessed in an EU Risk Assessment (http://ecb.jrc.it/home.php?CONTENU=/DOCUMENTS/Existing-Chemicals/RISK_ASSESSMENT/REPORT/) and C10-C14 LAB has previously been assessed in the OECD HPV Programme. LAB/C10-C14 LAB is a component (approximately 0.75%) of LAB alkylates bottoms.

Data from lab-synthesized LAB homologues, such as phenyl-C10 (C10 LAB) or phenyl-C12 (C12 LAB) as well as homologues such as phenyl-C18, which are outside the alkyl chain range for LAB are provided to illustrate how the aquatic toxicity of linear alkyl benzenes vary with alkyl chain length.

Physical-chemical properties

The LAB alkylate bottoms are all liquids at ambient temperatures. The density ranges from 0.89-0.92 at 15-20 ºC, with higher average molecular weights (318-480) than LAB (218-274 for C10-C14 LAB). The melting points range (based on weight-of-evidence) is -70 to ≤ -33 ºC and boiling point ranges overlap or are higher than that of LAB (278-314 ºC for LAB; 270-500 ºC for LAB alkylate bottoms). The range of vapour pressures is <0.01 to ≤7.5 hPa at 21-25 ºC (weight-of-evidence) and suggests limited volatility. Further, these compounds have low water solubility (<0.004 to <0.021mg/L) and high estimated log K_{ow} values (9.5 to 13.7).

Human Health

No specific data are available on the absorption, distribution or elimination of LAB alkylate bottoms. Metabolism on linear alkyl chains includes conversion of the terminal carbons of linear alkyl chains (alkanes) to carboxylic acids followed by metabolism of the resulting fatty acids. The carboxylic acid serves as a substrate for acyl-CoA synthetase, and the resulting acyl-CoA enters the β-oxidation pathway. Metabolism and biodegradation data on linear alkyl chains, LAB and linear alkylbenzene sulfonates (LAS) suggest that LAB alkylate bottoms will undergo metabolism and degradation in biological systems.

Inhalation studies in rats with the analogue substance LAB (CAS No. 67774-74-7) resulted in an LD_{50} of 71 mg/L. The dermal rat LD_{50} was >5000 mg/kg bw for CAS No. 68515-32-2 and >2000 mg/kg bw for the analogue substance LAB (CAS No. 67774-74-7). No clinical signs of toxicity were observed. The dermal rabbit LD_{50}s for CAS Nos, 129813-61-2 and 68855-24-3 were >2010 and >7940 mg/kg bw, respectively. Rabbits showed signs of reduced appetite and activity. The oral rat LD_{50}s for the LAB alkylate bottoms were >2000 mg/kg bw and for the analogue substance LAB (CAS No. 6774-74-7) >5000 mg/kg-bw. The only clinical sign of toxicity observed was a reduced appetite in one study.

LAB alkylate bottoms are slightly irritating to the skin (OECD TG 404) and not irritating to the eye of rabbits (OECD TG 405). LAB alkylate bottoms are not skin sensitisers in guinea pigs (OECD TG 406) and analogue LAB (CAS No. 67774-74-7) is not a sensitiser in humans.

Repeated-dose studies were available via inhalation for LAB, via the dermal exposure route for one LAB alkylate bottom and via oral feed for an LAB alkylate bottoms blend and LAB. In a repeated-dose inhalation toxicity study, Sprague-Dawley rats (15/sex/concentration), were exposed to LAB (respirable particles) at 0, 102, 298 or 580 mg/m^3 (~0, 0.102, 0.298 or 0.580 mg/L, respectively) for 6 hours/day, 5 days/week for 14 weeks. No deaths were observed, but respiratory effects (irritation and difficulty breathing) were evident in the mid- and high exposure concentrations. Body weights were depressed and liver weights and serum levels of hepatic enzymes were elevated at these levels, although no gross or histopathological changes were observed. Based on respiratory effects, body weight changes and changes in clinical chemistry, the NOAEL for repeated-dose inhalation toxicity was considered to be 102 mg/m^3(respirable particles).

In a repeated-dose dermal toxicity study, Wistar rats (6/sex/dose) were treated with 2000 mg/kg-bw/day (limit dose) LAB alkylate bottoms (CAS No. 68515-32-2) for 5 days/week for 28 days. No mortality was observed; however, a significant weight decrease was observed in female rats and acute multifocal hepatitis was observed in both sexes. The NOAEL for repeated-dose dermal toxicity was not established.

In a combined repeated-dose/reproductive/developmental toxicity screening study [OECD TG 422], an industry blend (containing all LAB alkylate bottoms products mixed in proportion to their production volume, as summarized in the table below) was administered by oral gavage to 60 male and 80 female Crl:CD(SD) rats at 0 (corn oil vehicle), 250, 500 and 1000 mg/kg-bw/day.

Component Class	Individual Products, weight %		Industry Blend, weight %
	Minimum	Maximum	Day 0
CnH2n-6	43.4	94.3	73.5
CnH2n-8	4.4	32.0	11.6
CnH2n-10	0.0	7.0	2.4
CnH2n-12	0.6	10.7	4.8

CnH2n-14	0.8	12.1	5.2
CnH2n-16	0.0	7.5	2.5

Clinical observations included body weight gain differences and changes in the thyroid of both sexes at all dose levels and in the thymus of the 1000 mg/kg-bw/day female rats. The significance of the effects seen in the thyroid at all dose levels is uncertain as it is generally accepted that humans are less susceptible than rats in relation to thyroid effects. The overall NOAEL for repeated-dose oral toxicity was considered to be 500 mg/kg-bw/day based on body weight reductions at 1000 mg/kg-bw/day. In a repeated-dose oral toxicity study, rats were administered 0, 2500, 5000, 7500 or 20000 ppm (~0, 125, 250, 375 or 1000 mg/kg-bw/day) LAB in the diet for 4 weeks. No deaths were observed. Body weights and food consumption were reduced at all exposure levels. No gross pathological changes were observed. The NOAEL was not established.

For LAB alkylate bottoms (CAS Nos 84961-70-6 and 85117-41-5) and LAB, *in vitro* bacterial reverse mutation assays (Ames test) using multiple strains of *Salmonella typhimurium* were negative for gene mutations, both with and without metabolic activation. An *in vitro* chromosomal aberration test with LAB alkylate bottom (CAS No. 85117-41-5) tested up to 80 nL/mL in Chinese hamster ovary (CHO) cells was negative with and without metabolic activation. LAB did not cause gene mutations *in vitro* in CHO cells and was not genotoxic in an *in vivo* rat bone marrow chromosome aberration test. Based on these data, LAB alkylate bottoms are considered not to be genotoxic *in vitro* or *in vivo*. No carcinogenicity data are available.

Reproductive toxicity data are available for an LAB alkylate bottoms blend and LAB. In a combined repeated-dose/reproductive/developmental toxicity screening study [OECD TG 422] with the LAB alkylate bottoms blend described above, no reproductive effects were observed at any dose up to the highest dose tested (1000 mg/kg-bw/day). Based on the lack of effects on reproduction parameters, the NOAEL for reproductive toxicity for LAB alkylate bottoms blend was 1000 mg/kg-bw/day. In a two-generation reproductive toxicity study, CD rats were given a single daily dose of LAB via gastric intubation at 5, 50 or 500 mg/kg-bw/day over a 35-week period. Evidence of toxicity was observed at the 500 mg/kg-bw/day dose level, with the most consistent effects being depressed weight gains in adults, smaller litters, fewer live pups, and decreased pup survival. At 50 mg/kg bw/day, the only effect was a temporary reduction in pup weight gain at day 7 that returned to normal at days 14 and 21. This temporary reduction occurred in one generation only, and thus was not consistent across generations. Based on decreased litter size and pup survival, the NOAEL for reproductive toxicity for LAB was 50 mg/kg-bw/day.

Developmental toxicity data are available for an LAB alkylate bottom (CAS No. 68855-24-3), the LAB alkylate bottoms blend and LAB. Pregnant Sprague-Dawley rats were administered 400, 800 and 1600 mg/kg-bw/day LAB alkylate bottom (CAS No. 68855-24-3) from gestation day 6 to day 15. On day 20 of gestation, the surviving animals were sacrificed and effects on the adults and fetuses were evaluated. No mortality was observed. Changes in maternal weight were observed at the two higher dose levels; however, no fetal effects were observed at any dose level. The NOAEL for developmental toxicity is 1600 mg/kg-bw/day. In a combined repeated-dose/reproductive/developmental toxicity screening study [OECD TG 422] with a LAB alkylate bottoms blend described above, no developmental effects were observed at the highest dose tested (1000 mg/kg-bw/day). The NOAEL for developmental toxicity was 1000 mg/kg-bw/day. Pregnant CD rats were administered 125, 500 and 2000 mg/kg-bw/day LAB on days 6 through 15 of gestation via oral gavage. Depressed maternal food consumption and weight gains were observed at 500 and 2000 mg/kg-bw/day during treatment which significantly increased in the post-treatment period. No treatment related increases were observed in soft-tissue malformations and variations; however, some skeletal variations (wavy ribs) and ossification variations were observed at the higher doses. Based on these effects, the NOAEL for both maternal and developmental toxicity was 125 mg/kg-bw/day. These results show that a minor component of the LAB alkylate bottoms exhibited reproductive/developmental toxicity at high doses; however, based on data for the LAB alkylate bottoms blend, this toxicity is not representative of the LAB alkylate bottoms mixture. Based on these screening-level data LAB alkylate bottoms are considered to have a low potential for reproductive/developmental toxicity.

The LAB alkylate bottoms possess properties indicating a low hazard profile for human health. Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD HPV Programme.

Environment

Based on studies conducted at concentrations greatly exceeding water solubility, LAB alkylate bottoms are not readily biodegradable. For C10-C14 dialkylbenzene, a major component (over 70%) of LAB alkylate bottoms, biodegradation ranged from 28-41% in 28 days and 43-54% in 48 days. These tests were conducted at concentrations higher than the water solubility of the materials and biodegradation may be more rapid at lower concentrations (as observed with LAB). Biodegradation for LAB at concentrations far exceeding the water solubility concentration ranged from 56 to 67%. Studies carried out in more natural systems (using concentrations ranging from 0.1 to 0.5 mg/L) showed LAB primary biodegradation greater than 90% with half-lives of 4-15 days. Based on structural similarities to LAB, LAB alkylate bottoms are also expected to undergo faster biodegradation at water soluble concentrations.

Level III fugacity modeling with equal and continuous distributions to air, water and soil compartments of representative LAB alkylate bottoms constituents (di- and trialkylbenzenes and diphenylalkanes) predicts predominant distribution to sediments (64-67%) and soil (28-30%) and lesser amounts to water (3.4-7.2%).

Predicted BCFs are 3.2 (estimated using EPI Suite v.3.20). In addition, because of the rapid metabolism of linear alkyl chains, LAB and LAS, and the presence in all LAB alkylate bottoms component structures of linear alkyl chains with unblocked terminal carbons, LAB alkylate bottoms are likely to show low bioaccumulation, similar to LAB and LAS.

Acute toxicity to several species of fish, *Daphnia*, and algae has been evaluated for LAB and two of the LAB alkylate bottoms. Studies conducted with fish using solvents to facilitate accurate dosing of the test media resulted in no effects at nominal concentrations up to 1000 mg/L. Similarly, new studies conducted on alkylate bottoms using water accommodated fractions (WAF) demonstrated no adverse effects at 100% WAF (loading rate = 1000 mg/L, measured = 0.024 and 0.020 mg/L). In addition to WAFs (NOECs = 0.0098 to >0.019 mg/L), studies on *Daphnia* and algae demonstrated no effects at saturation. Studies with C_{10}-LAB, the most water soluble component of LAB alkylate bottoms, show that these materials are not toxic at the limits of water solubility. ECOSAR modeling of key constituents also confirms that LAB alkylate bottoms are not predicted to be toxic at saturation The lack of acute aquatic toxicity at water soluble concentrations has been confirmed with the most water soluble component of the LAB alkylate bottoms, C_{10} LAB.

There are no chronic aquatic toxicity data on LAB alkylate bottoms. A 21-day *Daphnia* chronic study conducted on LAB indicated that reproduction and growth were affected at concentrations of 15 (LOEC) and 30 µg/L with a NOEC of 7.5 µg/L. ECOSAR-modeled LAB values are consistent with the potential for chronic toxicity below the water solubility limit. EPISuite modelling predicts that the LAB alkylate bottoms have higher Log Kows (>9.0), hence lower water solubility than LAB. Although no measured chronic toxicity data are available for LAB alkylate bottoms, these predicted data suggest that chronic effects would not be observed up to the water solubilities of the LAB alkylate bottoms. Because the LAB components make up less than 1% of the LAB alkylate bottoms, the LAB components are unlikely to produce chronic aquatic toxicity at the low water solubility of the LAB alkylate bottoms.

LAB alkylate bottoms have a low hazard profile for the environment. Adequate screening-level data are available to characterize the hazard for the environment for the purposes of the OECD HPV Programme.

Exposure

A survey of consortium members determined that total LAB alkylate bottoms production volume in 2005 in North and South America and Europe was between 50 and 100 kilotonnes. There are four primary processes by which LAB can be manufactured, and by which the LAB alkylate bottoms category co-products may be formed. In the final step of each process, the LAB alkylate bottoms are separated from the LAB by distillation. The LAB alkylate bottoms are predominantly used in non-consumer applications such as lubricating, transformer and other oils, as well as in auxiliary and marine diesel fuels and other miscellaneous uses. Some of the miscellaneous uses (e.g., car wash rust proofing, solvent cleaning bases for asphalt) may result in environmental releases to water and soil.

Occupational worker exposure is limited by engineering controls and the proper use of personal protective equipment, which are strict product stewardship requirements for LAB manufacture. For the closed system oils use (refrigeration/heat transfer fluids, transformer/dielectric oil), workers are protected from exposure by facility engineering controls for closed system processing and standard use of safety shoes, fire retardant clothing, safety glasses, gloves and other personal protective equipment (PPE). When used in auxiliary and marine diesel fuels, workers again use standard PPE to protect them from exposure. For sulfonated oil additives, the sulfonation reactions are conducted in closed manufacturing systems (reactor vessels) that are designed to limit any occupational exposure. However, given the widespread and dispersed use of these substances, proper use of PPE and other protective measures cannot be assured in all situations. Therefore, there is potential for some human (dermal and inhalation) exposure and environmental exposure.

The LAB alkylate bottoms are used primarily in closed system oils (refrigeration/heat transfer fluids, transformer/dielectric oil),, lubricating oils, marine fuels and other occupational settings. Furthermore, LAB alkylate bottoms are considered additives and thus generally make up small proportions of the final product, e.g. <1% of automobile or marine oils containing detergents. Therefore, consumer exposure to LAB alkylate bottoms is expected to be low.