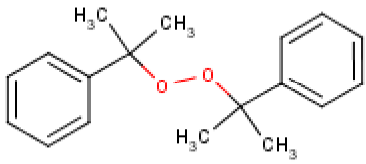
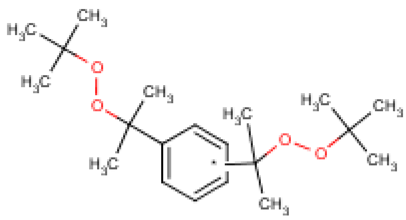
SIDS INITIAL ASSESSMENT PROFILE

Category Name	Aryl Substituted Dialkyl Peroxides
CAS No(s).	80-43-3 25155-25-3
Chemical Name(s)	1,1'-(Dioxydipropane-2,2-diyl)dibenzene (**DCUP**) [1,3(or 1,4)-Phenylenebis(1-methylethylidene)]bis[tert-butyl] peroxide (**DIPP**)
Structural Formula(s)	 80-43-3  25155-25-3

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SUMMARY CONCLUSIONS OF THE SIAR

Analogue/Category Rationale

The Aryl Substituted Dialkyl Peroxide category members are structurally similar showing trends in physical-chemical properties, ecotoxicity and similar toxicological properties. This category is defined as below:

- Physical / chemical similarity: The two materials in this category are not considered highly reactive, on a thermal or chemical basis. They are stable at neutral pH and ambient temperature. They each contain aryl and branched short chain alkyl groups with molecular weights, of 270 (DCUP) and 339 (DIPP) Daltons. They have log octanol water partition coefficients (log Kow) > 5.

- Similar structure: DCUP is composed of two isopropylbenzoyl groups and DIPP has both a substituted isopropyl benzoyl group and the *t*-butyl functional groups.

- Similar toxicological properties: Both the acute and repeated dose toxicity profiles for these materials are similar. The members of the class demonstrate low acute toxicity, little irritation, no sensitization, and are not genotoxic in *in vitro* studies. The category is adequate for the endpoints covered by this assessment however potential differences in the metabolic/degradation profiles between the two category members should be considered before extending the category rationale to other endpoints.

- Similar behaviour in the environment: The members of the class demonstrate low reactivity at neutral pH and ambient temperatures and are not expected to be highly reactive in the environment. DCUP and DIPP favour distribution to soil and sediment. DCUP and DIPP have low water solubility (<0.5 mg/L). Based on the available test data, the members of the category are not acutely toxic to aquatic organisms at the limit of water solubility, but are toxic to aquatic invertebrates on a chronic level.

Based on the chemical structures, similar physico-chemical properties and the existing toxicity information for the members of the category, read-across from DIPP to DCUP is appropriate for the human health and ecotoxicity endpoints. For DCUP, DIPP data are used as read-across for the fertility, developmental and acute fish toxicity endpoints. Hydrolysis data are not available for either category member; read across to a structurally similar alkyl substituted dialkyl peroxide is used to fill the endpoint.

Physical-chemical Properties

DCUP is a solid with a melting point of 39.8 °C (measured), a boiling point has not been determined as the substance decomposes without boiling upon heating, and a measured vapour pressure of <0.1 hPa at 60 °C. The measured octanol-water partition coefficient (log K_{ow}) is 5.6 at 25 °C, and the measured water solubility is 0.43 mg/L at 20 °C. DIPP is a solid with a melting point of 37-54 °C (measured), a boiling point has not been determined as the substance decomposes without boiling upon heating, and a measured vapour pressure (valid only for the liquid peroxides) of 0.6 hPa at 100 °C. Note that the vapour pressure of solid peroxide will be lower than the extrapolated value of the liquid. The measured octanol-water partition coefficient (log K_{ow}) is >5.5 and the measured water solubility is 0.04 mg/L, both at 20 °C.

Human Health

No toxicokinetic studies were available on the category members. Based on physical-chemical properties (e.g. water solubility and solid state), absorption would be expected to be low for DCUP and DIPP by the dermal route. Systemic effects in repeated dose studies with both substances supports absorption following oral exposure. *In vivo*, glutathione peroxidases are expected to catalyze the reduction of organic peroxides to the corresponding stable alcohols and water using cellular glutathione as the reducing agent.

Acute toxicity data with rats were available for the oral and dermal routes for DCUP and DIPP. The acute dermal LD_{50}s of the category members in rats was >2000 mg/kg bw [OECD TG 402]. The acute oral toxicity LD_{50}s of the category members in rats was >2000 mg/kg bw [OECD TG 401 or OECD TG 423]. Clinical signs of toxicity were not observed. The category members were not irritating to the skin of rabbits [OECD TG 404]; DCUP was not irritating to rabbit eyes, but DIPP was slightly irritating to rabbit eyes [both OECD TG 405]. In standard skin

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sensitization studies in mice [OECD TG 429], the substances were not considered skin sensitizers.

Repeated-dose toxicity data were available for DCUP and DIPP by the oral route of exposure in rats. In a 28-day study [OECD TG 407], 5 rats/sex were exposed to DCUP by gavage at 0, 60, 200 or 600 mg/kg bw/day for 28 days; an additional 5 rats/sex (satellite groups) in the 0 and 600 mg/kg bw/day groups were subjected to a 14 day recovery period. There was an increase in relative liver weights in both sexes, hypertrophy and degeneration of hepatocytes in both sexes, and mobilization of Kupffer cells in males observed at 600 mg/kg bw/day; there was an increase in relative liver weights in females and hypertrophy of hepatocytes in both sexes observed at 200 mg/kg bw/day. These changes were reversible during the recovery period. The NOAEL was 60 mg/kg bw/day. In a combined repeated-dose/reproductive/developmental toxicity screening test [OECD TG 422], rats (10/sex/dose) were exposed to DIPP by gavage at 0, 100, 300 or 1000 mg/kg-bw/day for 44 days (males) and ≥ 44 days (females). At 300 and 1000 mg/kg bw/day, increased relative kidney weights in both sexes, and an increased incidence and severity of hyaline droplets in proximal convoluted tubules in males was observed. The NOAEL was 100 mg/kg bw/day. In summary, the NOAELs following repeated oral exposure of the two category members are within a narrow range of 60 to 100 mg/kg bw/day.

Negative *in vitro* bacterial [OECD TG 471] and mammalian mutagenicity assays [OECD TG 476] were available for both members of the category. Both substances tested were negative for induction of bacterial and mammalian cell gene mutations. DIPP and DCUP were negative for the induction of mammalian chromosomal aberrations *in vitro* (OECD TG 473). DIPP and DCUP were not mutagenic *in vitro*.

No data are available for the carcinogenicity of the category members.

No reproductive and developmental toxicity studies were available for DCUP. Data by the oral route of exposure were available for DIPP. In a OECD TG 422 combined repeated-dose/reproductive/developmental toxicity screening test (see description of repeated-dose toxicity above for study details), effects in rats administered DIPP at 1000 mg/kg bw/day included a reduced number of pregnant dams, fewer corpora lutea, fewer implantation sites, fewer live offspring at first litter check, and a higher postnatal loss. In addition, the surviving pups at 300 and 1000 mg/kg bw/day had reduced body weight gain until day 4 post-partum. The NOAEL for maternal systemic (maternal)/reproductive/developmental toxicity is 100 mg/kg bw/day. Reproductive effects were not considered secondary to maternal toxicity. Based on these data, DCUP is expected to exhibit effects on reproductive/developmental toxicity.

The Aryl Substituted Dialkyl Peroxides possess properties indicating a hazard for human health [repeated-dose toxicity (liver or kidney effects following oral exposure) and reproductive/developmental toxicity]. Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

Hydrolysis studies were not available for the category members. However, in an OECD TG 111 study an analogous substance (an alkyl substituted dialkyl peroxide; Di-tert-butyl peroxide; CAS No 110-05-4) was stable to hydrolysis; the results of the tests at pH 4.0, pH 7.0 and pH 9.0 showed no significant degradation at 50 °C (less than 10% after 5 days). The Aryl Subsituted Dialkyl Peroxides are considered stable to hydrolysis; the molecules do not contain any functional groups sensitive to hydrolysis.

In the atmosphere, indirect photooxidation by reaction with hydroxyl radicals for DCUP and DIPP is predicted to occur with a half-life of 1.2 and 1.6 days, respectively. An OECD TG 301C study and OECD TG 301D study with DCUP resulted in 0 % and 18 % biodegradation after 28 days, respectively. An OECD TG 301D study with DIPP resulted in 0 % biodegradation after 28 days. The Aryl Substituted Dialkyl Peroxides were not readily biodegradable under aerobic conditions.

A level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments suggests that DCUP will distribute mainly to the sediment (56.6 %) and soil (39.8%) compartments with minor distribution to the water compartment (3.29%) and negligible amount in the air compartment (0.2%). Similarly a level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments suggests that DIPP will distribute mainly to the sediment (53.2 %) and soil (45.4%) compartments with minor

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distribution to the water compartment (1.2%) and negligible amount in the air compartment (0.1%). Henry's law constants have been estimated for DCUP and DIPP of 4.48 and 9.93 Pa-m^3/mole at 25 °C.

In an OECD TG 305 with DCUP, the measured BCF = 137 - 1470 (0.01 mg/L) and 181 - 667 (0.001 mg/L) suggested DCUP has a low to moderate potential to bioaccumulate in the environment. Using the Gobas model, and assuming no metabolism, the BCF for DIPP was estimated to be 45,294. With metabolism taken into account, the BCF was = 536 (hepatic blood flow only) and =209 (hepatic and arterial flow). DIPP may have the potential to bioaccumulate in the environment.

The following acute toxicity test results have been determined for aquatic species:

Fish, acute toxicity		
DCUP	Read Across from DIPP	
DIPP	[*Poecilia reticulata*] 96 h LC_{50} >water solubility*	nominal; semi-static
Invertebrate, acute toxicity		
DCUP	[*Daphnia magna]* 48 h EC_{50} >0.0.397*	measured; semi-static WAF
	[*Daphnia magna]* 48 h EC_{50} >water solubility*	measured; static
DIPP	[*Daphnia magna*] 48 h NOELR = ≥ 0.0219 mg/L	measured; static, highest concentration tested
Algae, acute toxicity		
DCUP	[*Pseudokirchneriella subcapitata*] 72 h ErC_{50} >water solubility* 72 h EbC_{50} >water solubility* NOECr > water solubility*	nominal
	[*Pseudokirchneriella subcapitata*] 72 h ErC_{50} >water solubility* 72 h EbC_{50} >water solubility* NOECr, NOECb > water solubility*	nominal
DIPP	[*Pseudokirchneriella subcapitata*] 72 h ErC_{50} >water solubility* 72 h EbC_{50} >water solubility*	measured
Chronic toxicity		
DCUP	[*Daphnia magna*] 21d EC_{50} reproduction = 0.231 mg/L 21d NOEC = 0.117 mg/L	measured; static renewal; based on average cumulative number of brood

*No effects at or below water solubility 0.43 mg/L at 20°C for DCUP and 0.04 mg/L at 20°C for DIPP

The Aryl Substituted Dialkyl Peroxides possess properties indicating a hazard for the environment (acute aquatic toxicity is not likely to occur at or below the water solubility of the substance, and chronic aquatic toxicity less than 1.0 mg/L for aquatic invertebrates). The substances are not readily biodegradable and have the potential to bioaccumulate. Adequate screening-level data are available to characterize the hazard to the environment for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

Worldwide production of DCUP was estimated to be approximately 10-50 kilo tonnes in year 2010. In the sponsor country (United States), the production of DIPP in 2005 was 1-10 million pounds (450 - 4500 tonnes). Worldwide production of DIPP was estimated to be approximately 1-10 kilo tonnes in year 2010. The dialkyl peroxides are most typically used as intermediates. The dialkyl peroxides have industrial uses. DCUP is used for the (co)polymerization of styrene and is used in the production of polyolefins and acrylics. It may also be used as a co-agent in the production of flame retardant, expandable polystyrene, and in the crosslinking of silicone materials. DIPP peroxide is used as an initiator (radical source) for the crosslinking of polymers above 170°C,

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including the crosslinking of polyethylene or rubber (ethylene propylene diene monomer, ethylene-vinyl acetate).

Potential releases to the environment (expected to be limited) and industrial worker exposure may occur during manufacture (open and closed systems), use and spills. The Aryl Substituted Dialkyl Peroxides may be used in products used for food contact. The US Code of Federal Regulations (Title 21) specifies that the use of these compounds in food contact products is not to exceed 1.5%.

During manufacturing processes in which Aryl Substituted Dialkyl Peroxides are used, the process materials are typically held at a thermal decomposition temperature for many half-lives. These products are typically incorporated at a use rate of 0.1-3% before heat exposure. However, after processing with heat exposure (e.g., extrusion or vulcanization), negligible quantities of the Aryl Substituted Dialkyl Peroxides remain. Thus, exposure to the consumer is also expected to be negligible.

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