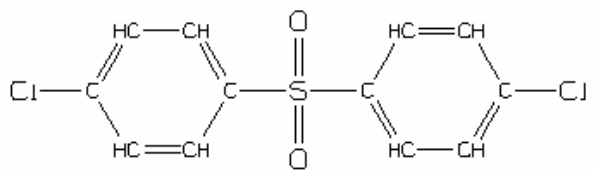
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	80-07-9
Chemical Name	4,4'-Dichlorodiphenyl sulfone
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Physical-chemical properties

4,4'-Dichlorodiphenyl sulfone (DCDPS) is manufactured as an off-white powder or as solid pellets. Based on EPI Suite (version 3.20) calculations it has a melting point of 146 °C and a boiling point of 390 °C. The calculated vapour pressure at 25° Celsius was low (1.08E-06 hPa). The measured water solubility (at 20° Celsius) of DCDPS is 0.86 mg/l, while the measured log K_{ow} (at 22° Celsius) is 3.9.

Human Health

The fate of uniformly ^{14}C labeled DCDPS has been studied, in rats, both after intravenous administration and after repeated oral exposure. Based on the results the substance is readily absorbed from the gastrointestinal tract, distributed to all tissues examined, concentrated in adipose tissue mainly as parent compound, and reached steady state after ~2 weeks. Excreted DCDPS equivalents were primarily present as metabolites. Five metabolites have been found and two of these were identified: 3-hydroxy-4,4'-dichlorodiphenyl sulfone and its glucuronide.

The acute oral LD_{50} (rat) was higher than 2000 mg/kg bw. Valid acute toxicity studies, using dermal or inhalation exposure, were not available.

No valid irritation or sensitisation studies were available.

Data from five valid dietary repeated dose studies, including one chronic study on rats and one chronic study on mice, are available. The rats, in the chronic study, were exposed to DCDPS via the diet during 105 weeks and the mice during 105-106 weeks. Based on the results from these chronic studies, an overall No Observed Adverse Effect Level (NOAEL) of 1.5 mg/kg bw/day was established for repeated dose toxicity. The NOAEL is based on liver effects e.g. centrilobular hepatocyte hypertrophy, bile duct hyperplasia and centrilobular degeneration identified in chronic studies. Decreased body weight, increased liver and kidney weight, increased incidence of nephropathy and decreased thymus weight were other effects that were evident at higher doses. During a 28-day study on rats, a slight enzyme induction in the liver was observed at a dose of 0.8 mg/kg bw/day but with no marked liver weight increase or other effects apparent. This slight enzyme induction, without any other corroborative effects is, in this case, not considered as an adverse effect.

DCDPS did not induce gene mutations in bacterial assays. In studies with mammalian cells, weak responses (1.7 to 3.1 fold vehicle control values) were obtained in the mouse lymphoma L5178Y assay without S9. The study was conducted according to GLP and OECD Guideline 476. The result of the sister chromatid exchange study in CHO cells was equivocal in the absence of S9 and negative in the presence of S9. In a HGPRT gene mutation assay with Chinese hamster ovary (CHO) cells DCDPS was negative in both the absence and presence of metabolic activation (S9). In a chromosomal aberration test with CHO cells, no induction of chromosomal aberrations, in presence and absence of S9, was observed. Based on these results it is concluded that the mutagenicity of DCDPS is equivocal *in vitro*. *In vivo*, positive results were obtained in a mouse bone marrow micronucleus study after repeated i.p. injection over a dose range of 200 to 800 mg/kg bw/day. In this study, the positive results were confirmed in a second experiment. In another study, negative results were obtained after a single i.p. injection of up to 1960 mg

DCDPS/kg bw. However, in this study the bone marrow might not have been sufficiently exposed. During an Unscheduled DNA Synthesis (UDS) assay, done according to OECD Guideline 486, DCDPS did not cause DNA damage in the rat. From these results it can be concluded that DCDPS is mutagenic *in vivo*.

Two carcinogenicity studies, performed according to currently accepted guidelines and GLP standards, are available for rat and mouse (see paragraph on repeated dose toxicity). In these 2-year studies, there were no increases in the incidences of neoplasms in the liver or any other organ in rats or mice, which were related to DCDPS exposure. From these studies it can be concluded that DCDPS is not a carcinogen.

An oral reproduction/developmental toxicity screening test has been performed according to GLP and OECD Guideline 421. The daily administration of DCDPS to rats by gavage at dose levels of 5, 15 and 50 mg/kg bw/day resulted in centrilobular hepatocyte hypertrophy and liver enlargement in adult animals of either sex from all treatment groups. The dose of 5 mg/kg bw/day is regarded as a Lowest Observed Adverse Effect Level (LOAEL) based on liver effects, for adult toxicity. During repeated dose studies liver effects were also observed and used for establishment of the NOAEL. The results of the reproduction/developmental toxicity screening test revealed no effects on fertility or developmental toxicity and therefore the highest dose of 50 mg/kg bw/day was regarded as NOAEL for fertility and developmental toxicity. A reduction in bodyweight gain was observed in offspring from rats treated with 50 mg/kg bw/day but maternal toxicity was evident at this dose level. Histological examinations of the reproductive organs during the reproduction/developmental toxicity study and during four valid repeated dose studies did not reveal any effects on the reproductive organs. It can be concluded that DCDPS has neither an effect on developmental toxicity nor on fertility.

Environment

The substance is considered to be hydrolytically stable based on an expected half-life greater than one year at 25°C. DCDPS is not readily biodegradable. EPI Suite (version 3.20) was used to calculate the rate of photodegradation of DCDPS. The half-life was calculated to be 18 days based on a mean hydroxyl radical concentration of 1.5×10^{6} OH-radicals $\cdot$ cm^{-3} over a 12-hour day. A level III fugacity model calculation, using a four compartment (air, water, soil and sediment) model has been conducted using EPI Suite version 3.20. An emission of 1.0 kg/h in the water compartment was hypothesized. Based on the results of the calculation, DCDPS is expected to partition to the aquatic compartment (80.8 %) with the remainder to sediment (18.9 %), soil (0.259 %) and air (0.00354 %). An emission of 1.0 kg/h to the soil compartment results in a partition to the soil compartment (99.7 %) with the remainder to water (0.221 %), sediment (0.0518 %) and air (0.00149 %). EPI Suite (version 3.20) calculations revealed a bioconcentration factor of 201. Measured BCF for fish of 75 and 82 (*Cyprinus carpio*) have been reported. There are, however, indications of biomagnification of DCDPS in air breathing organisms.

Aquatic ecotoxicity tests, which were performed according to GLP and standard guidelines, are available for fish, water fleas and algae. No mortality or effects on behaviour and general appearance were observed in a 96 hour limit test, performed at the water solubility limit, with zebra fish (*Brachydanio rerio*) at mean measured concentration of 0.98 mg/l. The acute EC_{50} (48 h) for water fleas (*Daphnia magna*) was > 0.93 mg/l. The NOEC (21-day) for the water flea (*Daphnia magna*) for reproduction was calculated to be 0.32 mg/l. The EC_{50} (72 h) based on biomass and growth rate for the algae (*P. subcapitata*) was > 0.80 mg/l. The NOEC (72 h) was 0.28 mg/l based on biomass. The LOEC was 0.49 mg/l which resulted in a biomass inhibition of 18 %. Terrestrial toxicity tests are not available for DCDPS.

Exposure

DCDPS is manufactured by Solvay in the USA and in India. The substance is also manufactured in the United Kingdom by Seal Sands Chemicals Ltd. The total production of these companies was estimated to be less than 18,000 tonnes in 2006.

DCDPS is manufactured also by other companies in China, India and the Russian Federation but the amount manufactured and the uses are unknown. However, Solvay is assumed to be the largest manufacturer of DCDPS. The information given below, regarding manufacturing and use, is based on data from the two Solvay production sites mentioned above.

DCDPS is used as starting material in the production of polysulfones, polyethersulfones and polyphenylsulfones. These polymers are a family of thermoplastics known as engineering plastics and are used in high-temperature applications. The polymers, which are thermally and chemically resistant, are used as coating on metals, as containers for holding food during heating or cooking and as components of food processing machinery and equipment. Recent analytical measurements showed that the residual

amount of DCDPS in these polymers ranged from 1.7 to 79 µg/g.

The majority (> 80 %) of DCDPS, produced by Solvay, is also polymerized by Solvay but it is also sold and transported in bulk quantities to customers (downstream users). However, for Solvay the global number of downstream users is limited (< 5). The downstream users of DCDPS are also using it for the production of polysulfones, polyethersulfones and polyphenylsulfones.

In Europe DCDPS has been detected both in the aquatic environment and in fish (1.8 – 190 ng/g fat), birds (5.2-2600 ng/g fat) and seals (21-700 ng/g fat) from the Baltic Sea. Based on a review of the available data from the Baltic region, it was suggested that DCDPS has a more local distribution than the more well-known long-range distributed PCB and DDT. The reason proposed was less distribution of DCDPS than of the POPs by the air pathway. A decreasing trend of the presence of DCDPS in the Baltic environment, as expressed in eggs of guillemot, could indicate historical sources to the contamination. However, the slow decrease of 1.6 % per year between 1971 and 2001 for DCDPS make ongoing emissions from current unknown uses seeming likely in the Baltic environment.

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

Human Health

The chemical is a candidate for further work. The chemical has properties indicating a hazard for human health (mutagenicity, repeated dose toxicity). Member countries are invited to perform an exposure assessment for workers, and if necessary a risk assessment.

Environment

The chemical is a candidate for further work. The chemical has properties indicating a hazard for the environment (, chronic toxicity to algae and to aquatic invertebrates between 0.1 -1 mg/l, lack of ready biodegradability and potential for persistency) and a potential for bioaccumulation. Member countries are invited to perform an exposure assessment for the environment, and if necessary a risk assessment.