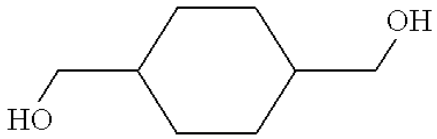
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	105-08-8
Chemical Name	1,4-Cyclohexanedimethanol
Structural Formula	*cis and trans* form 

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Following uptake of 1,4-Cyclo[^{14}C] hexanedimethanol (70% trans, 30% cis-isomers) via oral gavage in Sprague-Dawley rats, it is converted into the cyclohexanedicarboxylic acid and the 4-hydroxymethylcyclohexanecarboxylic acid. 1,4-Cyclohexanedimethanol was rapidly absorbed, and 95% was excreted in urine. The *cis-trans* ratio remained as it was. The elimination half life of this chemical in plasma was approximately 3 min.
The acute oral LD_{50} of 1,4-Cyclohexanedimethanol in rats ranged between 3200 and 6400 mg/kg bw. Slight prostration and vasodilatation were noted in treated animals. For acute dermal toxicity [OECD TG 402] the LD_{50} in rats was >2000 mg/kg bw. No clinical signs were reported. No human data on acute toxicity are available. No studies are available for acute inhalation toxicity.

No reliable skin/eye irritation or skin sensitization data are available.

In a repeated dose oral toxicity study in rats according to the OECD TG 408, 1,4-Cyclohexanedimethanol was administered via drinking water to 12 males and 10 females per dose at 0, 256, 479, 861 mg/kg (males) and 0, 440, 754, 1754 mg/kg (females) for 13 weeks. Death (one male and one female) and clinical effects like bloody or brown/red discolored urine, softened or reduced feces, and reductions in body weights were observed in males and females at 861 and 1754 mg/kg bw respectively. The mean body weight for male rats was significantly lower for 861 mg/kg bw treated group when compared to that of control group ($p<0.05$). Based on clinical effects, the NOAELs of the study were considered to be 479 mg/kg bw for males and 754 mg/kg bw for females.

In a bacterial reverse mutation assay with multiple strains of *Salmonella typhimurium*, 1,4-Cyclohexanedimethanol was negative both with and without metabolic activation [OECD TG 471 and 471-like]. An *in vitro* chromosomal aberration test in Chinese hamster lung (CHL/IU) cells was negative with and without metabolic activation [OECD TG 473]. In addition, this chemical did not induce significant increase in cells with chromosome aberrations or polyploidy, or endoreduplication in the rat bone marrow cells *in vivo* according to the OECD TG 475. The available information from genetic toxicity tests suggests that 1,4-Cyclohexanedimethanol is not genotoxic *in vitro/in vivo*.

No data are available for the carcinogenicity of 1,4-Cyclohexanedimethanol.

The reproductive toxicity of 1, 4-Cyclohexanedimethanol has been investigated in a reproductive and developmental toxicity screening test in rats [OECD TG421]. In this study, 1,4-Cyclohexanedimethanol was administered via drinking water to 12 males and 12 females per dose at 0, 256, 479, 861 mg/kg (males) and 0, 385, 854, 1360 mg/kg (females) for 13 weeks. 4 of 11 male rats exposed to 861 mg/kg bw had reduced sperm motility without statistical significance compared to the control group (the mean percent value was 69% for treated group and 90% for control group). However, this decrease did not induce any difference in fertility. Brown/red discoloured urine was observed in 5 of 12 male and 6 of 12 females dosed at 861 and 1360 mg/kg bw respectively. The NOAELs for this effect were considered to be middle dose (479 mg/kg bw for males and 854 mg/kg bw for females). The mean body weight for litters from dams on day 0 post partum and of pup survival from Day 0 to Day

4 (75.8% for treated group and 97.6% for control group) were lower than those for control group at 1360 mg/kg bw. There was no effect observed upon haematological, clinical biochemistry or histopathological examination at any dose. Based on decreases in sperm motility and survival of pups from dams, the LOAEL and NOAEL for reproductive/developmental toxicity were considered to be 1360 and 854 mg/kg bw, respectively. Fetotoxicity and maternal toxicity were only observed at the highest dose of 1360 mg/kg. This dose is in excess of the 1000 mg/kg bw limit dose recommended in the OECD TG 421. Overall, 1,4-Cyclohexanedimethanol is considered not to be a reproductive/developmental toxicant.

Environment

1,4-Cyclohexanedimethanol is a white solid with a melting point of 43°C (*cis*) and 67°C (*trans*), a boiling point of 286 °C (*cis*) and 283 °C (*trans*) and a measured vapour pressure of 0.041 Pa at 25 °C. The calculated *n*-octanol-water partition coefficient (log K_{ow}) is 1.49, and the water solubility is 920,000 mg/L at 20 °C.

1,4-Cyclohexanedimethanol did not hydrolyze under acidic, neutral or basic conditions after a 5-day period at 50 ºC. In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 0.5 days. 1,4-Cyclohexanedimethanol attained significant degradation (98% in 19 days) in an inherent biodegradation test conducted according to OECD test guideline 302B. No information is available on the ready biodegradability of the chemical.

Level III fugacity model with equal and continuous distributions to air, water and soil compartments suggests that 1,4-Cyclohexanedimethanol will distribute mainly to the soil (70 %) and water (29.8%) compartments with minor distribution to the air (0.081%) and sediments compartment (0.07 %). If released only to the water compartment, 1,4-Cyclohexanedimethanol stays in the water compartment (99.8 %) with negligible amounts in other compartments. A Henry law's constant of 4.13 x 10^{-9} $Pa.m^3$/mole at 25 °C suggests that volatilization of 1,4-Cyclohexanedimethanol from the water phase is expected to be moderate. A K_{oc} of 10 was estimated based on the log K_{ow}.

Bioaccumulation potential is expected to be low based on the Log K_{ow} of 1.49, which is supported by an estimated BCF value with BCFWIN v. 2.17 of 2.8.

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

Fish [*Oryzias latipes*];	96 h LC_{50} > 100 mg/L nominal concentration
Fish [*Pimephales promelas*];	96 h LC_{50} > 120 mg/L nominal concentration
Invertebrate [*Daphnia magna*]	48 h LC_{50} > 100 mg/L nominal concentration
Algae [*Pseudokirchneriella subcapitata*]	72 h ErC_{50} >120 mg/L nominal concentration
Algae [*Pseudokirchneriella subcapitata*]	72 h EbC_{50} >120 mg/L nominal concentration

1,4-Cyclohexanedimethanol is of low acute toxicity to aquatic organisms (fish, aquatic invertebrate and algae).

Exposure

1,4-Cyclohexanedimethanol is commercially produced with an annual production volume of 11,000 tonnes in the Republic of Korea (2007). Worldwide production volume is not available. 1,4-Cyclohexanedimethanol is used for polyester films and protective coatings. The substance is an intermediate reactant, promoting reduction of reaction time in esterification for polymers industry and any left over from the process will be collected.

No monitoring data for effluents or surface water are available from the production and processing sites in the sponsor country. Occupational exposures are expected to be minimal due to the processing in closed system and personal protective equipments.

1,4-Cyclohexanedimethanol is used as intermediate reactant, and there is therefore no known inclusion of the substance in final products. Therefore, the possibility of exposure for consumer is negligible.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human health:

The substance is of low priority for further work due to its low hazard potential.

Environment:

1,4-Cyclohexanedimethanol is currently of low priority for further work due to its low hazard profile.