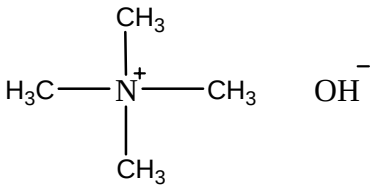
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	75-59-2
Chemical Name	Tetramethylammonium hydroxide
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Tetramethylammonium hydroxide (TMAH) is completely dissociated in the body of animals due to its strong alkaline property, forming tetramethylammonium (TMA) ion. TMA administered to the intestine was rapidly absorbed in rats and most of the absorbed dose was excreted unchanged via the urinary route.

The dermal LD_{50} value in female rats was 112 mg/kg bw. The oral LD_{50} value in male rats was between 34 and 50 mg/kg bw [OECD TG 401]. TMAH administered dermally or orally caused, variously, a decrease in locomotor activity, an ataxic gait, hypothermia, incomplete eyelid opening or eyelid closure, salivation, irregular respiration, bradypnea and clonic convulsions. There are no data available for acute inhalation toxicity of TMAH.

The substance is reasonably considered to be strongly irritating or corrosive to the skin and the eye of animals due to its strong alkaline property. There are no test results available for skin or eye irritation of TMAH. There are no data available for sensitisation of TMAH.

In a repeated dose dermal toxicity study, rats were exposed for 4 weeks (6 hours/day, 5 days/week) to TMAH at doses of 0, 5.5, 50, 120 and 250 mg/kg bw/day in male rats and 0, 2.5, 5.5, 10 and 50 mg/kg bw/day in female rats. In addition to erythema, edema and/or scabbing observed at the application sites in all of the treated animals, red ovaries were observed in female rats at 5.5, 10 and 50 mg/kg bw/day, and red lungs, urinary bladder calculus, dark eye and small seminal vesicles in male and/or female rats at 50 mg/kg bw/day. Based on these findings, the NOAELs for repeated dose dermal toxicity were considered to be 5.5 mg/kg bw/day in male rats and 2.5 mg/kg bw/day in female rats. In a repeated dose oral toxicity study in rats [OECD TG 407], TMAH was administered by gavage to male and female rats (5 or 10 animals/sex/group) for 28 days at doses of 0, 5, 10 and 20 mg/kg bw/day. No deaths were observed in either sex. In male rats, decreases in food consumption and relative heart weight were also observed at 10 and 20 mg/kg bw/day. In female rats, decreases in food consumption were also observed at 20 mg/kg bw/day. There was no effect observed on haematological, clinical or histopathological examination at any doses. Based on decreases in food consumption and relative heart weight, the NOAEL for repeated dose oral toxicity was considered to be 5 mg/kg bw/day in males and 10 mg/kg bw/day in females. There are no data available for repeated dose inhalation toxicity of TMAH.

A bacterial reverse mutation assay [OECD TG 471] on TMAH was negative with or without metabolic activation. An *in vitro* chromosome aberration test using CHL/IU cells [OECD TG 473] was also negative with or without metabolic activation. Although there is no study available for *in vivo* mutagenicity on TMAH, the chemical is considered to be not mutagenic based on negative outcomes in *in vitro* assays.

There are no data available for carcinogenicity of TMAH.

In a reproductive/developmental toxicity screening test in rats [OECD TG 421], TMAH was administered by gavage at doses of 0, 1, 5 and 20 mg/kg bw/day. No effect of TMAH was observed on any reproductive or

developmental parameters up to 20 mg/kg bw/day, the highest dose tested, while some toxic effects on parental animals (a decrease in food consumption, a decrease in locomotor activity) were observed at 20 mg/kg bw/day. Thus the NOAEL for reproductive/developmental toxicity was considered to be 20 mg/kg bw/day in rats.

Environment

TMAH has a water solubility of 1,000 g/l (estimated), a vapour pressure of 1.55 x 10^{-6} hPa (estimated), and a log Kow of -2.47 (estimated). Although an estimated Koc of 20.7 indicates a relatively low potential of the substance for adsorption onto soil and sediment, there is a possibility that TMA ion is adsorbed more than expected. A melting point for TMAH pentahydrate is 63°C.

A half life of TMAH by reaction with OH radicals in air was calculated to be 2.1 days (50.7 hr). TMAH has a strong alkaline property and is readily dissociated in water, forming TMA and hydroxyl ions. These physico-chemical properties indicate that TMAH is mainly distributed into the water compartment in the forms of TMA and hydroxyl ions in the environment. In a biodegradation test [OECD TG 301C], TMAH is readily biodegradable (BOD 96% after 14 days; the 10-day window was met). A bioconcentration factor of TMAH was calculated to be 3.16, indicating that the bioaccumulation potential of the substance is low.

The acute toxicity of TMA ion to fish was studied with tetramethylammonium chloride (TMAC) as a test substance, resulting in a value of 462 mg/l for the 96-hr LC_{50} in *Pimephales promelas*. Using the molecular weights of TMAH (91) and TMAC (109), this value is converted to 359 mg/l TMAH, indicating that the toxicity of TMA ion to fish is very low. The acute toxicity of TMAH to invertebrates was studied in *Daphnia magna*, resulting in a value of 3 mg/l for the 48-hr EC_{50} (pH7.6-9.5). Other studies conducted with *Ceriodaphnia dubia* gave 48-hr LC_{50} values of 1.3-1.5 mg/l for neutralized TMAH. These results demonstrate that the observed toxicities relate to the TMA ion and are not affected by pH deviations. The acute toxicity of TMAH to aquatic plants was studied in *Pseudokirchneriella subcapitata*, resulting in 72-hr EC_{50} values obtained on the basis of biomass and growth rate of 13 and 96 mg/l, respectively (pH8.2-11.2).

Chronic toxicity to invertebrates and algae has also been studied. The NOEC of TMAC regarding three brood survival and reproduction in *Daphnia magna* was 0.03 mg/l (converted to 0.02 mg/l TMAH using molecular weights of TMAH (91) and TMAC (109)), showing that TMA ion exerts strong chronic effects on daphnids. 72-hr NOECs of TMAH obtained on the basis of biomass and growth rate in *Pseudokirchneriella subcapitata* were 0.39 and 6.3 mg/l, respectively. No chronic toxicity data on fish are available.

Exposure

The annual production volume of TMAH in Japan was approximately 3,000 tonnes in 2004. The chemical is also produced in the United States and Korea while no data are available on the production volumes in these countries. All of TMAH is used for photolithography processes of semiconductors and liquid crystal panels (>97%) and electronic parts cleaning (<3%).

TMAH is produced in a closed system by electrolysis of aqueous solutions of TMAC or tetramethylammonium carbonate and is distributed to the market as aqueous solutions at various concentrations. In the Sponsor country, there is no process that generates wastewater at the production and formulation sites. Waste residues are derived only from containers and annual maintenance of plants. They are incinerated or biologically treated. Therefore, the release of TMAH into the environment from its manufacturing and formulation plants is minimal. At the user sites, several emission routes of TMAH after use were identified although no detailed information is available on each route. Therefore, the possibility is not excluded that some portion of TMAH used is released into the environment from user sites.

The monitoring data revealed that the TMAH concentrations in workplace atmospheres at a production site were minimal. In addition, workers are obliged to use personal protection equipments such as mask, safety glasses, gloves and protective garment. Thus the actual levels of occupational exposure to the substance via the dermal and inhalation routes are anticipated to be negligible. At the user site, TMAH is treated in a closed system. Although disposal of TMAH solution is the only process that might cause occupational exposure, such occupational exposure levels are considered to be negligible because of the low volatility of TMAH. Furthermore, workers use personal protection equipments such as masks, safety glasses, gloves and protective garment during operations.

Considering that TMAH is only used in the electronics industry as developers or cleaners and is completely washed away from the end products, such as semiconductors, liquid crystal panels and electronic parts, consumer exposure is also anticipated to be negligible.

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

Human Health: The chemical possesses properties indicating a hazard for human health (acute toxicity, corrosiveness and repeated dose toxicity). Based on data presented by the Sponsor country (relating to production in one country which accounts for an unknown fraction of the global production volume and relating to the use pattern in one country), exposure to humans is anticipated to be low, and therefore, this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by Sponsor country.

Environment: The chemical has properties indicating a hazard for the environment (acute aquatic toxicity EC/LC50 values between 1 and 100 mg/l). However the chemical is currently of low priority for further work for the environment because of its rapid biodegradation and its limited potential for bioaccumulation.