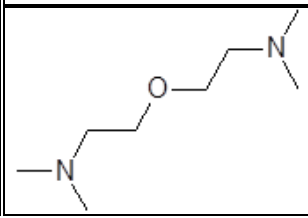
SIDS INITIAL ASSESSMENT PROFILE

CAS No(s).	3033-62-3
Chemical Name(s)	Ethanamine, 2-oxybis[N, N-dimethyl]- (DMAEE)
Structural Formula(s)	

SUMMARY CONCLUSIONS OF THE SIAR

Physical-chemical Properties

2-Oxibis[N,N-dimethyl]ethanamine (DMAEE) is a liquid with a melting point of -80 °C (measured), a boiling point of 189.9 °C at 1013 hPa (interpolated from vapor pressure curve) and a vapor pressure of 0.49 hPa at 20 °C (extrapolated from vapor pressure curve). The calculated water solubility (from K_{ow}) is 1000 g/L at 25 ^{o}C and the calculated octanol-water partition coefficient (log K_{ow}) is -0.54 (uncharged molecule). The estimated pKa values for the protonated form of DMAEE in water are 9.77 and 8.19 at 20 °C.

Human Health

Studies with rats and rabbits indicate DMAEE is rapidly absorbed following dermal or inhalation exposure. It is eliminated, largely unchanged, primarily in the urine. In rats, 53-58% or 24% is eliminated in urine as a percent of inhalation concentration or dermal dose, respectively. Some distribution to organs and tissues (ca. 6.4-8% in the liver, kidney, bone marrow, brain, fat (perirenal), heart, lung, muscle, spleen and testes/ovaries) was also seen after dermal exposure; up to 1% was distributed to tissues after inhalation. Based on the intravenous studies, the elimination half-life for DMAEE is ~13-14 hours in the rats, and 24-40 hours in the rabbit.

The 4-hour aerosol inhalation LC_{50} for DMAEE with male and female rats is 4 mg/L [BASF standard method]; the 6 hour vapor inhalation LC_{50} for DMAEE with male and female rats is 1.088 mg/L [similar to OECD TG 403]. Signs of toxicity were predominantly associated with site of contact effects (including respiratory changes, eye and nose irritation or corrosion), and hypoactivity. In one inhalation study, piloerection and effects on posture and gait were also seen. There were no findings at gross necropsy for surviving animals in either acute inhalation study. Site of contact effects (irritation/inflammation of the respiratory tract) was observed in animals that died (both studies). The dermal LD_{50} for rabbits was ca. 315 mg/kg bw (24 hours, undiluted test substance); severe skin necrosis was noted at the site of application [similar to OECD TG 402]. Other effects following dermal contact included hypoactivity and altered gait/posture. Also, in males in one study, dyspnea and mottled, red lungs in both sexes were the most common observations at necropsy. Oral (gavage) LD_{50} values for DMAEE range from 609 - 677 mg/kg bw (male and female rats) [OECD TG 401] up to 1045 mg/kg bw (male rats) [no guideline specified]. Clinical findings included hypoactivity, gasping/shortness of breath, ataxia, prostration, emaciation and unkempt fur. In one oral study, necropsy findings included pulmonary congestion and petechiae, gastric hemorrhages and liver congestion.

Neat DMAEE is corrosive when applied to the skin of rabbits [e.g., OECD TG 404]. It is injurious to eyes after direct instillation of undiluted and 10-15% aqueous solutions or irritating to the eye following whole body inhalation [no guideline specified]. Slight (marginal) increases in corneal thickness continued throughout the post-exposure period. It is also irritating to the respiratory tract in acute inhalation studies [similar to OECD TG 403].

DMAEE was not sensitizing in a standard guinea pig sensitization study [EU Method B.6]. In patch tests in humans who had symptoms of contact dermatitis, DMAEE has been associated with some allergic responses.

Rats (15/sex/group) were exposed to DMAEE by inhalation at 0, 0.22, 1.25 or 5.8 ppm (ca. 0, 0.0014, 0.008 or 0.036 mg/L, respectively) 6 hrs/day, 5 days/wk for 14 weeks. A 6-week recovery period was also included. Signs of ocular and respiratory irritation included swollen periocular tissue at all exposures and periocular and perinasal encrustation, cloudy eyes, and keratitis at 5.8 ppm. Color changes or opacity of the eyes were observed in one male and six females from the 5.8 ppm group, but were not present after 6 weeks of recovery. Microscopic lesions involving the eyes, nostrils, skin of the ears and eyelids, larynx, trachea, and lungs (bronchi and bronchioles) were seen at the highest exposure. The size and number of vacuoles in the mucosal epithelium increased with the duration of exposure. Decreased body weight was observed at the highest exposure. Urinalysis showed slight decreases in creatinine, sodium, potassium, and chloride at 5.8 ppm for both sexes. Changes in hematology and clinical chemistry were also noted at the highest concentration. Significant increases in male adrenal and testes weights relative to both body and brain weights were observed at 5.8 ppm, but no accompanying changes in histopathology were seen. Effects observed at the end of the recovery period included swollen periocular tissue (1.25 and 5.8 ppm) and microscopic lesions of the nasal cavity (all exposure groups). The LOAEC (for local effects) was determined to be 0.0014 mg/L due to various signs of irritation of the eye and respiratory tract at all concentrations. The NOAEC for systemic effects for males was 0.008 mg/L based on decreased body weights and changes in urinalysis at 0.036 mg/L. The NOAEC for systemic effects for females was 0.036 mg/L, the highest concentration tested.

Rabbits (10/sex/dose) were administered DMAEE in water dermally (under occlusive cover) at 0, 0.69, 2.0 or 5.3 mg/kg bw/day for 6 hrs/day, 5 days/wk for 13 weeks [no guideline was specified]. There were no signs of systemic toxicity. Skin irritation in both sexes included erythema, desquamation, edema and fissuring in a dose-response manner. Epidermal vacuolization occurred at 2 and 5.3 mg/kg bw/day and acanthosis occurred at all doses in both sexes with increasing severity. In most cases, the skin irritation effects were reversible during the recovery period. The NOAEL (systemic) was 5.3 mg/kg bw/day (highest dose tested). For local effects (based on dermatitis/skin irritation) the LOAEL was 0.69 mg/kg bw/day. In a nine-day dermal study in rats, skin irritation and necrosis was seen at all doses (7.1-9.2 mg/kg bw/day and higher); degeneration of the tubular epithelium and dilation of tubules was seen in the kidney at 5 and 10% dose (14-18 mg/kg bw/day and 28-37 mg/kg bw/day, respectively).

DMAEE has shown no evidence of mutagenicity *in vitro*, in the Ames bacterial test (similar to OECD TG 471) and the mammalian cell HGPRT assay (guideline not specified). A sister chromatid exchange assay with CHO cells gave equivocal results, while there was no evidence of genotoxicity in an *in vivo* mammalian erythrocyte micronucleus test (similar to OECD TG 474). The weight of evidence suggests that DMAEE is not genotoxic.

No data were available for the carcinogenicity of DMAEE.

Repeated inhalation exposure (14 weeks) of DMAEE by rats at concentrations of 0, 0.0014, 0.008 or 0.036 mg/L (measured) resulted in increased relative testes weights but no histopathological changes. There were no reproductive organ effects in female animals. Effects on reproductive organs were not observed in a 90-d repeated dose dermal study with rabbits. In a prenatal developmental toxicity study [no guideline specified], pregnant rabbits were exposed to DMAEE at ca. 0, 2.4, 12 or 24 mg/kg bw/day in water via the dermal route for 6 hrs/day from gestation days 6 through 18. The NOAEL for maternal systemic and local toxicity was ca. 2.4 mg/kg bw/day based on renal lesions and severe skin effects, respectively, at higher doses. The NOAEL for developmental toxicity was ca. 12 mg/kg bw/day based on decreased mean litter weight at 24 mg/kg bw/day.

DMAEE possesses properties indicating a hazard for human health (acute inhalation, oral and dermal toxicity; corrosive or irritating to the skin, eye and respiratory tract; repeated dose toxicity (site of contact and systemic effects); developmental effects at maternally toxic concentrations). Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

DMAEE is expected to be hydrolytically stable in the natural environment since it doesn't contain any functional group susceptible to hydrolysis. In the atmosphere, indirect photooxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 0.61 hours. In an OECD TG 302B inherent biodegradability study using activated sludge from an industrial wastewater treatment plant. DMAEE degraded <10% after 28 days. In a ready biodegradability study similar to OECD TG 301 F, DMAEE degraded 2% in 28 days. DMAEE is 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 DMAEE will distribute mainly to the soil (67.1%) and water (32.8%) compartments with minor distribution to the air and sediment compartments (<0.1%). It should be noted, however, that EPISuite predicts most environmental fate endpoints for DMAEE in its uncharged form. Therefore, there will be some differences between predicted and actual results. A Henry's law constant of 3.79 x 10^{-10} Pa-m^3/mol (Bond Estimate) and 1.21 x 10^{-5} Pa-m^3/mol (Group Estimate) at 25 °C suggests that volatilization of DMAEE from the water phase is not expected to be high. The model estimate is for the uncharged molecule. DMAEE is not expected to bioaccumulate in the aquatic environment based on an estimated BCF value of 3.16 L/kg wet-wt.

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

Fish [*Brachydanio rerio*]	96 h LC_{50} = 131 mg/L (nominal concentrations confirmed by measured values; semi-static; unbuffered, pH 8.4 to 9.8)
Invertebrate [*Daphnia magna*]	48 h EC_{50} = 102 mg/L (measured; static; buffered, pH 7.7-7.9)
Algae [*Pseudokirchnerella subcapitata*]	72 h ErC_{50} = 24 mg/; 72 h EyC_{50} = 4.7 (measured; static; buffered, pH 8.2 to 9.2)
[*Pseudokirchnerella subcapitata*]	72 h ErC_{50} = 23 mg/L (nominal; static; unbuffered, pH 7.7 to 9.9)

DMAEE possesses properties indicating a hazard for the environment (acute aquatic toxicity values for algae between 1 and 100 mg/L). The chemical is not readily biodegradable and is not expected 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

DMAEE is commercially produced with an annual production volume in the United States (sponsor country) of 450 to < 4500 metric tons in 2005. DMAEE is produced in closed systems. DMAEE is used as a polyurethane catalyst for flexible foam, semi-rigid foam and rigid foam. It is a powerful blowing catalyst in polyurethane foam. The amine in the foam is released during and right after foaming in the plant, where air handling removes the material. What is left of the amine after the initial foaming will slowly be released over time. Possible exposures for workers might be via inhalation or dermal routes. There are no known consumer uses of DMAEE.