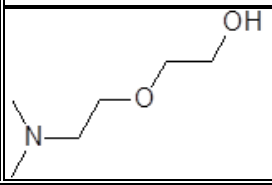
SIDS INITIAL ASSESSMENT PROFILE

CAS No(s).	1704-62-7
Chemical Name(s)	2-[2-(Dimethylamino)ethoxy]ethanol (**DMEE**)
Structural Formula(s)	

SUMMARY CONCLUSIONS OF THE SIAR

Analogue/Category Rationale

The sponsored substance, **DMEE** is structurally similar to 2-(2-aminoethoxy)ethanol (CAS RN 929-06-6); the substances differ only by the presence of two methyl groups on the terminal nitrogen. Both substances are dialkyl mono alkanolamines. The physico-chemical properties of both substances are similar. **DMEE** is readily absorbed and rapidly eliminated (mostly unchanged) in the urine; 2-(2-aminoethoxy)ethanol is expected to exhibit the same behavior based on similarities in both structural and physical chemical properties. The available data indicate that both the mammalian toxicology of **DMEE** and 2-(2-aminoethoxy)ethanol are also comparable, with corrosive properties and effects at the site of contact related to the alkaline properties predominate observed effects.

Data for 2-(2-aminoethoxy)ethanol for the endpoints including sensitization, repeated dose toxicity, reproductive toxicity and *in vivo* mutagenicity are used to fill these endpoints for the sponsored substance. 2-(2-aminoethoxy)ethanol data (for example, irritation) are also presented alongside data for the sponsored substance for other endpoints for the purpose of comparison.

Read Across Strategy

Substance	Sensitization	Repeated dose toxicity	*In vivo* mutagenicity	Effects on fertility and developmental toxicity
Sponsored substance: **DMEE**	READ ACROSS TO SUPPORTING SUBSTANCE			
Supporting substance: 2-(2-aminoethoxy)ethanol	X	X	X	X

X = data available

Physical-chemical Properties

DMEE is a liquid with a melting point of < -20 °C (measured), a boiling point of 203.5 °C at 1013 hPa (measured value, extrapolated from vapour pressure curve), and a vapor pressure of 0.11 hPa at 20 °C (extrapolated from vapour pressure curve). The measured octanol-water partition coefficient (log K_{ow}) is -0.778 at pH 9.9 and at 20 °C, and is miscible in all proportions with water. The pKa is 9.3 at 25 °C (measured).

Human Health

DMEE is readily absorbed and rapidly eliminated (mostly unchanged) in the urine when rats were exposed via dermal contact or intravenously.

Acute inhalation of a saturated vapour atmosphere of **DMEE** [similar to OECD 403] produced signs of local (eye) irritation but no mortality, effects on body weight or gross findings at necropsy; the 4 hour LC50 was >0.39 mg/L (highest concentration tested). The 8 hour saturated vapour inhalation LC50 for 2-(2-aminoethoxy)ethanol was >0.0087 mg/L [only concentration tested; guideline not specified, RL =4]. There

were no deaths, clinical signs, effects on body weight or significant findings at gross necropsy. The dermal LD50 for DMEE in rabbits was ca. 1653 mg/kg bw (female rabbits) and ca. 2033 mg/kg bw (male rabbits) [similar to OECD 402]. Both local site of application effects (necrosis), as well as systemic toxicity (salivation, sluggishness, unsteady gait, red nasal/oral discharge, tremors, prostration and effects on lung and liver), were observed. For 2-(2-aminoethoxy)ethanol , the dermal LD50 for the rabbit [OECD 402] was >3000 mg/kg bw (only dose tested). Clinical signs included both systemic (decreased activity, abnormal gait and stance, diarrhea, and dyspnea) and local effects (site of application: necrosis and sloughing of the skin, clear mucous and discharge, and yellow discoloration of fur). Terminal necropsy of the animals revealed local effects (severe irritation and/or yellow discoloration of the underlying muscle tissue at the application site, necrotic or discolored yellow fascia), and mottled lungs and pale kidneys. DMEE was more irritating at lower dose levels than 2-(2-aminoethoxy)ethanol, but neither show significant systemic effects. In an acute oral study [similar to OECD 401] the LD50 for **DMEE** was >2150- <3830 mg/kg bw in female and male rats. Clinical signs included dyspnea, apathy, staggering, piloerection and a poor general state, salivation, abnormal position, atonia, paresis, cyanosis and dehydration. Gross necropsy of animals that did not survive to study termination included site of contact effects in the stomach/small intestine; similar findings were not observed for surviving animals. Acute oral LD50s for 2-(2-aminoethoxy)ethanol in rats [OECD 401 or similar] were 2558 and ca. 3400 mg/kg bw (combined sexes). For the latter study, the acute oral LD50 was ca. 3000 (females) and ca. 3700 (males) mg/kg bw. Clinical signs of toxicity included signs of poor condition, staggering, prostration, decreased activity, dyspnea, diarrhea, piloerection, tremors, abnormal gait and stance, discolored urine. Findings at gross necropsy included effects on the gastrointestinal tract (site of contact), mottled kidneys and adhesion of the liver to the stomach and small intestines.

DMEE is corrosive to the skin [OECD 404 or Department of Transportation (D.O.T.) Skin Irritancy Test] and causes irreversible effects to the eyes [OECD 405]. Respiratory irritation data are not available, but acute inhalation of **DMEE** vapor at 0.39 mg/L for 4 hours by rats was not irritating to the respiratory tract [OECD Guideline 403]. However, as described below, repeated inhalation of **DMEE** vapor by rats (guideline not specified) caused nasal irritation (at 0.23 mg/L) and histologic lesions in the nasal cavity (at 0.1 and 0.23 mg/L; in two animals at 0.017 mg/L). 2-(2-Aminoethoxy)ethanol is corrosive to skin [OECD 404] and causes irreversible effects to the eyes [similar to OECD 405]. Bronchitis was noted in rats exposed to a saturated atmosphere of 2-(2-aminoethoxy)ethanol [similar to OECD 403].

Sensitization data were not located for **DMEE**. In an OECD 406 study, 2-(2-aminoethoxy)ethanol was not considered a skin sensitizer; similar results are expected for **DMEE**.

A standard repeated dose study was not located for **DMEE** by any route of exposure. Rats (10/sex/group) were exposed to **DMEE** by whole body vapor inhalation (guideline not specified) at 0, 3.1, 18.9, and 42.7 ppm (measured; 0, 0.017, 0.1, and 0.23 mg/L) 6 hrs/day for nine exposures over eleven days. Nasal irritation (0.23 mg/L group only), decreased body weight gain and increased blood carbon dioxide levels (0.23 mg/L males only), ophthalmologic findings (corneal crystals at 0.1 and 0.23 mg/L) and histologic lesions in the nasal cavity (0.1 and 0.23 mg/L, both sexes; 0.017, two females). The findings of decreased body-weight gain and increased blood carbon dioxide levels are a reflection of local damage. The study duration was insufficient for the determination of an NOAEC for **DMEE**. Rats (10/sex/group) were exposed to 2-(2-aminoethoxy)ethanol aerosol by nose only inhalation [OECD 422] for 6 hrs/day for 46-48 days (females) or 29 days (males) at concentrations of 0, 0.00388, 0.0166, and 0.0412 mg/L (measured; nominal concentrations were 0, 0.004, 0.016 and 0.04 mg/L). Repeated inhalation had no systemic effects in male and female Wistar rats. Treatment-related microscopic changes were observed in the larynx in the high dose group and consisted of increased squamous metaplasia of the respiratory epithelium and chronic (active) inflammation to a marginal or slight degree. These treatment-related findings (squamous metaplasia and chronic [active] inflammation) were also observed in the mid-dose group, however, to a lesser severity degree. These changes were considered local effects, not systemic. The NOAEC (systemic) for 2-(2-aminoethoxy)ethanol was 0.04 mg/L (nominal; no findings for any endpoint). The NOAEC (local) for 2-(2-aminoethoxy)ethanol was 0.004 mg/L (nominal; based on local effects on the respiratory tract); the NOAEC (systemic and local) are applicable to **DMEE**.

Rabbits (5/sex/group) were exposed to **DMEE** by the dermal route at 0 (control), 50, 250 or 500 mg/kg bw/day for a total of nine exposures over an eleven day period. Crusting or scaling dermatitis and epidermitis described as excoriation and encrustation were noted at the application at necropsy. There were no clinical signs of systemic

toxicity. Hematology changes (increased segmented heterophils at 500 mg/kg bw/day; increased total leukocyte count in females only at 500 mg/kg bw; increased platelets in males at all doses; decreased hemoglobin and hematocrit levels in males at 500 mg/kg bw) and organ weight effects (reduction in absolute/relative adrenal weight in males at 500 mg/kg bw; increased relative liver weight in males at 250 and 500 mg/kg bw) were observed. These changes were probably secondary changes in consequence of the skin barrier destruction and a subsequent infection. Similar findings have been reported to occur in rabbits for other irritating /corrosive compounds as well as in an interlaboratory evaluation. The study duration was insufficient for the determination of an NOAEL for **DMEE**. Similar findings of local but not systemic effects following dermal exposure were noted in a 14 day range-finder with Sprague-Dawley rats with 2-(2-aminoethoxy)ethanol, as well as in a 9-day study with New Zealand white rabbits with **DMEE**. More specifically, when rats (5/sex/group) were exposed to 2-(2-aminoethoxy)ethanol by the dermal route at 0 (control), 250, 500, 1000 or 1500 mg/kg bw/day for 6 hrs/day, under occlusive cover, for 14 days dermal irritation (erythema and/or edema), as well as scab formation, sloughing, fissuring and black areas on the dosing site were observed; no signs of systemic toxicity were observed. Rats (10/sex/group) were exposed to 2-(2-aminoethoxy)ethanol by the dermal route at 0 (control), 17, 87 or 175 mg/kg bw/day for 6 hrs/day, under occlusive cover, for 90 days [OECD 411]. Repeated dermal exposure had no systemic effects in male and female Sprague-Dawley rats as the effects observed were due to animals responding to infection rather than toxic properties of the tested chemical; the NOAEL (systemic) was 175 mg/kg bw/day. The NOAEL (local) for 2-(2-aminoethoxy)ethanol was 17 mg/kg bw/day, based on gross and histopathological changes of the skin at the site of contact; the NOAEL (systemic and local) are applicable to **DMEE**.

DMEE [OECD 471, 473 and 476] and 2-(2-aminoethoxy)ethanol [OECD 471 or similar, EU Method B.21, OECD 482] were not mutagenic *in vitro*. 2-(2-aminoethoxy)ethanol was not mutagenic in vivo [EPA OPP 84-2; similar to OECD TG 474]. **DMEE** is not expected to be mutagenic *in vivo* based on data for 2-(2-aminoethoxy)ethanol.

No data are available for the carcinogenicity of **DMEE** nor 2-(2-aminoethoxy)ethanol.

No data are available for the reproductive toxicity of **DMEE**. In an aerosol inhalation study with 2-(2-aminoethoxy)ethanol in rats [OECD 422], the NOAEC for reproductive performance and fertility was 0.04 mg/L (highest concentration tested). The NOAEC for developmental toxicity (embryotoxic / teratogenic effects) was 0.04 mg/L (highest concentration tested). In a repeated-dose 90-day dermal toxicity study with 2-(2-aminoethoxy)ethanol in rats [OECD 411], the NOAEL for effects on reproductive organs was >175 mg/kg bw/day (the highest dose tested). **DMEE** is not expected to be a reproductive toxicant based on these data with 2-(2-aminoethoxy)ethanol, and the NOAEL is applicable to **DMEE**.

DMEE possesses properties indicating a hazard for human health [acute toxicity, corrosive to skin, eye and respiratory tract irritation and local toxicity following repeated-dose exposure,]. Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

An OECD 111 study was not located for **DMEE**. Based on the lack of hydrolisable groups in the molecule, **DMEE** is expected to be resistant to hydrolysis and therefore the hydrolysis study was not conducted. As the measured dissociation constant (pKa) for the amino group is 9.3, **DMEE** mainly exists in its protonated form at environmentally relevant pH values.

In the atmosphere, indirect photooxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of 1.1 hours. In an OECD Guideline 302 B using non-adapted activated industrial sludge there was 10-20% degradation of the test substance (DOC removal) in 28 days under aerobic conditions, indicating **DMEE** is not readily biodegradable.

A level III fugacity model calculation with equal and continuous distributions to air, water and soil compartments suggests that **DMEE**, as the uncharged molecule, will distribute mainly to the soil (62.2 %) and water (37.7%) compartments with minor distribution to the air and sediment compartments (<0.1%). However, as the model does not take into account the charged form of the molecule at environmental relevant pH-values (pH 5-9), the model may underestimate distribution of DMEE into water. A Henry's law constant of 2.79E-06 Pa-m^3/mol (Bond Estimate) at 25 °C suggests that volatilization of **DMEE** from the water phase is not

expected to be high. Based on estimated K_{oc} values of 1 or 0.846 (25 ^{o}C) using the first-order MCI or the KOC-estimate from log Kow, respectively, the neutral form of **DMEE** is expected to have a low adsorption potential. However, as the amine is expected in its protonated form at environmental relevant pH values the KOCWIN-estimates may underestimate the adsorption as cationic amines will likely adsorb more strongly to soils containing organic carbon and clay than the neutral molecule.

DMEE has a low potential to bioaccumulate in the aquatic environment based on an estimated BCF value of 3.16 L/kg wet-wt (modelled as the uncharged molecule).

Acute aquatic toxicity data are available for **DMEE**.

The following acute toxicity test results have been determined for aquatic species:
Fish [*Leuciscus idus*] 96 h LC_{50} = ca. 320 mg/L (nominal; static; unbuffered); No toxic effects at 464 mg/L (nominal; static; buffered)
Invertebrate [*Daphnia magna*] 48 h EC_{50} >100 mg/L (nominal; confirmed by meausurements; static; unbuffered)
Algae [*Pseudokirchnerella subcapitata*] 72 h ErC_{50} = 160 mg/L (growth rate method; nominal; confirmed by measurements, unbuffered) 72 h EbC_{50} = 73 mg/L (area under growth curve method; nominal; confirmed by measurements, unbuffered)
72 h NOErC = 40 mg/L (growth rate method; nominal; confirmed by measurements, unbuffered)

DMEE does not possess properties indicating a hazard for the environment (acute aquatic toxicity > 100 mg/L). The chemical is not readily biodegradable and has a low 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

DMEE is commercially produced with an annual production volume of 2380 tonnes in the United States for the year 2012. Worldwide production volume is not available. **DMEE** is used to catalyze polyurethane foams (PU) foams (rigid and flexible foams). It is used in sealants, coatings, fillers, and putties. DMEE may also be used as a PU spray foam that would be applied by professional insulators (non-industrial spraying, roller application or brushing).

DMEE is generally used in closed systems (process, batch synthesis or formulation, mixing or blending for formulation of preparations and articles, transfer from/to large vessels, transfer into small containers (dedicated filling line)) with no exposure or occasionally with controlled exposure (batch synthesis or formulation). **DMEE** is used as a lab reagent. Exposures as outlined may occur during manufacturing, industrial use or professional user. There are no consumer uses/exposures of **DMEE.**