SIDS INITIAL ASSESSMENT PROFILE

Chemical Name	2-aminoethanol
CAS Number	141-43-5
Structural Formula	$HO\text{-}CH_2\text{-}CH_2\text{-}NH_2$

SUMMARY CONCLUSIONS OF THE SIAR

Analogue Justification

The hydrochloride salt (MEA-HCl; CAS 2002-24-6) was used for the two generation reproduction toxicity study in rats. Once dissolved and dissociated there is no difference expected in the toxicity of MEA and the hydrochloride salt.

Physical-chemical Properties

2-Aminoethanol (monoethanolamine; MEA) is an organic, colorless, viscous liquid with an unpleasant, fishy, ammoniac odour. The melting point was measured at 4 °C at atmospheric pressure and the measured boiling point was 167 °C at 101 kPa. The measured density of 1.02 g/cm^3 at 20 °C is slightly higher than that of water. The vapor pressure of 0.5 hPa at 20 °C can be calculated from a regression, which was derived by dynamic vapor pressure measurements. MEA is completely miscible with water at ambient temperature. The measured n-octanol/water partition coefficient (log K_{ow}) was determined to be -2.3 at 25 °C (pH 6.8 - 7.3). A measured pKa value (expected to be the value for the protonated form of MEA) in water is 9.5. The pKa of MEA itself is likely to be in the high 20s or 30s.

Human Health

MEA is present in nature as a nitrogenous base in phospholipids, which constitute the building blocks of cell membranes in animals. MEA applied to skin preparations *in vitro* showed steady state penetration rates of 123.1 (mouse) > 73.8 (rabbit) > 42.5 (rat) > 7.9 (human) µg/cm²/h. MEA is metabolized to acetaldehyde and ammonia; the reaction is catalyzed by ethanolamine deaminase and further degraded to CO_2 via the formation of ethanolamine-O-phosphate. MEA was shown to be a natural metabolite in the urine of rats, cats, dogs, rabbits and humans. MEA is also metabolized to ammonia and acetaldehyde by ethanolamine deaminase, the latter one is further metabolized to CO_2.

MEA has moderate acute oral toxicity, but has low toxicity after inhalative or dermal exposure.

The inhalation LC_{50} for 6 hours exposure was >520 ppm (1300 mg/m^3) and using modified Haber's law the calculated 4 h LC_{50} was >1487 mg/m^3. Also no mortalities were reported upon exposure of rats to saturated vapor concentrations of MEA for 8 h.

The key oral LD_{50} values were 1089 and 1515 mg/kg bw in male and female rats.

The dermal LD_{50} value was 2504 mg/kg in the male rabbit and 2881 mg/kg in the female rabbit.

The unspecific clinical effects seen in acute studies consisted of sluggishness, prostration, unkempt appearance, piloerection, lacrimation, emaciation, kyphosis and unsteady gait beside local irritant effects in the form of eyrthema, edema, ecchymosis, descquamation, necrosis, ulceration, and scabs after dermal exposure.

MEA is corrosive to the skin and corrosive or causes severe eye irritation in laboratory animals.

MEA is not a skin sensitizer in animals.

Available information in humans is ambiguous as there are negative but also several reports of dermatitis and positive epicutaneous test reactions to MEA, particularly in metalworkers exposed regularly to cooling lubricants.

The inhalation exposure of rats to MEA for 28 days caused concentration-related lesions in larynx, trachea and lung. No histopathological effects were seen in any other organ outside the respiratory tract. The NOAEC for systemic toxicity is the highest concentration tested of 150 mg/m³. The NOAEC for local portal of entry effects was the lowest tested concentration of 10 mg/m³. In a two-generation oral reproductive toxicity study with MEA-HCl, the NOAEL for general systemic toxicity was 300 mg/kg bw/day based on reduced body weight gain and/or food consumption. Repeated dose dermal toxicity studies have not been conducted.

MEA did not induce reverse mutations in *Salmonella typhimurium* or *Escherichia coli* and had no effect on gene conversion in *Saccharomyces cerevisiae*. In mammalian *in vitro* systems, MEA did not induce chromosomal aberrations in rat hepatocytes, gene mutation in mouse lymphoma cells or Chinese hamster lung fibroblasts. In the hamster embryo cells no morphological transformation were induced. *In vivo*, MEA showed no chromosome-damaging effect or any impairment of chromosome distribution in the course of mitosis in a mouse micronucleus test. Overall, information from both *in vitro* and *in vivo* tests that cover relevant endpoints indicates that MEA is not genotoxic.

No reliable data are available to assess the carcinogenicity of MEA.

A two-generation reproduction toxicity study in rats with dietary MEA-HCl administration demonstrated clear NOAELs for systemic and reproductive toxicity including effects on fertility at 300 mg/kg bw/day. Only at 1000 mg/kg bw/day, which is generally accepted as a limit dose level, minor effects were noted. Males at this dose showed a minor functional impairment of fertility in the form of decreased weights of epididymides and cauda epididymidis and reductions in the number of homogenization resistant caudal epididymal sperm. However, there was neither an effect on mating success nor histomorphological evidence of testicular toxicity. Females at this dose had decreased numbers of implants and increased resorption rates resulting in smaller litters associated with indications of systemic toxicity. There was virtually no effect on the pre- and postnatal development of the progeny in both generations up to the limit dose level of 1000 mg/kg bw/day representing a NOAEL for developmental toxicity.

MEA was investigated for prenatal developmental toxicity in several oral studies in rats. Studies conducted according to GLP and OECD guidelines indicated a NOAEL for maternal toxicity in the range of 120 – 300 mg/kg bw/day. There was no indication of prenatal developmental toxicity including teratogenicity in these studies up to the highest dose levels tested (450 – 500 mg/kg bw/day). A non-GLP and non-guideline study with low numbers of pregnant rats (10 per dose) was primarily designed to evaluate whether MEA would more affect specific fetal subtypes dependent on their *in utero* position relative to siblings of the same or opposite sex. This test used atypical interpretation criteria and was performed with Long-Evans strain rats, which is clearly susceptible to developmental toxicity, as ca. 14% of dead or malformed foetuses were seen in the control group. Embryotoxicity was seen that included increases in *in utero* deaths and numbers of pups with morphological changes (up to approximately 50% when combined) currently predominantly classified as variations. The LOAEL for developmental toxicity was 50 mg/kg bw/day.

In mice, limited developmental toxicity in the form of decreased numbers of viable litters was only noted in the Chernoff and Kavlock oral screening test at a dose level of 850 mg/kg bw/day that caused also maternal mortality.

Prenatal developmental toxicity of MEA following dermal application was investigated in rats and rabbits. In rats, maternal toxicity was indicated by reduced maternal body weight gain. In addition, moderate to severe skin irritation was recorded. The NOAEL for maternal toxicity was 75 mg/kg bw/day. Although the observed maternal skin irritation represented a certain level of stress, no indication for prenatal developmental toxicity and especially no morphological alterations were induced up to the highest dose level tested. The NOAEL for prenatal developmental toxicity including teratogenicity was 225 mg/kg bw/day. Marked skin irritation occurred in rabbits but there was no indication of any systemic effect. The NOAEL for local effects was 10 mg/kg bw/day and the NOAEL for systemic maternal toxicity, prenatal developmental toxicity including teratogenicity was 75 mg/kg bw/day (the highest dose tested).

MEA is not a developmental toxicant after dermal exposure. Oral GLP, guideline developmental toxicity studies additionally suggest that MEA is not a developmental toxicant at maternally toxic doses. An indication of developmental toxicity was observed in one oral study conducted under non-GLP and non-guideline conditions with a very sensitive strain of rat. Minor effects on reproductive performance and fertility, without histopathological correlate or influence of mating success, were only noted at the limit dose of 1000 mg/kg bw/day, a dose also associated with systemic toxicity in the parents.

MEA possesses properties indicating a hazard for human health (at low doses, corrosive or irritating to eyes, skin, respiratory tract, and/or site of contact, and reproductive/developmental toxicity (postimplantation loss) at high doses). Adequate screening level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

MEA is expected to be hydrolytically stable in the natural environment, since it does not contain any hydrolysable groups. The molecule will exist as a cation in water at environmentally relevant pH. It should be noted, however, that EPISuite predicts certain environmental fate endpoints in their uncharged forms. Therefore, there will be some differences between predicted and actual results.

Based on an AOP v1.92-estimate uncharged MEA is indirectly photo-degraded in the atmosphere by reaction with hydroxyl radicals with a half-life ($t_{1/2}$) of about 10.74 hours assuming a hydroxyl radical concentration of 500,000 molecule/cm³ and a 24-h day.

Level III fugacity modelling, using loading rates of 1000 kg/h each for air, soil and water, provides the percent distribution when the MEA is released simultaneously to all three compartments. Distribution to air, water, soil and sediment was calculated to be 0.46%, 40.6%, 58.9% and 0.08%, respectively. Based on model results the main target compartments of MEA are water and soil. The Henry's law constant for the uncharged molecule was calculated with HENRYWIN v3.20 (Bond estimation method) to be 0.000037 $Pa.m^3/mol$ at 25 °C. A pH corrected Henry's law constant at pH 7 of 0.00000963 $Pa.m^3/mol$ at 25 °C (estimated) suggests that volatilization of MEA from the water phase is not expected.

There are several ready biodegradation studies (OECD TG 301) available for MEA. In one of the studies, OECD 301 A study (DOC-die-away-test), MEA was inoculated in non-adapted, domestic sludge under aerobic conditions. Degradation was followed by DOC analysis at frequent intervals over a 21-day period. The initial concentration was 20 mg DOC/L. Elimination after 1, 4, 6, 11, 13 and 21 day was 9%, 97%, 95%, 95%, 95% and 94%, respectively. Thus, MEA was shown to be readily biodegradable. This was confirmed by at least 5 other reliable biodegradability tests.

Based on the measured partition coefficient (log K_{ow}) of –2.3 and an estimated bioconcentration factor (BCF) of 3.16, MEA is not expected to bioaccumulate**.**

The aquatic toxicity MEA to fish, invertebrates, algae and microorganisms was comprehensively investigated. Taking into account very high solubility of MEA in water, results based on nominal concentrations are as valid as based on measured concentration. The lowest reliable acute toxicity values for aquatic species are as follows:

Goldfish (*Carassius auratus*, fish)	96-h LC_{50} = 170 mg/L (measured; pH 10.1)
Daphnia magna (invertebrates)	48-h EC_{50} = 32.6 mg/L (measured; pH 7.3-9.1)
Pseudokirchneriella subcapitata (algae)	72-h E_rC_{50} = 2.8 mg/L (nominal; pH 8.0-9.7)
	72-h NOE_rC = 1 mg/L (nominal; pH 8.0–9.7)
Pseudomonas putida. (microorganisms)	17-h EC_{50} = 110 mg/L (nominal, pH 8.1-9.8)
Domestic activated sludge (microorganisms)	30-min EC_{10} >1000 mg/L (nominal)

In an early-life stage reproduction toxicity test in Japanese killifish (*Oryzias latipes*), the NOEC (30 days) was

1.24 mg/L and LOEC was 3.55 mg/L.

Chronic exposure to Brook trout *(Salvelinus fontinalis)* for up to 100 days resulted in NOECs (60 or 100 days (days) of >14.1 mg/L or >20 mg/L for survival, length and weight. The NOEC (100 days) for reproduction was 1.77 mg/L.

In a chronic toxicity test on reproduction of the water flea *Daphnia magna*, the NOEC (21 days) was 0.85 mg/L for reproduction and the EC_{50} (21 days) was 2.52 mg/L for reproduction as well.

MEA possess properties indicating a hazard for the environment (acute aquatic toxicity values between 1 and 100 mg/L and chronic aquatic toxicity values <1 mg/L). The chemical is 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

MEA is synthesized in a continuous, closed process by reacting one mole of ethylene oxide (EO) with one mole of ammonia.

The estimated production, imports, exports, and consumption of ethanolamines (MEA, DEA, and TEA) in 2011 by major consuming regions in thousand metric tons was as follows:

	Annual Capacity (year-end)	Production	Imports	Exports	Consumption
North America (United States, Canada, Mexico)	775	663	57	154	566
Central and South America	110	77	29	4	103
Western Europe	427	386	92	78	400
Central and Eastern Europe	57	41	12.5	16.9	36.6
Africa	0	0	7.7	0	7.7
Middle East	30	20	15.2	12.5	22.7
Asia	975	421	182	133	470
Oceania	0	0	7	0	7
Total	2,374	1,608	402	397	1,612
SOURCE: CEH estimates.					

Synthesis of MEA takes place in a closed continuous process. Therefore worker exposure during manufacture is limited. Major uses of ethanolamines in 2007 were for the production of surfactants, herbicides and gas treatment applications.

MEA is present in many household products and personal care products, such as laundry detergents, fabric softeners, oven and grill cleaners, glass and surface cleaners, disinfectants, mildew and mold removers, floor strippers and cleaners, grout cleaner, kitchen cleaners, household degreasers, personal care and hand cleaners and soaps, in hair color formulations and mousses. The typical reported concentration ranges for MEA in personal care products are 1 - 18%outbind://28/ - _msocom_1 , however, for floor strippers up to 30% and for grout and tile cleaners up to 99% are reported for single products

The exposure of MEA to the environment from industrial settings is anticipated to be low because synthesis and production of MEA takes place in a closed continuous process. Transfer of this material is in closed pipe systems rather than in open systems to minimize loss. There may be low level losses in process waters, which are discharged to a waste water treatment system. MEA is stored in closed tanks or pressurized cylinders and transported in tank cars and tank trucks, and smaller amounts are transported in drums, pressurized cylinders or Intermediate Bulk Containers (IBCs). Its use as a dispersing agent for agricultural chemicals will result in its direct release to the environment. In addition, emission to the environment is expected from use of consumer products (laundry detergents and cleaning agents). The possibility of a release to air or environment is low and

even if there is a release, MEA is readily photo- and biodegradable.

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