FOREWORD INTRODUCTION

ETHYLENEDIAMINE

CAS N°: 107-15-3

SIDS INITIAL ASSESSMENT REPORT
For 13th SIAM
(Bern, Switzerland November 6-9, 2001)

Chemical Name: Ethylenediamine

CAS No.: 107-15-3

Sponsor Country: United States/ICCA

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History: Documents were prepared and reviewed by industry prior to submission to sponsor country. Data searches consisted of searching available literature, databases and internal consortia files. Sponsor country conducted reviews of submitted data and offered comments to industry. It should be noted that a Concise International Chemical Assessment Document (CICAD) is available for this chemical and may be located at www.inchem.org. Industry prepared and resubmitted documents for consideration at SIAM 13.

Testing: No testing (x)
Testing ( )

Comments:

Deadline for Circulation: September 14, 2001
Date of Circulation:

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	107-15-3
Chemical Name	Ethylenediamine
Structural Formula	NH_2-CH_2-CH_2-NH_2

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Acute toxicity of ethylenediamine (LD50, rat, oral range from 637 mg/kg to 1850 mg/kg; LC50, rat, inhalation >29 mg/l and LD50, rabbit, dermal 560 mg/kg) is considered to be low to moderate. Due to the high alkalinity, ethylenediamine is corrosive to the skin and eyes. It is a dermal and respiratory sensitizer in humans and has been reported to cross-sensitize for chemicals of similar structure. In repeat dose studies, decreased body weight along with decreased water and feed consumption were observed. Every attempt was made to minimize the irritating nature of EDA and reduce the pH by using EDA-2HCL. Hepatocellular pleomorphism was noted in every study following dietary administration of longer than 13 weeks duration. Gavage administration resulted in effects in the eyes and kidneys. Kidney effects consisted of degenerative and regenerative changes in the tubular epithelium. The Lowest-Observable-Adverse-Effect-Level (LOAEL) is 100 mg/kg/day with a No-Observable-Effect-Level (NOEL) of 20 mg/kg/day observed in the chronic dietary feeding study. Ethylenediamine was rapidly excreted with most of the material eliminated in the urine within 24 hours. Ethylenediamine has produced weakly positive results, 2-3 times greater than control values, in several Ames tests, which may or may not be related to an impurity. Subsequent studies conducted with purer material were negative. All other tests including several *in vitro* assays (CHO gene mutation, sister chromatid exchange with CHO cells and UDS with primary rat hepatocytes) and a rat dominant lethal assay were negative. The weight of evidence from both *in vitro* and *in vivo* tests indicates that ethylenediamine is unlikely to be genotoxic. In chronic bioassays via two routes of exposure there was no carcinogenic effect. In developmental toxicity studies, growth retardation was noted at maternally toxic levels. However, there was no evidence of developmental toxicity at maternally toxic doses when compared with a pair-fed control. There was no effect on reproductive parameters at levels, which produced parental toxicity.

Environment

Ethylenediamine's vapor pressure is 12hPa at 20^0C, the log P_{ow} range is from –1.3 to –2.04 and the water solubility is110 g/L. It should be noted that while EDA does not have as high of a stability constant as several higher molecular weight ethyleamines, it does have the potential to chelate copper. Based on physical chemical properties, EDA is not expected to bioaccumulate. Ethylenediamine is expected to be readily biodegradable in the environment with > 80% degraded within 28 days. The estimated photodegradation half-life is 8.9 hours. Using the level III Fugacity Model by Mackay, most of EDA at steady state will partition to the water compartment. The 96 hr LC50 in fish is 115 mg/L while the 96 hr algae biomass EC50 is 61 mg/L. In the most sensitive aquatic organism, *Daphnia magna*, the 48 hr LC50 is 3-46 mg/L with a 21-day reproduction test No-Observable-Effect-Concentration (NOEC) of 0.16 mg/L.

Exposure

In the United States (US), ethylenediamine is a major industrial chemical used primarily as a closed-system intermediate in the production of chelating agents. It is also used to produce polyamide resins, ethylene bis-stearamide, gasoline and lube oil additives and cationic surfactants. Production in Western Europe is 58,000 tonnes, 41,000 tonnes in the US and 5,000 tonnes in Japan. In the US, environmental releases are not anticipated based on the manufacturing process and use conditions. Since it is primarily an industrial intermediate in the US, exposures are anticipated to be restricted to product transfer and maintenance operations. Exposures in the workplace are

typically below 10 ppm (TWA). In the U.S., the only known use of EDA in consumer products is via the pharmaceutical industry in the production of aminophylline for the treatment of severe asthma. In the U.S. this use is regulated and restricted to consumers under medical supervision. Based on varied information provided by registries from some OECD member countries (Sweden, France, Switzerland, Finland and Denmark) it would appear that the concentration of unreacted EDA in products sold to consumers is low, typically less than 0.5%. However, it is recommended that each OECD Member country evaluate their exposure scenarios to determine the chemical's priority for further work.

NATURE OF FURTHER WORK RECOMMENDED

Based on data indicating EDA possibly being present in consumer products, national or regional exposure information gathering may need to be considered to clarify the possible extent of exposure to consumers.

FULL SIDS SUMMARY: Ethylenediamine

CAS NO: 107-15-3		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point	--	--	10.9-11.1 °C
2.2	Boiling Point	--	--	17°C
2.3	Density	--	--	0.899 g/cm3
2.4	Vapour Pressure	--	--	12 hPa at 20°C, 17.06 hPa at 25°C
2.5	Partition Coefficient (Log P_{ow})	--	--	-1.3 to –2.04
2.6 A.	Water Solubility	--	--	110 g/L at 20°C
B.	pH	--	--	11.8 at 5 g/L
	pKa	--	--	pK1 7.56
				pK2 10.71
2.12	Oxidation: Reduction Potential	--	--	No data
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation	--	Calculated	8.9 hours
3.1.2	Stability in Water	--	Calculated	Does not contain functional groups for hydrolysis.
3.2	Monitoring Data	--	Measured	Limited occupational air sample data, concentrations are usually below 10 ppm, the ACGIH TLV.
3.3	Transport and Distribution	--	Fugacity estimates	Primarily distributes to water compartments.
3.5	Biodegradation	--	Measured	Extensive degradation under aerobic conditions.
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Pimephales promelas*	96-hour lethality	LC50 = 115.7 – 210 mg/L
4.2	Acute Toxicity to Aquatic Invertebrates *(Daphnia)*	*Daphnia magna*	48-hour lethality	LC50 = 3.0 – 46 mg/L
4.3	Toxicity to Aquatic Plants e.g. Algae	*Chlorella pyrenoidosa*	96-hour growth	EC50 = 61 mg/L
4.5.1	Chronic Toxicity to Fish	*Gasterosteus aculeatus*	28-day growth	NOEC > 10 mg/L
4.5.2	Chronic Toxicity to Aquatic Invertebrates (*Daphnia*)	*Daphnia magna*	21-day reproduction	NOEC=0.16 mg/L
4.6.1	Toxicity to Soil Dwelling Organisms	--	--	No data
4.6.2	Toxicity to Terrestrial Plants	*Lactuca sativa*	21-day EC50	EC50 = 208 mg/L (nutrient, semi-static, nominal)
			14-day EC50	EC50 = 692 mg/kg (soil, static, nominal)
4.6.3	Toxicity to Other Non-Mammalian Terrestrial Species (Including Birds)	--	--	No data

CAS NO: 107-15-3		SPECIES	PROTOCOL	RESULTS
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat	Acute lethality	LD50 = 637-1850 mg/kg
5.1.2	Acute Inhalation Toxicity	Rat	Acute toxicity	LC50 > 29 mg/L
5.1.3	Acute Dermal Toxicity	Rabbits	Acute lethality	LD50 = 560 mg/kg
5.2.1	Dermal Irritation	Rabbit	Dermal irritation	70% aqueous solution burns within 6-12 minutes.
5.2.2	Eye Irritation	Rabbit	Eye irritation	Severe irritation with permanent damage
5.3	Sensitization	Guinea Pig	Modified Maguire, Maximization,	Positive
5.4	Repeated Dose Toxicity	Rat	3-month dietary toxicity	LOAEL = 250 mg/kg/day NOAEL = 50 mg/kg/day
		Rat	3-month oral toxicity	LOAEL = 100 mg/kg/day
5.5	Genetic Toxicity *In Vitro*			
A.	Bacterial Test (Gene mutation)	*Salmonella typhimurium*	Mutagenicity	With activation: - weakly positive in TA100 and TA1535 Without activation: - negative
B.	Non-Bacterial *In Vitro* Test	Chinese Hamster Ovary	Gene mutation assay	Negative
		Chinese Hamster Ovary	Sister chromatid exchange	Negative
		Rat hepatocytes	Unscheduled DNA Synthesis	Negative
5.6	Genetic Toxicity *In Vivo*	Rat	Dominant Lethal	Negative
		Drosophila	SLRL	Negative
5.7	Carcinogenicity	Rat	Oral toxicity	Negative
		Rat	Dermal	Negative
5.8	Toxicity to Reproduction	Rat	Two-generation repro	LOAEL (adults) = 150 mg/kg/day NOEL (adults) = 50 mg/kg/day NOEL (offspring) = 500 mg/kg/day
5.9	Developmental Toxicity/ Teratogenicity	Rat	Teratology	LOAEL (adults) = 250 mg/kg/day NOEL (adults) = 50 mg/kg/day LOAEL (fetuses) = 1000 mg/kg/day NOEL (fetuses) = 250 mg/kg/day
5.11	Experience with Human Exposure	Human	Dermal sensitization	Positive
			Respiratory sensitization	Positive

SIDS Initial Assessment Report

1. IDENTITY

IUPAC name: Ethylenediamine

CAS number: 107-15-3

Molecular formula: $C_2H_8N_2$

Structural formula: NH_2-CH_2-CH_2-NH_2

Synonyms: alpha.,.omega.-Ethanediamine, .beta.-Aminoethylamine, 1,2-Diaminoethane, 1,2-Ethanediamine, 1,4-Diazabutane, Dimethylenediamine

Purity: >99%

Physical and chemical properties:

ITEMS	RESULTS
Appearance	Colorless to yellow liquid
Melting Point	10.9-11.1°C
Boiling Point	117°C
Vapor Pressure	12hPa at 20°C 17.06 hPa at 25°C
Partition Coefficient (log Pow)	-1.3 to -2.04 (measured values)
Water Solubility	110g/L at 20°C
pK1 pK2	7.56 10.71

As with several higher molecular weight ethyleneamines, such as diethylenetriamine (DETA), triethylenetetramine (TETA) and tetraethylenepentamine (TEPA), EDA has the ability to chelate copper, albeit at a much lower affinity than TETA and TEPA. Below is a table which summarizes the stability constants of these materials.

Stability Constants for Ethylenediamine, Diethylenetriamine, Triethylenetetramine and Tetraethylenepentamine

Metal	EDA	DETA	TETA	TEPA
Copper	10.71	15.9	20.4	23.1
Cobalt	5.96	8.0	11.1	13.5
Zinc	5.87	8.8	12.1	15.3
Iron	4.34		7.8	9.96
Manganese	2.77		4.9	6.6

Source: Smith, R.M. and Martell, A.E. (1975). Critical Stability Constants Vol. 2. Plenum Press.

2. GENERAL INFORMATION ON EXPOSURE

Ethylenediamine (EDA) is a major industrial chemical with approximately 90 million lbs. (41,000 tonnes) produced in the US, 128 million lbs. (58,000 tonnes) produced in Western Europe and 11 million lbs. (5,000 tonnes) produced in Japan in 1994 (Somogyi et al, 1996). There are two plants in the US, five plants in Western Europe and two plants in Japan (Greiner, et al., 1999). There are two processes used to produce EDA: The ethylene dichloride (EDC) process and the ethylene oxide/monoethanolamine (EO/MEA) process. In each process the starting materials are reacted with ammonia. In the EO/MEA process, EO reacts with ammonia to form MEA which then reacts with ammonia to form EDA.

Since EDA is used as an industrial intermediate, its uses are predominantly in enclosed systems and for these uses there is little occasion for human exposure. The greatest exposures occur during product transfer and maintenance operations. Due to the highly reactive nature of EDA, it is essentially consumed during reactions. During these manufacturing processes, residual EDA is typically removed by distillation. Low levels of EDA, typically in the low ppm range would be expected in the final product. EDA is a very reactive molecule and will react with acids, oxides and other materials. Thus the concentration of EDA may be lower than estimated. Based on manufacturing processes and use conditions, significant releases are not expected to the terrestrial environment.

EDA is used primarily as an intermediate in the production of chelating agents, such as ethylenediaminetetraacetic acid (EDTA). Ethylenediamine is also used as an intermediate in the production of polyamide resins, ethylene bis-stearamide, gasoline and lube oil additives, cationic surfactants and, in Europe, fungicides (Greiner et al., 1999). To a lesser extent EDA has been used as an intermediate in the production of fabric softeners and bleach activators. In the production of these materials, EDA is the initial reactant and may undergo one, two, three or four subsequent reactions prior to the manufacture of the final product. The concentration of unreacted EDA decreases with each subsequent reaction. EDA is also added to refinery streams as a scavenging agent due to its high degree of reactivity.

Ethylenediamine is used within the pharmaceutical industry to produce aminophylline for the treatment of acute severe asthma (Merck, 1999). In the U.S., this use is restricted to consumers under medical supervision. At the present time, there is only one aminophylline producer (PDR, 2000) and the amount sold into this market is probably quite small. It has been used in the past as a stabilizer in topical creams containing neomycin (Van Hecke, 1975). However, recent formulations of topical creams do not appear to contain ethylenediamine (PDR, 2000).

2.1 Environmental Fate

The Level I Fugacity Model of Mackay predicts the percentages of ethylenediamine in water, air and soil at equilibrium are 98.1, 1.9 and <0.1%, respectively (Davis, 2001). The Level III Fugacity Model of Mackay calculations were determined using four simulations: one with 1000 kg/hour emitted to air only, one with 1000 kg/hour emitted to water only, one with 1000 kg/hour emitted to soil only, and one using the default emissions of equal amount to soil, air and water (1000 kg/hour for each). For each scenario, the majority of ethylenediamine was predicted to be in the water compartment. Using the default emissions of equal amount to soil, air and water (1000 kg/hour for each) the percentages of ethyleneamine in water, air and soil are estimated to be 78.1, 0.1 and 21.8%, respectively (Table 1) (Davis, 2001).

The fugacity model predictions for partitioning of EDA into the soil/sediment compartment is a function of the K_{ow} and water solubility, which is reasonable for most non-polar organic species. However, for polar or ionizable compounds such as EDA, chemical sorption to soil/sediment can involve other mechanisms. For example, studies with the EDA have shown that interaction of protonated amines and negatively charged soil is possible (Davis 1993). The mean Koc value was 4766 (range 2071-7051). These results demonstrate that at environmentally relevant pHs, EDA is likely to sorb to soil to a greater extent then predicted by their water solubility and K_{ow} alone. Thus, the fugacity model predictions likely underestimate the adsorption capacity of EDA to soil and sediment.

Table 1: LEVEL III Distribution of Ethylenediamine

	% distribution		
	Air	Water	Soil
Air only – 1000 kg/hour	5.5	60.2	34.3
Water only – 1000 kg/hour	<0.1	99.9	<0.1
Soil only – 1000 kg/hour	<0.1	62.2	37.7
Combined– 1000 kg/hour into air, water and soil compartments	0.1	78.1	21.8

Hydrolysis of ethylenediamine would not be expected under environmental conditions (pH 5 to 9) since the molecule does not contain functional groups susceptible to hydrolysis (Larson et al., 1994, Boethling et al., 2000). This assessment is supported by computerized estimations of hydrolysis rates (Meyland et. al., 1996) based on structure activity relationships which predict no reaction.

In the atmosphere rapid photochemical-oxidative degradation occurs through OH radicals, for which a half-life of 8.9 hours has been calculated (Atkinson, 1987). Ethylenediamine is readily biodegradable, as greater than 80% was degraded after 28 days in the closed bottle test. In the modified MITI (OECD 301C), 93-95% was biodegraded (JCIE, 1992). Since >90% was degraded after 10 days in the Zahn-Wellens test (Voelskow, 1990) material can also be considered inherently biodegradable. Based on a Bioconcentration Factor of 0.07, EDA is not expected to bioaccumulate (Veith, 1980).

2.2 Human Exposure

Occupational Exposure

Exposure Guideline: The ACGIH TLV, OSHA PEL, NIOSH REL values are 10 ppm TWA. The TLV is based on irritation, asthma and sensitization. ACGIH has also added a “skin” designation (ACGIH 2000). Numerous other countries, including Australia, Belgium, Denmark, Finland, France, Japan, Sweden, Switzerland and Turkey, have the same TWA. One country, the Netherlands, has adopted a lower value of 7.2 ppm (18 mg/m3) TWA. France and Sweden have adopted short-term-exposure-limits (STELs) of 15 ppm while Finland and Switzerland have adopted STELs of 20 ppm.

In a 1967 study of an ethylenediamine production facility, the concentration of ‘total nitrogen’ was measured and concentration of ethylenediamine in the atmosphere was determined assuming all of the material was ethylenediamine (Soule 1967). The highest concentration measured was 4 ppm EDA.

According to a UK risk assessment document, there have been 5 studies which have measured the concentration of ethylenediamine at production plants under various conditions (Brooke et al., 1997). Ethylenediamine was only detected at one plant under a ventilation hood at a tanking site (Hansen et al., 1984). The EDA concentration in the air was about 0.41 ppm (equivalent to 1.025 mg/m^3) after 3 hours of sampling. At all other plants, the concentration was below the level of detection (level of detection in these four plants was 0.05 ppm in two plants, 0.1 ppm in one plant and 0.41 ppm in one plant) (Brooke et al., 1997).

In 1975-1981, a plant using a formulation containing 50-100% EDA was monitored for the concentration of EDA in air (cited in Brooke et al., 1997). The percentage of exposures exceeded 10 ppm in 5% of the samples in 1975 and 1980. For most years, >99.8% of the samples were less than the TLV of 10 ppm.

In 1982, NIOSH measured worker exposure to a number of chemicals in a pattern and blade shop for Boeing Vertol Company, Philadelphia, PA (Liss and Chrostek, 1983). Airborne concentrations of ethylenediamine were below the limit of detection, 0.0005 mg/sample.

Concentrations of ethylenediamine measured in the air around workers in the road paving industry were <0.02 mg/m^3 (equivalent to <0.008 ppm) (Levin et al., 1994). For this use, which is typically conducted during warm weather where the paving material is heated, the concentration measured was negligible.

Consumer Exposure

In the U.S., the only confirmed use of EDA in consumer products is within the pharmaceutical industry to produce aminophylline for the treatment of severe asthma (Merck, 1999). This use is restricted to consumers under medical supervision. EDA has not been reported to be present in any additional consumer products and this is believed to be due to the reactive properties of the chemical when formulating such products.

Some OECD member countries (Sweden, France, Switzerland, Finland and Denmark) provided varied information from their respective product registries. In general, the product registries were unable to provide additional information regarding other components (chemicals) that were present in the consumer products in which EDA was reported to be present. These other components are believed to be acids, oxides and other materials, which react with EDA. This was confirmed by France, as oxides are reported as being present in some of the products which ultimately results in the concentration of the EDA in the final product being much lower than implied by the data from the product registries. In addition, Switzerland provided information that the concentration of EDA present in a final product decreases with every additional reaction of EDA. It would appear that the concentration of unreacted EDA in products sold to consumers is low, typically less than 0.5%.

Indirect Exposure

Indirect Exposures via the environment are not anticipated.

3. EFFECTS ON HUMAN HEALTH

Most of the repeated dose studies have been conducted with the dihydrochloride salt of EDAadministered by the oral route. To briefly summarize, EDA is converted in the stomach to EDA-dihydrochloride due to naturally occurring HCl in the stomach. There is little difference in toxicity observed between EDA and EDA-2HCl when one corrects for molecular weight differences via the oral route. Greater differences are observed via other routes of administration.

a) Toxicokinetics

Metabolic and pharmacokinetic studies of ethylenediamine in relation to oral, endotracheal and intravenous dosing were conducted in rats (Yang and Tallant, 1982). Male Wistar rats were dosed with single doses of ^{14}C-EDA-2HCl at 5, 50 or 500 mg/kg and the fate of ^{14}C-EDA derived radioactivity was followed for 24 or 48 hours. Urinary excretion was the primary route of elimination accounting for 42-65% of the administered dose with most of the material excreted within 24 hours. Fecal excretion ranged from 5-32% depending on the route of administration and/or dosage. Expired air contained 6-9% of the administered radioactivity in the form of $^{14}CO_2$. A relatively large percentage, 11-21%, remained in the various organs and carcass at the end of the 48-hour experimental period. The radioactivity was distributed throughout the body although thyroid, bone marrow, liver and kidney contained relatively higher concentrations. In the urine, depending on the dosage level, 2-49% of the radioactivity was unchanged parent compound. A major metabolite, N-acetylethylenediamine accounted for approximately half of the urinary radioactivity. The fate of EDA in the rat following oral or endotracheal dosing is similar particularly at the two lower doses.

A pharmacokinetic study was done with rats as part of the chronic bioassay (Yang, Tallant, and McKelvey, 1984). Young naïve Fischer 344 rats and those on test for 6 or 18 months from the control and 350 mg/kg/day groups were dosed orally with 50 mg/kg of ^{14}C-EDA-2HCl. Plasma kinetics were followed for 24 hours. Similar excretion percentages in the urine feces and expired air were observed in this study as were observed in Wistar rats. However, the volume of distribution decreased from naïve to 6-month old to 18-month old animals which would result in the concentration of EDA in the plasma increasing over time. The volume of distribution for old rats was 25-50% of that of new rats. This is most likely because a significant part of the body weight increase was due to an increase in body fat. EDA, being highly water soluble, has little to no affinity for fat tissue.

Aqueous ^{14}C-EDA solutions of 10, 25 or 50% were applied percutaneously over a 7x7 cm area on the back of rats with occlusion for 24 hours (Yang et al., 1987). Recovery of ^{14}C from the plasma, urine and feces and at the end of the study from selected tissues, carcass and skin of the dosing area was low with 70, 75 and 83% recovered from the 10, 25 and 50% EDA solutions, respectively. Kinetic measurements were obtained only from animals treated with 25 or 50% EDA, but not from the 10% treatment group due to analytical limitations. The uptake of ^{14}C-EDA percutaneously was relatively slow in comparison with the uptake following oral administration. Greater than 50% of the test material was absorbed from the 25 or 50% solutions. However, full-thickness epidermal necrosis was observed at this concentration. Thus the amount absorbed was probably greater than one would see with intact skin. At the lowest concentration only 12% of the material applied was absorbed. At this same concentration, >50% of the applied dose remained on the application site. As with oral administration, urinary excretion was the predominant route of excretion.

Pharmacokinetic and metabolism studies of EDA in relation to oral or intravenous dosing were conducted in mice (Leung, 2000). Male Swiss Webster mice received an iv dose of 50 mg/kg or an oral gavage dose of 5, 50 or 500 mg/kg of ^{14}C-EDA-2HCl and the fate of ^{14}C-EDA derived

radioactivity was followed for 48 hours. Approximately 54 – 70% of the dosed radioactivity was recovered in the urine within 24 hours. The principle urinary metabolite was N-acetylethylenediamine. During the 48 hour study, another 10% was eliminated as CO2 and another 5-14% was eliminated in the feces. Most of the material was eliminated from the body within 24 hours.

Conclusions: Following oral exposure, i.v., or intratracheal administration, ethylenediamine was rapidly excreted with most of the material eliminated in the urine. Dermal absorption plays a minor role except when necrosis was observed. As with ingestion, most of the absorbed material was quickly eliminated in the urine. The volume of distribution in older animals is much less than young animals due to the higher fat content in the older animals. Plasma levels in older rats were 2-4x greater than for younger rats.

b) Acute toxicity

Acute toxicity data is reported for mice, rats and rabbits (Table 2). The pH of this material is relatively alkaline, 11.8 at a concentration of 5000 mg/L in water, and the material can severely irritate the gastrointestinal tract following ingestion or burn the skin following dermal application. The oral LD50 in rats ranged from 637-1850 mg/kg. The range of differences in the reported oral LD50 values may be due to the dilution volume used to administer the test material. It is unknown whether the differences in the dermal LD50 values are due to the species or the dilution volumes.

Table 2: Acute toxicity of ethylenediamine in experimental animals.

Route	Animals	Values	Type	Reference
Oral				
	Rat	637 mg/kg	LD50	Union Carbide (1984)
	Rat	1850 mg/kg	LD50	Du Pont (1983)
	Rat	1050 mg/kg		Olson (1951)
	Rat	~1500 mg/kg	LD50	Peters (1982)
Inhalation	Mice	Between 400 and 800 mg/kg	LD50	Peters (1982a)
	Rat	>29 mg/l	LC50	Du Pont (1983)
Dermal	Rat	~1000 mg/kg	LD50	BASF (1978)
	Rabbit	560 mg/kg	LD50	Du Pont (1983)

Irritation and Corrosiveness

Application of an aqueous solution of 70% EDA to the skin caused complete destruction within 6 to 12 minutes in the rabbit (Hollingsworth, 1951). A 10% solution in water also caused a burn within 24 hours (Olson, 1958). A 0.1% solution was non-irritating to the skin following multiple applications.

Application of neat material to the eye resulted in severe irritation and permanent injury (Olson, 1958). A 10% solution in water caused moderate corneal damage and extensive conjunctivitis. A 1% solution was essentially non-irritating.

Vapors of ethylenediamine are mildly irritating to the eye after 10 seconds at 200 ppm while 400 ppm is intolerable (Pozzani and Carpenter, 1954).

Vapor exposure for 5-10 seconds produced tingling of the face and irritation of the nasal mucosa at 200 ppm and severe nasal irritation at 400 ppm (Pozzani and Carpenter, 1954).

Conclusions: Due to the high alkalinity, exposure to EDA can readily cause corrosion to the skin and eyes.

Sensitization

Ethylenediamine induced positive results in Guinea Pig skin sensitization tests (Goodwin et al., 1981, Henck et al., 1980). In the modified Maguire method, 0.1 ml containing 10% EDA applied during the induction and challenge phase produced a positive response in all guinea pigs tested. In addition ethylenediamine has been shown to be a cross sensitizer for diethylenetriamine, triethylenetetramine, aminoethylethanolamine and piperazine in Guinea Pigs (Leung et al., 1997).

Conclusions: It is a dermal sensitizer in guinea pigs (for human experience see section g) and has been reported to cross-sensitize for chemicals of similar structures.

c) Repeated dose toxicity

Dietary: In a 7 day dietary study, male and female rats were fed target concentrations of 150, 500 or 1500 mg/kg/day of EDA·2HCl (Yang et al., 1983). Actual dosages were somewhat higher with males ingesting 200, 630 or 1940 mg/kg/day, respectively, and females somewhat higher doses. Although no deaths occurred during the study, one high-dose female rat was euthanized on day 6 due to clinical effects. High dose males gained less weight while high dose females actually lost weight and this was reflected in a reduced feed consumption. Absolute liver and kidney weights of the high dose males and females were reduced and relative kidney weight of the middle and high dose female rats were increased. The No-Observed-Effect-Level was 200 mg/kg/day and the Lowest-Observed-Adverse-Effect-Level (LOAEL) was 630 mg/kg/day.

In a three month dietary study, male and female rats were fed targeted doses of 0, 50, 250 or 1000 mg/kg/day of EDA·2HCl (Yang et al., 1983). Water consumption was comparable to control values at all dose levels in males but was decreased in a dose-response manner in female rats at all 3 dose levels. There were no deaths and no abnormal clinical signs noted during the study. Body weight gains were significantly decreased in the high dose group which affected a number of absolute and relative organ weights in both males and females. Slight reductions in serum glucose levels and an elevation of alkaline phosphatase, AST and ALT activities were observed in the high dose group. An elevation of ALT activity was also observed in the intermediate dose male rats. Urinary pH in the high dose group was decreased in both males and females. There were no dose-related gross lesions in any animal on the study. The most significant histopathologic lesion, hepatocellular pleomorphism, was observed primarily in the high dose female and, to a lesser extent, male rats. The LOAEL was 250 mg/kg/day for a 13 week study in rats. Since the water consumption was only slightly decreased at 50 mg/kg/day, the No-Observed-Adverse-Effect-Level (NOAEL) was considered to be approximately 50 mg/kg/day.

In a 7-day dietary study, male and female mice were fed target concentrations of 156, 625 and 2500 mg/kg/day of EDA-2HCl (Yang et al., 1983). High dose males and females lost weight. This was reflected in a reduced feed consumption in the high dose animals. Absolute liver and kidney weights of the high dose males and females were significantly reduced from control values while the relative liver and kidney weights of the same animals were slightly reduced. The LOAEL was 2500 mg/kg/day while the NOEL was 625 mg/kg/day.

In a two-year bioassay, 100 male and 100 female Fischer 344 rats were fed ethylene dichloride at 0, 20, 100 or 350 (M) or 360 (F) mg/kg/day for 24 months with interim sacrifices of 10 rats/sex/dose at 6 and 12 months; and 15-20 rats/sex/dose at 18 months (Hermansky et al., 1999). Mortality was essentially the same through the first 20 months. Mortality increased relative to controls in male and female rats ingesting 350 mg/kg/day after 22 months and in female rats ingesting 100 mg/kg/day after 24 months. Toxicity, as exemplified by reductions in body weight gain at the high dose and decreased absolute weights of liver, kidney and spleen in high dose males, was observed. Hepatocellular pleomorphism was first observed in intermediate and high dose females at 12 months but was not observed in high dose males until the final sacrifice. Rhinitis and tracheitis were seen with greater frequency in high level males at 12, 18 and 24 months and in high level females at 18 months. At 24 months, rhinitis persisted at a significantly greater frequency in high level females while tracheitis did not. The NOEL for chronic toxicity was 20 mg/kg/day. The carcinogenicity data are summarized in section e.

Oral Gavage: In a 16 day study, rats received 0, 100, 200, 400, 800 or 1600 mg/kg five days/week for a total of 12 treatments (Peters 1982). All animals ingesting 1600 mg/kg died prior to the third dose and one male and 2 females ingesting 800 mg/kg died prior to the scheduled termination. All rats administered 100-800 mg/kg EDA lost weight although the weight loss was less severe in the female rats. Histopathologic changes were observed in the kidneys of rats administered 200-800 mg/kg and lymph nodes of rats adminstered 400-800 mg/kg. The NOAEL was 100 mg/kg.

In a 13-week study, rats received 0, 100, 200, 400, 600 or 800 mg ethylenediamine/kg by gavage on weekdays only (Peters 1982). At the highest dose, 6 male and 1 female of 10 rats/sex died during the study. Decreased body weight gains were noted in 200 - 800 mg/kg group of males and in the 400 - 800 mg/kg group of females. These changes ranged from –20% in 200 mg/kg male group to –47% in 800 mg/kg male group and –10% in 400 mg/kg female group to –50% in 800 mg/kg female group. Males appeared to be more severely affected than females. Thymus to body weight mean ratios of the dose group decreased as a function of increasing dose at 200 mg/kg in males and 600 mg/kg in females. However, there were no accompanying histopathologic changes. Histopathologic changes were noted in the eyes, kidneys and uterus. Eye lesions were present to some degree in 100-800 mg/kg rats. In the more severe cases the retina was lacking all the normal layers while in less severe cases there was only rosetting and focal cellular losses. Renal tubular lesions were only observed in the 600 and 800 mg/kg groups. These lesions were characterized by degeneration, regeneration and occasional necrosis of the tubular epithelium. Hypoplasia of the uterus was noted in the high dose group and was attributed to inanition. The LOAEL was 100 mg/kg based on the eye effects.

In a 16-day study, mice received 0, 50, 100, 200, 400 or 600 mg ethylenediamine/kg body weight five days/week for a total of 12 treatments (Peters 1982a). All animals in the 600 mg/kg group died by the fourth day of the study. Three of 5 female mice in the 400 mg/kg group died during the in-life phase. All other animals survived to the end of the study. Weakness and inactivity were observed in mice that died during the study. Absolute and relative organ weights were unaffected. There were no significant gross lesions at necropsy. Histopathologic changes were observed in the kidney of mice dosed with 100 - 400 mg/kg and in the spleen of mice dosed with 400 mg/kg. The LOEL was 100 mg/kg while the NOEL was 50 mg/kg.

In a 13-week study, mice received 0, 25, 50, 100, 200 or 400 mg ethylenediamine/kg body weight five days/week (Peters 1982a). One male mouse in the 400 mg/kg group died which was attributed to EDA. There was no apparent dose-response relationship in either sex with respect to body weight changes. Absolute and relative organ weight changes were unaffected in any dose groups. There were no treatment-related gross lesions. Histopathologic changes were only observed in the kidneys of mice receiving 400 mg/kg and primarily in males. The kidney lesion was characterized

by mild to moderate acute degeneration and/or necrosis of the renal tubular epithelium. The effect was more marked in the male mouse that died. The NOEL was 200 mg/kg and the LOEL was 400 mg/kg.

Dermal: In a lifetime skin painting study, 25µl of a 1% aqueous solution of test material from Dow and Union Carbide was applied 3 times/week to male mice (Depass et al., 1984). This was the highest dose which did not result in irritation at the application site or body weight loss. Mean survival of male mice from the Dow material was slightly shorter than from the Union Carbide material or for the control mice (598, 639 and 626 days for Dow, UCC and control groups, respectively). However, the survival curves were similar for the first 600 days of the study.

Conclusions: In repeated dose studies, decreased body weight and water and feed consumption have been observed and are probably related to the irritating nature of EDA and it's high pH. Hepatocellular pleomorphism has been observed in several dietary studies of varying duration. The lowest LOAEL was 100 mg/kg/day with a NOEL of 20 mg/kg/day in the chronic dietary feeding study.

d) Genotoxicity

Genetic toxicity *in vitro*

In two Ames Salmonella assays, weakly positive results were reported but no data were presented (Hedenstedt, 1978 and Hulla, 1981). The purity of test material used was not reported. Weakly positive responses were reported in strains TA100 and TA1535 but not in strains TA98 and TA1537 using the Ames Salmonella assay (Haworth, et al., 1983). The purity of this test material was reportedly 99.8% pure. In another study, slightly positive mutagenic activity was observed with a Dow sample of EDA but not with a Union Carbide sample of EDA (Mueller and Dabney, 1979). The Dow sample of EDA was positive with metabolic activation in strains TA100 and TA1535 but not without metabolic activation or in strains TA98 and TA1538 with and without metabolic activation. Subsequent tests of product from Dow and Union Carbide were negative in the Ames test (Domoradzki, J.Y. 1979). Additional tests several years later of a Union Carbide sample resulted in a borderline result in strain TA100 (Guzzie, 1987). The cause of the weakly positive response has been hypothesized to be due to an impurity (Hedenstedt, 1978). Ethylenediamine was negative in the CHO gene mutation assay, sister chromatid exchange with CHO cells, UDS assay with primary rat hepatocytes (Slesinski, 1983).

Ethylenediamine has the ability to chelate metals, most notably copper, albeit at a much lower affinity than DETA, TETA and TEPA. However, it's weak chelant ability probably did not produce the borderline positive result in the Ames test.

Genetic toxicity in vivo

Ethylenediamine was negative in dominant lethal (Slesinski, 1983) and *Drosophila melanogaster* SLRL assay when administered in the diet at 10,000 or 20,000 mg/kg or when injected at a dose of 1500 mg/L (Zimmering, S. et al., 1985).

Conclusions: Ethylenediamine has produced weakly positive results, 2-3 fold greater than control values, in several Ames tests which may or may not be related to an impurity. Subsequent studies conducted with purer material were negative. All other tests including several *in vitro* assays and a rat dominant lethal assay were negative. The weight of evidence from both *in vitro* and *in vivo* tests indicates that ethylenediamine is unlikely to be genotoxic. It was also negative in chronic bioassays via two routes, oral and dermal.

e) Carcinogenicity

In a two-year bioassay, 100 male and 100 female Fischer 344 rats were fed 0, 20, 100 or 350 (M) or 360 (F) mg/kg/day for 24 months with interim sacrifices of 10 rats/sex/dose at 6 and 12 months; and 15-20 rats/sex/dose at 18 months (Hermansky et al., 1999). Mortality was essentially the same through the first 20 months. Mortality increased relative to controls in male and female rats ingesting 350 mg/kg/day after 22 months and in female rats ingesting 100 mg/kg/day after 24 months. Decreased numbers of pituitary adenomas and testicular interstitial cell adenomas were evident in high level males. There was no evidence, under the conditions of this study, that chronic feeding of ethylenediamine dihydrochloride, at levels as high as 350 mg/kg/day, exhibited a carcinogenic effect in the Fischer 344 rat. Repeated dose effects from this study are summarized in section c.

In a lifetime skin painting study, 25µl of a 1% aqueous solution of test material from Dow and Union Carbide was applied 3 times/week to male mice (Depass et al., 1984). No epidermal tumors were seen on the mice, which received either EDA sample. One mammary gland adenocarcinoma was noted in the mice dosed with the Dow Chemical Co. material. One myosarcoma was noted at the base of the tail in the mice dosed with the Union Carbide material. One sebaceous adenoma of the skin of the thorax was noted in the control group. Neither product was considered to be carcinogenic under the conditions of the study protocol.

Conclusions: In animals, ethylenediamine was not carcinogenic by either the dermal or oral route.

f) Toxicity to reproduction

Effects on fertility

In a two-generation reproduction study, male and female rats were fed 0, 50, 150 or 500 mg/kg/day of EDA-2HCl in the diet (Yang et al., 1984a). The parent generation (F0) and the F1 generation were each bred once. Similar effects to those noted in the 3 month repeated dose study were observed in both sexes for the F0 and F1 parents, albeit at lower doses. These effects included decreased body weight gain, decreased liver weight, increased kidney weights and hepatocellular pleomorphism in the high dose group, decreased body weight gain in the middle dose F_0 females and increased kidney weight in the middle dose F_1 females. The observation of effects at lower doses is most likely due to the increased feed consumption noted in females during the last two weeks of lactation where there can be a 2-5 fold increase in dietary intake. There was no reproductive effect noted in any dose group as regards fertility, pup survival, number of pups born alive and number of pups weaned per litter. For the adults, the lowest LOAEL was 150 mg/kg/day, which may have been much higher due to the increased feed consumption. The NOEL was 50 mg/kg/day for the adults and 500 mg/kg/day for reproductive parameters.

Developmental toxicity

In a teratology study, female rats were fed 0, 50, 250 or 1000 mg/kg/day of EDA·2HCl in the diet on days 6-15 of gestation (DePass et al., 1987). Maternal effects, such as decreased weight gain and feed consumption, were noted in the intermediate and high dose groups. In the high dose group, fetal weight and crown-rump length were significantly reduced and the percentage of litters with resorptions, with skeletal variants and with missing (left and right cartoid branch off the brachiocephalic artery at the same time, thus there is no innominate) or shortened innominate artery was increased. However, the missing innominate artery would not affect blood supply to areas served by these arteries. Additional oral gavage studies were conducted at 1000 mg/kg/day to determine whether the effects observed in the offspring were directly due to EDA·2HCl. In the first

study, food intake was decreased in dams receiving EDA·2HCl. In the second study, a paired-feeding study, male and female fetal weights and crown-rump lengths were significantly less than the negative control group and the pair-fed control group. In addition, the length of the innominate artery in male and female pups was shorter than for the pair-fed control and negative control groups. However, both the EDA·2HCl and the pair-fed control group had two fetuses from different litters with missing innominate artery. Missing innominate artery has been observed in the offspring of rats placed on diets deficient in folic acid (pteroylglutamic acid) and vitamin A. The authors concluded the shortened innominate artery from pups fed EDA·2HCl is not a teratologic effect since it would result in no functional deficit and may not be an irreversible change. It may be part of an overall growth retardation effect of EDA·2HCl along with reduced fetal weight. Therefore the authors concluded that EDA·2HCl was not teratogenic in the Fischer 344 rat. However, the LOAEL for the fetuses was 1000 mg/kg/day with a NOEL of 250 mg/kg/day. In these studies the NOEL for maternal toxicity was 50 mg/kg/day and the LOAEL was 250 mg/kg/day.

Conclusions: Although significant growth retardation was observed in fetuses from dams receiving 1000 mg/kg/day, levels which resulted in maternal toxicity, there was no evidence of a teratogenic effect. There was no evidence of reproductive toxicity at levels as high as 500 mg/kg/day in rats in a two generation study.

g) Other human health related information

Ethylenediamine has been positive in a number of human dermal sensitization studies (Eriksen, 1979, English and Rycroft, 1989). The first case reports on hypersensitivity appeared in the late fifties and concerned pharmacists handling aminophylline preparations (Baer et al., 1959). During a 20 year period, between 1967 and 1987, the International Contact Dermatitis Group (ICDRG) included ethylenediamine as part of its standard patch test series. The standard patch test series was conducted on different test populations consisting of 89-3216 individuals from several countries, including Poland, Canada, USA, Scotland, Sweden, Italy, Denmark and Germany. These individuals probably had some type of dermal irritation prior to visiting the physician's office. The percentage positive for these various groups ranged from 0-17%. The higher incidence is probably due to individuals with 'angry back syndrome'. In the seventies ethylenediamine had been nominated the second or the fifth most common contact allergen. In most cases sensitization was caused by topical preparations containing ethylenediamine as stabilizer (e.g. Mycolog in the US, Tri-Adcortyl in Great Britain, Kenacomb in Australia, Assocort and Halciderm Combi ointment in Italy). Mycolog is no longer produced in the US (PDR, 2000).

Cases of occupational sensitization in production facilities have only rarely been reported (Hagmar et al., 1982; Lewinsohn and Ott, 1991; Ng, 1991). Delayed-type asthma was observed in workers with rhinorrhea, sore throat and a hacking cough being observed first. Occasionally dual-type asthma has been observed. There have been no cases of immediate-type asthma reported. Humans sensitized to EDA have also been shown to be sensitive to diethylenetriamine, triethylenetetramine, tetraethylenepentamine and to a lesser extent, piperazine (Balato, 1986).

Conclusions: It is a dermal and respiratory sensitizer in humans.

3.2 Initial Assessment for Human Health

The critical effects from acute exposure to ethylenediamine are primarily due to the pH of the material. Based on animal data, ethylenediamine is corrosive to the skin and eyes. Even dilute solutions have caused burns to the skin. Ingestion may also cause burns to the mouth and

gastrointestinal tract. It has been a positive skin sensitizer in several guinea pig and human studies and has been demonstrated to be a cross sensitizer with other amines. EDA has also caused delayed-type asthma.

In repeated dose studies, decreased body weight, feed and water consumption and liver pleomorphism have been noted in nearly every study via the dietary route. However, when EDA was given by oral gavage, effects were noted in the eyes and kidneys. Kidney effects consisted of degenerative and regenerative changes in the tubular epithelium. In developmental toxicity studies, growth retardation was noted at maternally toxic levels. However, there was no evidence of developmental toxicity at maternally toxic doses when compared with a pair-fed control. There was no effect on reproductive parameters at levels, which produced parental toxicity. In summary, the lowest LOAEL is 100 mg/kg/day with a NOEL of 20 mg/kg/day observed in the chronic dietary feeding study.

The weight of evidence suggests that ethylenediamine is not genotoxic. It was also negative in chronic bioassays following administration via two routes, oral and dermal.

4. Hazards to the Environment

4.1 Aquatic Effects

4.1.1 Acute Toxicity

The chemical was neutralized in solution prior to performing toxicity testing. As a result, the pH was not considered to be a factor.

The 96 hr LC50 in the most sensitive fish species, *Pimephales promelas*, is 115 mg/L (see Table 3). An old study reports a 24 hr LC50 between 30 and 60 mg/L in *Semolitus atromaculatus* and does not appear to be consistent with the results of other studies.

Daphnia are the most sensitive species tested. The 48 hr LC50 for *Daphnia magna* ranges from 3-26.5 mg/L. One study using adult daphnids reports a 96-hr LC50 value of 0.88 mg/L which is slightly lower than the 48 hr values. But since Daphnia tests are usually conducted with first instar organisms (less than 24 hr old) and, typically, are not fed during the exposure period, it is unclear whether the mortality was due to toxicity from ethylenediamine or due to starvation. The 48 hr LC50 values in Daphnia range from 3-46 mg/L.

The 48-, 72- and 96-hr algal biomass EC50 values were >100, 71 and 61 mg/L, respectively, in 3 freshwater green algal species.

Conclusion: On an acute toxicity basis the most sensitive species is *Daphnia magna* where the 48 hr LC50/EC50 is 3-46 mg/L.

Table 3: Acute Toxicity in Aquatic Organisms

Species	Duration	Parameter measured	Results (mg/L)	Reference
Fish				
Oryzias latipes	24	LC50	1000	Tonogai, et al. (1982)
Semolitus atromaculatus	24	LC50 static	>30 <60	Gillette et al. (1952)
Oryzias latipes	48	LC50	1000	Tonogai, et al. (1982)
Leuciscus idus melanotus	48	LC50 static	405	Juhnke and Luedemann (1978)
Salmo trutta	48	LC50	230	Woodiwiss and Fretwell (1974)
Pimephales promelas	96	LC50 semistatic	115.7	Curtis and Ward (1981)
Pimephales promelas	96	LC50 static	210	Union Carbide
Pimephales promelas	96	LC50 static	210	Bartlett (1978).
Pimephales promelas	96	LC50	>11.5	NAPM (1974)
Poecilia reticulata	96	LC50 static	275	van Leeuwen (1985)
Poecilia reticulata	96	LC50 semistatic	640	AKZO Research (1989)
Poecilia reticulata	96	LC50	1545	Van Wijk (1994)
Invertebrates				
Artemia salina	24	LC50	14	Price et al. (1974):
Daphnia magna	24	EC50	14	Kuehn et al. (1989)
Daphnia magna	24	EC50	19	Bringmann and Kuehn (1982)
Daphnia magna	48	EC50	17	AKZO Research (1989)
Daphnia magna	24	LC50	16	Bringmann and Kuehn (1977):
Daphnia magna	48	LC50 static	3.0	Bartlett, E.A. (1978).
Daphnia magna	48	LC50	4.5	Union Carbide

Daphnia magna	48	LC50	26.5	van Leeuwen (1985)
Daphnia magna	48	LC50	46	Van Wijk (1994)
Daphnia magna	96	LC50	0.88	NAPM (1974)
Algae				
Scenedesmus subspicatus	48	EC50	>100	Kuehn and Pattard (1990)
Selenastrum capricornutum	72	EC50	71	Akzo Research to Delamine (1990)
Chlorella pyrenoidosa	96	EC50	61	van Leeuwen (1985)

***** *Poecilia reticulta* - guppy
Pimephales promelas – fathead minnow
Leuciscus idus – golden orf
Oryzias latipes – Japanese medaka
Semolitus atromaculatus – creek chub
Salmo trutta – brown trout
Artemia salina – brine shrimp
Daphnia magna – water flea
Scenedesmus subspicatus – green algae
Selanstrum capricornutum – green algae

4.1.2 Chronic Toxicity

In the case of chronic toxicity, the NOEC was >10 mg/L in a fish 28 day early life stage study (Akzo, 1992). In Daphnia, the NOEC ranged from 0.16 – 2 mg/L in two 21-day reproduction studies (Kuehn et al., 1989 and Akzo, 1992).

Conclusion: In the case of chronic toxicity, the lowest NOEC was 0.16 mg/L in a Daphnia 21 day reproduction study.

4.2 Terrestrial effects

For *Lactuca sativa* the 21day EC_{50} =208 mg/L(nutrient solution, semi-static, nominal) and the 14-day EC_{50}= 692 mg/kg (soil, static, nominal). (Hulzebos et al. 1993)

4.3 Other Environmental Effects

4.4 Initial Assessment for the Environment

Ethylenediamine is expected to be readily biodegradable in the environment with 80% degraded within 28 days. The 96 hr LC50 in fish is 115 mg/L while the 96 hr algae biomass EC50 is 61 mg/L. In the most sensitive aquatic organism, *Daphnia magna*, the 48 hr LC50 is 3-46 mg/L with a 21-day reproduction test No-Observable-Effect-Concentration (NOEC) of 0.16 mg/L.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusion

Physical/chemical property, production, use and distribution

The production volume in the US was approximately 90 million lbs. in 1994 (SRI, 1996). Essentially all of the ethylenediamine produced in the US is used as an intermediate for industrial use. A very small amount is used in the pharmaceutical industry. Ethylenediamine is a highly water soluble liquid at room temperature. Based on Level III Fugacity Model of Mackay, the majority of ethylenediamine would be expected in water. Ethylenediamine is readily biodegradable in water with 80% degraded within 28 days. It has a half-life of 8.9 hours in air. Any EDA released into the environment would be expected to degrade quickly.

Aquatic Toxicity
The 96 hr LC50 in fish is 115 mg/L while the 96 hr algae biomass EC50 is 61 mg/L. In the most sensitive aquatic organism, *Daphnia magna*, the 48 hr LC50 is 3-46 mg/L with a 21-day reproduction test No-Observable-Effect-Concentration (NOEC) of 0.16 mg/L.

Human Health

Acute toxicity of ethylenediamine is considered to be low to moderate. This chemical is corrosive to skin and eyes. It has caused dermal sensitization primarily in the pharmaceutical industry. It has been reported to cross-sensitize for chemicals of similar structures. EDA has also caused a delayed-type asthma. Hepatocellular pleomorphism was observed in subchronic and chronic studies via the dietary route. However, when EDA was administered by gavage effects were noted in the eyes and kidneys. The kidney changes consisted of degenerative and regenerative changes in the tubular epithelium. Although EDA produced growth retardation at maternally toxic doses in animal studies, there was no evidence of a teratogenic effect. EDA was negative in chronic bioassays by two separate routes of exposure.

5.2 Recommendations

The toxicity of ethylenediamine to the environment, animals and humans is well characterized. It is recommended that ethylenediamine be considered low priority for further hazard characterization. OECD member countries should evaluate their exposure scenarios to determine the chemical's priority for further work.

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I U C L I D

Data Set

Existing Chemical	:	ID: 107-15-3
CAS No.	:	107-15-3
EINECS Name	:	ethylenediamine
EINECS No.	:	203-468-6
TSCA Name	:	1,2-Ethanediamine
Molecular Formula	:	C2H8N2

Producer Related Part

Company	:	The Dow Chemical Company
Creation date	:	16.10.2000

Substance Related Part

Company	:	The Dow Chemical Company
Creation date	:	16.10.2000
Memo	:	
Printing date	:	05.09.2002
Revision date	:	
Date of last Update	:	05.09.2002
Number of Pages	:	315
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	???

1.0.1 OECD and Company Information

Type :
Name : AgrEvo Prode Tech
Partner :
Date :
Street : Usine de Saint Marcel BP 1
Town : F-13367 Marseille
Country : France
Phone : 00334(91)244545
Telefax : 00334(91)244646
Telex :
Cedex : 11
05.09.2002

Type :
Name : Bakelite Italia S.p.A.
Partner :
Date :
Street : Via Mazzini, 792-4
Town : I-21058 Solbiate Olona (VA)
Country : Italy
Phone : +39/(0)331/355-225
Telefax : +39/(0)331/376-390
Telex :
Cedex :
05.09.2002

Type :
Name : BASF AG
Partner :
Date :
Street : Karl-Bosch-Str
Town : 67056 Ludwigshafen
Country : Germany
Phone :
Telefax :
Telex :
Cedex :
05.09.2002

Type :
Name : BASF Antwerpen N. V.
Partner :
Date :
Street :
Town : 2040 Antwerpen 4
Country : Belgium
Phone :
Telefax :
Telex :
Cedex :
05.09.2002

Type :
Name : Bayer AG
Partner :
Date :
Street :

Town : 51368 Leverkusen
Country : Germany
Phone :
Telefax :
Telex :
Cedex :
05.09.2002

Type :
Name : Berol Nobel AB
Partner :
Date :
Street :
Town : 444 85 Stenungsund
Country : Sweden
Phone : +46-303-85000
Telefax : +46-303-84659
Telex :
Cedex :
05.09.2002

Type :
Name : DELAMINE BV
Partner :
Date :
Street :
Town : 9930 AB Delfzijl
Country : Netherlands
Phone :
Telefax :
Telex :
Cedex :
05.09.2002

Type :
Name : Dow Benelux N. V.
Partner :
Date :
Street : Herbert H. Dowweg 5
Town : 4530 Terneuzen
Country : Netherlands
Phone :
Telefax :
Telex :
Cedex :
05.09.2002

Type :
Name : RHODIA CHIMIE
Partner :
Date :
Street : 25 QUAI PAUL DOUMER
Town : 92408 COURBEVOIE CEDEX
Country : France
Phone :
Telefax :
Telex : 01 47 68 12 34
Cedex :
05.09.2002

Type :
Name : RHODIA LTD
Partner :
Date :
Street : OAK HOUSE - REEDS CRESCENT
Town : WD1 1QH WATFORD
Country : United Kingdom
Phone :
Telefax :
Telex : 01923 211 700
Cedex :
05.09.2002

Type :
Name : Rohm and Haas France S.A.
Partner :
Date :
Street : 371 rue L. van Beethoven
Town : 06565 Valbonne
Country : France
Phone :
Telefax :
Telex :
Cedex :
05.09.2002

Type :
Name : Union Carbide Benelux
Partner :
Date :
Street : Norderlaan 147
Town : 2030 Antwerpen
Country : Belgium
Phone :
Telefax :
Telex :
Cedex :
05.09.2002

Type :
Name : Warwick International Limited
Partner :
Date :
Street : Dock Road
Town : CH8 9HE Mostyn, Holywell, Clwyd
Country : United Kingdom
Phone : 0745 560651
Telefax : 0745 561702
Telex : 61640
Cedex :
05.09.2002

1.0.2 Location of Production Site

1.0.3 Identity of Recipients

1.1 General Substance Information

Substance type : organic
Physical status : liquid
Purity : >= 99 % w/w
Test substance : Ethylenediamine
29.08.2001 (1)

Substance type : organic
Physical status : liquid
Purity : ca. 100 % w/w
Remark : Analysis of a 19 month old sample used in toxicity tests indicated the water content was nil and no impurities were identified by infrared.
Test substance : Ethylenediamine dihydrochloride
29.08.2001 (2)

1.1.0 Details on template

1.1.1 Spectra

1.2 Synonyms

.alpha.,.omega.-Ethanediamine
02.06.1994

.beta.-Aminoethylamine
02.06.1994

1,2-diaminoethane
31.05.1994

1,2-ethanediamine
31.05.1994

1,2-Ethanediamine (9CI)
19.12.1994

1,2-ETHANEDIAMINE - EDA, EDA-HP, EDA-UHP
27.05.1998

1,2-Ethylenediamine
05.09.2002

1,4-Diazabutane
02.06.1994

Dimethylenediamine
10.05.1994

Dimethylenediamni
02.06.1994

EDA
02.06.1994

Edamine
02.06.1994

Ethylene diamine

24.05.1994

Ethylenediamine
08.04.1994

Ethylenediamine (8CI)
19.12.1994

Remark : 1,2 - Diaminoethane
Dimethylenediamine
Source : Berol Nobel AB Stenungsund
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

09.05.1994

1.3 Impurities

1.4 Additives

1.5 Quantity

Production during the last 12 months :
Import during the last 12 months :
Quantity produced : 100 000 - 500 000 tonnes in 1994
Remark : Worldwide production
15.01.2001 (3)

Production during the last 12 months :
Import during the last 12 months :
Quantity : 100 000 - 500 000 tonnes in
05.09.2002

1.6.1 Labelling

Labelling : as in Directive 67/548/EEC
Symbols : C
Nota : other RM: H
Specific limits : yes
R-Phrases : (10) Flammable
(21/22) Harmful in contact with skin and if swallowed
(34) Causes burns
(42/43) May cause sensitization by inhalation and skin contact
S-Phrases : (1/2) Keep locked up and out of reach of children
(23) Do not breathe ...
(26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
(36/37/39) Wear suitable protective clothing, gloves and eye/face protection
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

05.09.2002

1.6.2 Classification

Classification : as in Directive 67/548/EEC
Class of danger : corrosive
R-Phrases : (34) Causes burns
05.09.2002

Classification : as in Directive 67/548/EEC
Class of danger : harmful
R-Phrases : (21/22) Harmful in contact with skin and if swallowed
05.11.2000

Classification : as in Directive 67/548/EEC
Class of danger :
R-Phrases : (10) Flammable
05.09.2002

Classification : as in Directive 67/548/EEC
Class of danger :
R-Phrases : (42/43) May cause sensitization by inhalation and skin contact
05.09.2002

1.7 Use Pattern

Type : type
Category : Non dispersive use
14.02.2002

Type : type
Category : Use in closed system
10.02.2000

Type : type
Category : Use resulting in inclusion into or onto matrix
10.02.2000

Type : type
Category : Wide dispersive use
14.02.2002

Type : industrial
Category : Chemical industry: used in synthesis
10.02.2000

Type : industrial
Category : Fuel industry
30.08.2001

Type : industrial
Category : Paints, lacquers and varnishes industry
10.02.2000

Type : industrial
Category : Paper, pulp and board industry
05.09.2002

Type : industrial

Category : Polymers industry
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10.02.2000

Type : use
Category : Intermediates
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10.02.2000

Type : use
Category : other: Used in epoxy resin curing agents
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.08.2001

Type : use
Category : other: Used in the manufacture of Cleaning/washing agents and disinfectants (tetraacetylethylenediamine, TAED)
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.08.2001

Type : use
Category : other: Used in the manufacture of additive oils and fuels
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.08.2001

Type : use
Category : other: Used in the manufacture of chelating agents
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.08.2001

Type : use
Category : other: Used in the manufacture of diverse chemicals
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10.02.2000

Type : use
Category : other: Used in the manufacture of fungicides for Europe
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.08.2001

Type : use
Category : other: Used in the manufacture of surfactants
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.08.2001

1.7.1 Technology Production/Use

1.8 Occupational Exposure Limit Values

Type of limit : MAC (NL)
Limit value : 25 mg/m3
05.09.2002 (4)

Type of limit : MAK (DE)
Limit value : 25 mg/m3
Short term exposure
Limit value : 50 mg/m3
Schedule : 30 minute(s)

Frequency : 4 times
Remark : Group D: Not enough data for final classification concerning pregnancy risks.
05.09.2002 (5)

Type of limit : MAK (DE)
Limit value : 25 mg/m3
05.09.2002

Type of limit : MAK (DE)
Limit value : 10 ml/m3
Short term exposure
Limit value : 20 ml/m3
Schedule : 30 minute(s)
Frequency : 4 times
05.09.2002 (6)

Type of limit : MAK (DE)
Limit value : 25 mg/m3
Remark : hautresorptiv, sensibilisierend
05.09.2002 (7)

Type of limit : MAK (DE)
Limit value : 25 mg/m3
Remark : hautresorptiv, sensibilisierend
05.09.2002 (7)

Type of limit : MAK (DE)
Limit value : 10 ml/m3
Short term exposure
Limit value : 20 ml/m3
Schedule : 30 minute(s)
Frequency : 4 times
05.09.2002

Type of limit : MAK (DE)
Limit value : 25 mg/m3
Remark : hautresorptiv, sensibilisierend
05.09.2002 (7)

Type of limit : OES (UK)
Limit value : 25 mg/m3
Remark : Long-term exposure limit (8-hour TWA reference period)
05.09.2002 (8)

Type of limit : TLV (US)
Limit value : 25 mg/m3
05.09.2002 (9)

Type of limit : TLV (US)
Limit value :
Remark : TLV: 10 ppm skin
05.09.2002 (10)

Type of limit : other
Limit value : 18 mg/m3
29.08.2001 (11)

1.9 Source of Exposure

Memo : Information was supplied from Denmark, Finland, France, Sweden and France on products listed in their registries.

Remark : The concentration of EDA listed in the consumer products is the highest concentration listed and many products contained much lower concentrations.

Result : Number of products varied from 17 (Finland) to 189 (Switzerland).

Product registries varied in the reporting requirement based on EDA present in consumer products in which some of the other components in each product were not provided. These other components are believed to be acids, oxides and other materials, which react with EDA. This was confirmed by France, as oxides are reported as being present in some of the products which ultimately result in the concentration of the EDA in the final product being much lower than implied by the data from the product registries.

Switzerland provided information that the concentration of EDA present in a final product decreases with every additional reaction of EDA.

In countries that differentiated between consumer and industrial applications, <25% of the products were sold into consumer application.

All identified consumer products contained <0.5% EDA.

In Denmark 6 tons/year is sold.

14.02.2002 (12)

Remark : Routes of manufacturing in Dow:

Reaction of ethylene dichloride with NH3, neutralisation with NaOH and salt remocal. Separation of ethylenediamine by fractionated distillation. Manufacturing process completely closed. Estimated fugitive emissions of ethylenediamine to the hydropshere and atmosphere < 0.5% and < 0.05%, respectively.

26.05.1994

Remark : As the quantities of this substance placed on the EU market by Union Carbide Benelux N.V. are normally sourced from the manufacturing facilities of its U.S. parent comany, no exposure can arise within the EU from the manufacture of these quantities. The comments below on exposure are restricted to the uses for which Union Carbide believes its customers use this substance.

Major use(s): As chemical intermediate for fungicides, chelating agents, polyamides etc.

Sources of human exposure: Negligible human exposure assuming appropriate industrial hygiene and personal protective precautions are observed.

Sources of environmental exposure: In waste water streams from chemical processes, the substance readily biodegrades.

20.05.1994

Remark : No data
05.05.1998

Country : United Kingdom
Remark : The substance is imported into the UK and delivered in approved construction Iso-tanks directly from the manufacturer. It is used only at the UK site of this submission.

Acceptance is based on the provision of SPC data by the supplier, rather than by sampling and testing at the point of use, in order to reduce unecessary exposure to this material.

The storage of the substance - and the abatement techniques employed in its use - are described in our Integrated Pollution Control application which has been submitted to, and approved by, HMIP.

The substance is reacted with acetic anhydride to make tetraacetyl ethylene diamine (TAED), the subject of a separate submission. The reaction is quantitative; there is no carry-over of the substance into the final product. The substance is delivered in bulk, stored in bulk and metered into the reaction vessels.

We consider the process to be "closed".
25.05.1994

Remark : Article summarizes data from 5 plants, only one of which is referenced, Hansen, et al., (1984).

Chemical synthesis - Measured exposure data
"Color indicator tubes have been used to monitor for EDAduring disconnection of the transfer hose from a tanker following transfer of EDA to storage tanks. Airborne concentrations of EDA were below the limit of detection (0.05 ppm).

Transfer of EDA from 200 liter drums to storage tanks involves the use of an enclosed pumping system. An organic vapor meter, calibrated for diethylamine, has been used to monitor for EDA at 30 second intervals during charging of storage tanks from 200 liter drums. EDA levels were below the limit of detection (0.1 ppm).

Personal sampling for EDA has been conducted at one UK based plant. This involved using pumped XAD tubes (80/40 mg) treated with 1-naphthylisothiocyanate at a flow rate of between 0.01-0.1 liters/minute. Subsequent analysis based on NIOSH method 2540 gave results below the limit of detection (average limit of detection = 0.41 ppm).

At another UK based plant, EDA was not detected in the workplace during background monitoring using color indicator tubes (detection limit 0.05 ppm).

Hansen et al., 1984, monitored for EDA using an impinger sampling method in a petrochemical plant producing EDA and a plant using EDA for making EDTA. EDA was detected only

under a ventilation hood at a tanking site. The EDA concentration in the air was about 0.41 ppm after 3 hours of sampling at 750 ml/minute.

Use of formulations - Measured exposure data
"Franklin, Strange and Geesaman, (1987) have investigated EDA exposure levels at a large-scale coating operation. Pure or 50% EDA was used as a solvent in the application of polymers and pigments to an aluminised polyethylene terephthalate film substrate by a coating machine in an enclosed environment and in the presence of exhaust ventilation. Background air sampling was carried out in the coater machine environment from 1975 to 1981. A total of 1,053 measurements of EDA in air were made using the standard NIOSH method (NIOSH, 1978). The percentage of EDA measurements in coater machine environment that exceeded 1 ppm was below 3% for most years but reached 20 and 25% in 1975 and 1980 respectively. The percentage of exposures exceeding 10 ppm were below 0.2% for most years but reached 5% in 1975 and 1980. It is important to note that these EDA concentrations were from the use of pure or 50% EDA formulations."

References
Franklin, Stange and Geesaman (1987). unreferenced

Hansen, L., Kristiansson, B. and Sollenberg, J. (1984). A method for the determination of ethylenediamine in workroom air. Scand J Environ Health 10:95-98.

16.01.2001 (13)

Remark : An industrial hygiene survey was conducted on a ethylenediamine production plant. Air samples were taken in the process area on March 7 and 8, 1967. Because the sampling-analyzing technique would not allow differentiation between various amines, the analyses were made as "total nitrogen" and the corresponding air concentrations were first calculated assuming the nitrogen to be present as ammonia and secondly as ethylene diamine. Data presented assumes all of the nitrogen was from ethylenediamine.

The concentration measured in the control room, where operators spend as much as 70 percent of their time, was 1.5 or 2.0 ppm as ethylenediamine.

The highest concentration measured in the workplace was 4.4 ppm.

The actual exposure to ethylenediamine is probably lower than presented.

Sample Number	Description of Sample	EDA (ppm)
1	General area sample	0.7
2	Breathing zone of operator during sample taking	4.4
3	General area in control room	2.0
4	General area in control room	1.5
5	General area on ground level of process area	1.8

16.01.2001 (14)

Result : Paper presents sampling and analysis of EDA in air. Concentration of EDA was measured in two plants. One was a petrochemical plant producing EDA and five othe amines, and the other was a factory using EDA for making ethylenediaminetetraacetic acid.

In these investigations EDA was found only at a site for tanking which occurred under a ventilation hood. The EDA concentration in the air was about 1 mg/m3 after 3 hours of sampling at 750 ml/min.

16.01.2001 (15)

Remark : Three commercial amine products used as wetting agents in bitumen were studied. The bitumen emulsion used contained 4-6% binder which contained approximately 0.2% amine. The amount of EDA present in the wetting agents was <0.5% in each case.

The concentration of EDA present in air during road paving operations was <0.02% in each instance.

16.01.2001 (16)

1.10.1 Recommendations/Precautionary Measures

1.10.2 Emergency Measures

1.11 Packaging

1.12 Possib. of Rendering Subst. Harmless

1.13 Statements Concerning Waste

1.14.1 Water Pollution

Classified by : KBwS (DE)
Labelled by : KBwS (DE)
Class of danger : 2 (water polluting)
05.09.2002

1.14.2 Major Accident Hazards

Legislation : Stoerfallverordnung (DE)
Substance listed : no
No. in directive :
05.09.2002 (17)

Legislation : Stoerfallverordnung (DE)
Substance listed :
No. in directive :
Remark : Anhang: II Nr. 3
05.09.2002

1.14.3 Air Pollution

Classified by : TA-Luft (DE)
Labelled by : TA-Luft (DE)
Number : 3.1.7 (organic substances)
Class of danger : II
05.09.2002
Classified by : other: VCI
Labelled by :
Number : 3.1.7 (organic substances)
Class of danger : II
05.09.2002

1.15 Additional Remarks

Remark : FDA; Ethylenediamine is an indirect food additive for use only as a component of adhesives.
21 CFR 175.105 (4/1/86)
03.06.1994
Remark : Disposal: Incineration of ethylenediamine at federal approved incineratiors.
10.05.1994
Remark : Disposal: Incinerate in a furnace where permitted under national and local regulations.

Transport: Ethylenediamine is a class 8 product according the ADR/RID/IMDG/ICAO regulations.
The substance has to be (un)loaded with a vapour return line.

Ethylenediamine is shipped in road/rail tankcars, tankcontainers/ISOtanks and smaller packages (e.g. drums).
31.05.1994
Remark : No data
05.05.1998
Remark : The substance is delivered by road in approved Iso-tanks, of a design appropriate for the classification of this material. The vehicles are identified according to U.N. Transport Regulations and carry the appropriate TREM cards.
25.05.1994

1.16 Last Literature Search

1.17 Reviews

Memo : CICAD #15 is a review of ethylenediamine
07.02.2002

1.18 Listings e.g. Chemical Inventories

2.1 Melting Point

Value : = 11.1 ° C
Sublimation :
Method : other: adiabatic calorimeter
Year : 1975
GLP : no data
Test substance : other TS: 99.90 moles percent pure
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (18)

Value : 10.9 ° C
Sublimation :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.06.2001 (19)

Value : 8 ° C
Sublimation :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (20)

Value : 8.5 ° C
Sublimation :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (21)

Value : 8.5 ° C
Sublimation :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (22)

Value : 10.7 ° C
Sublimation :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (23)

Value : 11 ° C
Sublimation :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (24) (25)

2.2 Boiling Point

Value : = 117 ° C at
Decomposition :
Method : other:: measured with an ebulliometer as part of vapor pressure determination
Year : 1975
GLP : no data
Test substance : other TS: 99.90 moles percent pure
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (18)

Value : 115 ° C at 1013 hPa
Decomposition :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (24)

Value : 116 - 117 ° C at
Decomposition :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (26)

Value : 116 ° C at 1013 hPa
Decomposition :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (20)

Value : 117 - 118 ° C at

Decomposition :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (23)

Value : 117 ° C at 1013 hPa
Decomposition :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.06.2001 (19)

Value : 117 ° C at
Decomposition :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (27)

Value : 117 ° C at 1013 hPa
Decomposition :
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (25)

2.3 Density

Type : density
Value : .899 g/cm3 at 20° C
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (21)

Type : density
Value : .9 g/cm3 at 15° C
Method :
Year :
GLP :

Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (28)

Type : relative density
Value : .898 at 20° C
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (23) (25)

Type : density
Value : .8995 at 20° C
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (29)

Type : density
Value : .902 g/cm3 at 20° C
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (20)

Type : relative density
Value : .893 - .906 at 25° C
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (24)

2.3.1 Granulometry

2.4 Vapour Pressure

Value : 12 hPa at 20° C
Decomposition :
Method
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint
19.06.2001 (19)

Value : = 17.06 hPa at 25° C
Decomposition :
Method other (measured): used static inclined-piston method at low-pressure and comparative ebulliometer at high pressure range
Year : 1975
GLP : no data
Test substance : other TS: 99.90 moles percent pure
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (18)

Value : 12 at 20° C
Decomposition :
Method
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (20)

Value : 13.33 at 20° C
Decomposition :
Method
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (24)

Value : 13.86 hPa at 20° C
Decomposition :
Method
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (30)

Value : 14.26 hPa at 20° C
Decomposition :
Method
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (31)

Value : 13.33 hPa at 21.5° C
Decomposition :
Method
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (32)

Value : 70 hPa at 50° C
Decomposition :
Method
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (23)

2.5 Partition Coefficient

Log pow : = -1.3 at ° C
Method other (measured): no data
Year : 1982
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (33)

Log pow : = -2.04 at ° C
Method other (measured): no data
Year : 1991
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (34)

Method other (calculated): Advanced Chemistry 4.56
Year : 2000
GLP :
Test substance : as prescribed by 1.1 - 1.4
Result : Predicted Log Kow

pH	Log Kow
5	-5.87
6	-5.08
7	-4.12
8	-3.13
9	-2.18

16.11.2001 (35)

Log pow : = -1.52 at ° C
Method other (calculated): no data
Year : 1991
GLP : no data
Test substance :
Source : Union Carbide Benelux Antwerpen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.04.1994 (36)

Log pow : = -1.36 at ° C
Method
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Remark : highly water soluble expected to be completely protonated at natural pH
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.06.2001 (37)

Log pow : -1.221 at ° C
Method other (calculated)
Year :
GLP :
Test substance :
Remark : The log octanol/water partition coefficient (log KoW) is estimated using the Pomona-MedChem structural fragment method.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.1994 (24) (38)

Log pow : = -1.2 at ° C
Method other (calculated): A. Leo, CLOGP-3.63 (1991) Daylight, Chemical Information Systems,Inc. Irvine, CA USA
Year : 1991
GLP :
Test substance :
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
05.11.2000 (39)

2.6.1 Water Solubility

Value : at 20 ° C
Qualitative :
Pka : at 25 ° C
PH : 12.2 at 110 g/l and 12.2 ° C
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.06.2001 (23)

Value : 100 other: % by weight at 20 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C
Method :
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.06.2001 (40)

Value : at ° C
Qualitative : miscible
Pka : at 25 ° C
PH : at and ° C
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (41) (19) (42)

Value : at ° C
Qualitative : miscible
Pka : at 25 ° C
PH : at and ° C
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (24)

2.6.2 Surface Tension

2.7 Flash Point

Value : = 34 ° C
Type : closed cup
Method : other: no data
Year : 1990
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (43)

Value : 38 ° C
Type :
Method : other: DIN 51 755
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (23)

Value : 38 ° C
Type : closed cup
Method : other: Pensky-Martens Closed Cup (ASTM D 93)
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (44)

Value : 40.5 ° C
Type : closed cup
Method : other: Tag closed cup (ASTM D 56)
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (45)

Value : 42 ° C
Type : closed cup
Method : other: Abel Penshy closed cup
Year : 1990
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (46)

Value : 42.2 ° C
Type : open cup
Method : other: Tag open cup (ASTM D 1310)
Year :
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (47)

Value : >= 43 ° C
Type : closed cup
Method : other: no data
Year : 1984
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (48)

2.8 Auto Flammability

Value : = 385 ° C at
Method :
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Remark : Flammability group G2
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (49)

Value : = 390 ° C at
Method :

Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Remark : Flammability group G2
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (50)

Value : 400 ° C at
Method : other: DIN 51794
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.2001 (20)

Value : 405 ° C at
Method : other: DIN 51 794
Year :
GLP :
Test substance :
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.05.1994 (23)

Value : 406 ° C at
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.1994 (24)

2.9 Flammability

2.10 Explosive Properties

Result : no data
Remark : Lower explosion limit: 2.5 Vol.-%
upper explosion limit: 16.3 Vol.-%
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
28.04.1994 (20)

Remark : Lower explosion limit: 2.7 Vol.-%
upper explosion limit: 16.6 Vol.-%
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
08.04.1994 (50)

Remark : Lower explosion limit: 4.2 Vol.-%
upper explosion limit: 14.4 Vol.-%
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.05.1994 (51) (47)

Remark : Explosionsgrenzen in Luft: 3.1 - 18.0 vol.%
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.05.1994 (23)

Remark : Lower flammability limit: 2.6% vol
Upper flammability limit: 14.2% vol
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.1994 (24)

2.11 Oxidizing Properties

2.12 Additional Remarks

Remark : pH-value 11.8 at 5 g/l water
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
22.04.1994 (52)

Remark : pk1 7.44
pk2 10.17
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.04.1994 (53)

Remark : pk1 7.56
pk2 10.71
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.04.1994 (21)

Remark : Gefaehrliche Reaktionen: Exotherme Reaktion mit Saeuren.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.05.1994 (23)

Remark : vapour density (air = 1): 2.07
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.1994 (24) (47)

3.1.1 Photodegradation

Indirect photolysis

Sensitizer	:	OH
Conc. of sens.	:	500000 molecule/cm3
Rate constant	:	= .00000000004324 cm3/(molecule*sec)
Degradation	:	= 50 % after 8.9 hour(s)
Deg. Product	:	
Method	:	other (calculated): according to Atkinson
Year	:	1987
GLP	:	
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

19.06.2001 (54)

3.1.2 Stability in water

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	at degree C
t1/2 pH9	:	at degree C
Result	:	Hydrolysis of ethylenediamine would not be expected under environmental conditions (pH 5 to 9) since the molecule does not contain functional groups susceptible to hydrolysis
Reliability	:	(2) valid with restrictions

19.06.2001 (55) (56)

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	at degree C
t1/2 pH9	:	at degree C
Deg. Product	:	
Method	:	other (calculated)
Year	:	2001
GLP	:	
Test substance	:	
Result	:	Computerized estimations of hydrolysis rates based on structure activity relationships predict no reaction will occur.

17.05.2001 (57)

3.1.3 Stability in soil

3.2 Monitoring data

3.3.1 Transport between environmental compartments

Type	:	fugacity model level I
Media	:	
Air (level I)	:	
Water (level I)	:	
Soil (level I)	:	
Biota (level II / III)	:	

Soil (level II / III) :
Method :
Year : 2001
Method : Mackay Level 1 Fugacity Model Version 2.11, Trent University, 1999 was used.

Input Parameters used in calculation of Ethylenediamine

Property	Value	Source
Chemical type	1	Partitions into all 3 media
Molecular mass	60.1	
Water solubility	1.00E+6	Measured value
Vapor Pressure	1600	Calculated from 12mm Hg
Melting Point	10	Verschueren, 2001
Est. Henry's Law Constant	0.096	Calculated by EQC
Kaw	3.88E-5	Calculated by EQC
Log Kow	-2.04	Hansch (1995).
Temperature	25	
Amount of Chemical input to system	100,000	Level 1 default

Result : Level 1 fugacity calculates the amount of ethylenediamine present in the three primary environmental compartments: air, water and soil at equilibrium. The percentages of ethylenediamine in water, air and soil predicted by the equilibrium model are 98.1, 1.9 and <0.1%, respectively. Negligible amounts of the chemical partition into the fish compartment, which is consistent with the low Kow. At equilibrium EDA partitions almost exclusively to water and these results are consistent with the physical properties of EDA, namely the high water solubility and low air-water and octanol-water partition coefficients.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (58)

Type : fugacity model level III
Media :
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method :
Year : 2001
Method : Level III Fugacity Based Environmental Equilibrium Partitioning Model Version 2.10, Trent University (1999) was used. Four simulations were conducted: one with 1000 kg/hour emitted to air only, one with 1000 kg/hour emitted to water only, one with 1000 kg/hour emitted to soil only and one using the default emissions of equal amount to soil, air and water (1000 kg/hour for each).
Result : Using the default emissions of equal amount to soil, air and water (1000 kg/hour for each compartment), the percentage of ethylenediamine in bulk water, air and soil predicted by the Level III model are 78.1, 0.1 and 21.8% respectively. Regardless of the media to which EDA is released, most of the EDA at steady state is in the water phase. These results are consistent with the physical properties of EDA, namely the high water solubility and low air-water and octanol-water partition coefficients.

LEVEL III Distribution of Ethylenediamine

	% distribution		
	Air	Water	Soil
Air only 1000 kg/h	5.5	60.2	34.3
Water only 1000 kg/h	<0.1	99.9	<0.1
Soil only 1000 kg/h	<0.1	62.2	37.7
Combined 1000 kg/h into all 3 compartments	0.1	78.1	21.8

Reliability : (2) valid with restrictions
19.06.2001 (59)

Type : adsorption
Media : water - soil
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : other: OECD Guideline #106
Year : 1991
Remark : Adsorption studies were conducted using six different test soils consisting of sand, 2 sandy loams, sandy clay loam, silty loam and clay. Studies were conducted also, at aqueous phase pH adjusted to 3, 4, 5 9 and 11. Desorption from a sandy loam soil was also measured.
Result : Koc mean 4766 (range 2071-7051)

Batch equilibrium adsorption studies were conducted which showed a log Koc of 3.68, indicating relative immobility in soil. However, the mobility of the amine may increase substantially in soils under high ionic strength or extremely basic conditions.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : >97% radiolabeled [1,2-14C] ethylenediamine dihydrochloride with a specific activity of 9.9 mCi/mmol was used. Nonlabeled HPLC grade ethylenediamine was obtained from Aldrich Chemical Co., Milwaukee, WI.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
19.06.2001 (60) (61)

Type : volatility
Media :
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method :
Year :
Remark : Volatilization from water or soil is expected to be negligible. No removal from water was reported in a 4-hour aeration test.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : >97% radiolabeled [1,2-14C] ethylenediamine dihydrochloride with a specific activity of 9.9 mCi/mmol was used. Nonlabeled HPLC grade

ethylenediamine was obtained from Aldrich Chemical Co., Milwaukee, WI.

Reliability : (1) valid without restriction
18.07.2001 (62)

Type : adsorption
Media : other: adsorption to algae (solids)
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : other
Year : 1992
Remark : Studies on adsorption of 14C-labelled ethylenediamine were conducted in acidic media on the algae Vaucheria sp.. Sorption of ethylenediamine on algae occurs via an ion-exchange process at pH= 5. Ethylenediamine is protonated at this pH and displaces equivalent amounts of Ca and Mg which are associated to the cell wall anions.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 14C-labeled ethylenediamine from Amersham. No percentage purity supplied.
Reliability : (4) not assignable
18.07.2001 (63)

3.3.2 Distribution

Media : water - air
Method :
Year :
Remark : Log air/water partition coefficient (log Kaw) is -7.15.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
31.05.1994 (64) (65)

3.4 Mode of degradation in actual use

3.5 Biodegradation

Contact time :
Degradation : > 80 % after 28 day
Result :
Deg. Product :
Method : other: Closed bottle test
Year :
GLP :
Test substance :
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.06.2001 (66)

Contact time :
Degradation : > 90 % after 10 day
Result :

Deg. Product	:	
Method	:	other: Zahn-Wellens test
Year	:	
GLP	:	
Test substance	:	
Remark	:	Inherently biodegradable
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

16.11.2001 (66)

Type	:	aerobic
Inoculum	:	activated sludge
Concentration	:	100mg/l related to related to
Contact time	:	
Degradation	:	% after 28 day
Result	:	
Deg. Product	:	
Method	:	
Year	:	1992
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	% Biodegradation: 93 - 95 (NH3) related to BOD sludge conc.: 30 mg/l Method: "Biodegradation test of chemical substance by microorganisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "301C, Ready Biodegradability: Modified MITI Test I" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

19.06.2001 (67)

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Concentration	:	50mg/l related to related to
Contact time	:	
Degradation	:	10 % after 5 day
Result	:	readily biodegradable
Kinetic of test substance	:	15 day 87.5 **%** 28 day 94 **%** **%** **%** **%**
Deg. Product	:	
Method	:	Directive 84/449/EEC, C.6 "Biotic degradation - closed bottle test"
Year	:	1989
GLP	:	yes
Test substance	:	other TS: Delamine purity: > 99 %
Remark	:	closed bottle test
Source	:	Union Carbide Benelux Antwerpen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
18.07.2001 (68)

Type : aerobic
Inoculum : other: activated sludge, acclimated
Concentration : 50mg/l related to Test substance
related to
Contact time :
Degradation : 81 % after 10 day
Result : other: biodegradable
Deg. Product :
Method : other: BOD standard
Year :
GLP : no data
Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Temperature: 20 degree C, 28 days of acclimatisation
Reliability : (2) valid with restrictions
18.07.2001 (69)

Type : aerobic
Inoculum : other: microbial seed
Contact time :
Degradation : 100 % after 20 day
Result : readily biodegradable
Kinetic of test substance : 5 day 68 **%**

10 day 100 **%**
20 day 100 **%**
%
%
Deg. Product :
Method : other: BOD20
Year :
GLP :
Test substance :
Remark : test description: Price,K.S., Waggy, G.T., Conray, R.A.,
"Brine Shrimp Bioassay and Seawater BOD of Petrochemicals",
J.Water Poll. Control Fed., Vol 26, No. 1, January 1974.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
18.07.2001 (70)

Type : aerobic
Inoculum : activated sludge
Contact time :
Degradation : ca. 70 % after 70 day
Result :
Deg. Product :
Method : other: activated sludge simulation test
Year :
GLP : no
Test substance :
Remark : The degradation degree depended on the retention time.
3 hours retention time: 70 % degradation
6 hours retention time: 90 % degradation
Source : Union Carbide Benelux Antwerpen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : 70 % after 70 days
19.01.2001

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 200mg/l related to Test substance
related to
Contact time :
Degradation : 97.5 % after 5 day
Result : readily biodegradable
Deg. Product :
Method : other: based on COD
Year :
GLP : no data
Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
18.07.2001 (71)

Type : aerobic
Inoculum : other: adapted settled domestic wastewater
Deg. Product :
Method : other: no data
Year :
GLP : no data
Test substance : no data
Remark : Degradation: 5 day : 36 %
10 day : 45 %
15 day : 56 %
20 day : 70 %
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : based on a theoretical oxygen demand of 1.33 mg O2/mg
25.04.1994 (72)

Type : aerobic
Inoculum : other: not adapted
Deg. Product :
Method : other: no data
Year :
GLP : no
Test substance : no data
Remark : Degradation: 5 day : 2 %
10 day : 14 %
15 day : 16 %
20 day : 16 %
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : synthetic seawater, not adapted; based on a theoretical oxygen demand of 1.33 mg O2/mg
25.04.1994 (72)

Type : aerobic
Inoculum : other: not adapted settled domestic wastewater
Deg. Product :
Method : other: no data
Year :
GLP : no data

Test substance : no data
Remark : Degradation: 5 day : 24 %
10 day : 44 %
15 day : 55 %
20 day : 47 %
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : based on a theoretical oxygen demand of 1.33 mg O2/mg
25.04.1994 (72)

Type : aerobic
Inoculum : other: no data
Deg. Product :
Method : other: see below
Year :
GLP : no data
Test substance : other TS: no further specification
Remark : BOD in sea water studied in order to investigate the biodegradability and self-purification in seawater. The initial concentrations of ethylenediamine was 7 - 10 mg (related to theoretical oxygen demand of 3.73 g).
A BOD5 of 0.619 g O2/g and a degradation of 17.9 % was detected. Standard procedures with fresh water revealed a BOD5 of 0.019 g O2/g and a degradation ratio of 0.55 %.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
18.07.2001 (73)

Type : aerobic
Inoculum :
Contact time :
Degradation : 62 % after 20 day
Result :
Kinetic of test substance : 5 day 2 **%**
10 day 11.5 **%**
20 day 62 **%**
%
%
Remark : Industrial BOD as % THOD
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
18.07.2001 (74)

Type :
Inoculum : other: Dow Michigan Division 437 wastewater treatment plant and City of Midland Michigan wastewater treatment plant.
Contact time : 20 day
Degradation : % after
Result :
Kinetic of test substance : 5 day = 2.4 **%**
20 day = 87.8 **%**
%
%
%
Deg. Product :

Method : other: American Public Health Association, American Water Works Association and Water Pollution Control Federation. Standard Methods for the Examination of Water and Wastewater, 14th Ed. New York. 1965.
Year : 1978
GLP : no
Test substance : other TS: Production grade material is typically 99+% pure.
Remark : BOD measured after 5, 10 and 20 days in municipal and industrial inoculum. Method of analysis - Clifford Dennis A. (1968). Automatic measurements of total oxygen demand: A new instrumental method. 23rd Annual Purdue Industrial Waste Conference. Purdue University, Lafayette, Indiana. Nil after 5 and 10 days and 2.28 p/p after 20 days in the municipal inoculum. It was 0.06, 0.40 and 2.16 p/p after 5, 10 and 20 days, respectively, in the industrial inoculum.
Reliability : (2) valid with restrictions
18.07.2001 (75)

3.6 BOD5, COD or BOD5/COD ratio

Remark : degradation (BOD5): 24 %
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.04.1994 (73)

Remark : COD: 1300 mg/g
ThOD: 1330 mg/g
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.04.1994 (72)

Remark : TOD 3450 mg/g (N-NO3)
COD 1330 mg/g
BOD5 10 mg/g
BOD5 (adapt.) 1000 mg/g
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.04.1994 (76)

3.7 Bioaccumulation

BCF : .07
Remark : BCF calculated from the log octanol/water partition coefficient via Veith's equation.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
18.07.2001 (77)

Remark : Because of its low Pow (-1.36) and its high water solubility, ethylenediamine is regarded to have no bioaccumulation potential for animals and plants.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
18.07.2001 (78)

Remark : Very low accumulation on algae
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.04.1994 (79)

3.8 Additional remarks

Remark : Impact on conventional biological treatment systems:
1085 mg/l inhibitory;
108.5 mg/l no effect;
225 mg/l degraded after adaptation
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
18.07.2001 (76)

Remark : Impact on biological wastewater treatment systems:
At very low concentrations in water (about 10 ppm), ethylenediamine is biodegradable in a biological wastewater treatment system. However, at about 500 ppm concentration or higher, it can be toxic to the biomass in a treatment system.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
18.07.2001 (47)

4.1 Acute/prolonged toxicity to fish

Type	:	semistatic
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	115.7
Method	:	other: open system, no further data
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	This study is considered to be a critical study since the lowest 96 hr LC50 value.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature: 21 - 23 degree C; pH: 7.2 - 7.9; hardness: 40 - 48 mg CaCO3/l
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

30.08.2001 (80)

Type	:	static
Species	:	Semolitus atromaculatus (Fish, fresh water)
Exposure period	:	24 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC0	:	30
LC100	:	60
Method	:	other: closed vessels
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	This study is considered to be less reliable since it is not consistent with results from other studies and used a species that is not commonly used.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature: 15 - 21 degree C; pH: 8.3
Reliability	:	(4) not assignable

30.08.2001 (81)

Type	:	static
Species	:	Oryzias latipes (Fish, fresh water)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	1000
Method	:	other: JISKO 102: Testing method for industrial waste water, Japanese Industrial Standards Committee
Year	:	
GLP	:	no data
Test substance	:	no data
Method	:	Ten Oryzias latipes, about 2 cm in length and 0.2 g in weight, were placed in 2 liter of solution. No additional information provided although the test followed Japanese Industrial Standards, 1971.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature: 25 degree C; deionized water pH - 7.0
Reliability	:	(2) valid with restrictions

14.02.2002 (82) (33)

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
LC50	:	= 210
Method	:	other: In general accordance with OECD guideline 203
Year	:	1978
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	LC10 was 174 mg/L (124-194 mg/L confidence intervals) and LC90 was 252 mg/L (227-349 mg/L confidence intervals).
Test condition	:	Groups of 10 fish/concentration were exposed to EDA. Static study conducted using dechlorinated Lake Huron water. Water temperature was maintained at 12C. LC50 determined by Finney's method of probit analysis. No additional information supplied in report. Nominal concentrations of 0, 75, 87, 115, 155, 210, 280, 370, 490 and 650 mg/L.
Test substance	:	Purity unstated. Production grade material was typically 99+% pure.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

06.07.2001 (83)

Type	:	semistatic
Species	:	Poecilia reticulata (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	640
Method	:	Directive 84/449/EEC, C.1 "Acute toxicity for fish"
Year	:	
GLP	:	yes
Test substance	:	other TS: Delamine, purity: > 99%
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(1) valid without restriction

18.07.2001 (68)

Type	:	semistatic
Species	:	Poecilia reticulata (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	
LC50	:	1545
Method	:	other: EEC Directive 79/831, Annex V, Part C.
Year	:	1994
GLP	:	no data
Test substance	:	other TS: >99%
Method	:	The tests were semistatic in Dutch standard water.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

18.07.2001 (84)

Type	:	static

Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	210
Method	:	other: EPA-ASTM procedures
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Test references: (1) Methods for Measuring the Acute Toxicity of Effluents toFreshwater and Marine Organisms, EPA/600/4-85/013, March 1985. (2) Annual Book of ASTM standards, Water and Environmental Technology, Vol. 111.04, (1990).
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.07.2001 (70)

Type	:	static
Species	:	Poecilia reticulata (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	275
Conf. lmts.	:	180 - 560
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1985
GLP	:	no data
Test substance	:	other TS: Supplied by Baker Chemicals. No additional information supplied.
Method	:	Stock solutions were prepared fresh each day and test solutions were renewed daily. Tests on the amines (presume this includes ethylenediamine) were conducted in sealed vessels. LC50 values and their 95% confidence intervals were calculated according to Litchfield and Wilcoxon method. No additional information supplied.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.07.2001 (85)

Type	:	field observation
Species	:	Salmo trutta (Fish, fresh water, marine)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	230
Method	:	other: open system
Year	:	
GLP	:	no data
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature: 9 - 11; pH: 7.6 - 8.0; hardness: 210 - 290 mg CaCO3/l

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
18.07.2001 (86)

Type : other: growth inhibition
Species : other: Pimephales promelas cells
Exposure period : 2 hour(s)
Unit : mg/l
Analytical monitoring : no data
NI50 : 3152
Method : other: no data
Year :
GLP : no data
Test substance : no data
Remark : NI = neutral-red-inhibition; NI50 = concentration at which 50% decrease in neutral red uptake into cells
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.01.2001 (87)

Type : static
Species : Leuciscus idus melanotus (Fish, fresh water)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no
LC0 : 360
LC50 : 405
LC100 : 450
Method : other: DIN 38 412, part 15
Year :
GLP : no
Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
18.07.2001 (88)

Type : static
Species : Oryzias latipes (Fish, fresh water)
Exposure period : 24 hour(s)
Unit : mg/l
Analytical monitoring : no data
LC50 : 1000
Method : other: JISKO 102: Testing method for industrial waste water, Japanese Industrial Standards Committee
Year : 1982
GLP : no data
Test substance : no data
Method : Ten Oryzias latipes, about 2 cm in length and 0.2 g in weight, were placed in 2 liter of solution. No additional information provided although the test followed Japanese Industrial Standards, 1971.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Temperature: 15 - 20 degree C; pH: 7.0, distilled water
Reliability : (2) valid with restrictions
14.02.2002 (82) (89)

Type : static
Species : Pimephales promelas (Fish, fresh water)
Exposure period : 96 hour(s)

Unit	:	mg/l
Analytical monitoring	:	
LC50	:	> 11.5
Method	:	
Year	:	1974
GLP	:	
Test substance	:	no data
Remark	:	This study is inconsistent with results from other species for the same time period. Therefore it is not considered to be valid.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

30.08.2001 (76)

4.2 Acute toxicity to aquatic invertebrates

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
EC50	:	17
Method	:	Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year	:	
GLP	:	Yes
Test substance	:	other TS: Delamine, purity: > 99%
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

18.07.2001 (90)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	4.5
Method	:	other: EPA/ASTM procedures
Year	:	
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	test details: (1) Methods for Measuring the Acute Toxicity of Effluents toFreshwater and Marine Organisms, EPA/600/4-85/013, March 1985. (2) Annual Book of ASTM Standards, Water and Environmental Technology, Vol. 111.04, (1990)
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(1) valid without restriction

18.07.2001 (70)

Type	:	Static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	No

LC10	:	c = .18
LC50	:	c = 3
LC90	:	c = 48.5
Method	:	other: In general accordance with OECD Guideline 202
Year	:	1978
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Considered a critical study, since this study was of an appropriate duration, in the most common species tested and was the most sensitive. Groups of 10 Daphnids/container with 3 replicates/concentration were exposed to EDA. Nominal concentrations of 0, 1.0, 3.2, 10, 32, 100 mg/L only. Static study conducted using dechlorinated Lake Huron water. Water temperature was maintained at 20C. LC50 determined by Finney's method of probit analysis. No additional information supplied in report.
Result	:	LC50 was 3.0 mg/L (95% confidence limits are 1.5-5.0 mg/L) at 48 hours. LC10 was 0.18 mg/L (0.03-0.5 mg/L) and LC90 was 48.5 mg/L (25-162 mg/L)
Test substance	:	Purity is unstated. Production grade material was typically 99+% pure.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

30.08.2001 (83)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	26.5
Confidence Intervals	:	= 20.4 - 34.4
Method	:	other: modified OECD 202
Year	:	1985
GLP	:	no data
Test substance	:	no data
Remark	:	95% confidence limits: 20.4 - 34.4
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Stock solutions were prepared fresh each day and test solutions were renewed daily. Tests on the amines (presume this includes ethylenediamine) were conducted in sealed vessels. Daphnids were fed 1 x 10(8) cells/liter C pyrenoidosa. LC50 values and their 95% confidence intervals were calculated according to Litchfield and Wilcoxon method. No additional information supplied.
Reliability	:	(2) valid with restrictions

31.08.2001 (91)

Type	:	Static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	
LC50	:	c = 46
Method	:	other: EEC Directive 79/831, Annex V, Part C.
Year	:	1994
GLP	:	no data

Test substance	:	other TS: >99% pure
Method	:	The test temperature was 20C, the photoperiod 8:16 light:dark. Dutch standard water (pH 8, bicarbonate hardness 1.4 meq/L) was used as test medium. The effect parameter was immobility of individuals and tests were considered valid if >80% survived in the controls. No additional information supplied in paper.
Result	:	The daphnia LC50 46.0 mg/L with a standard deviation of 4.9 based on 4 datapoints.
Reliability	:	(2) valid with restrictions

31.08.2001 (92)

Type	:	
Species	:	Artemia salina (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	14
Method	:	other: no data
Year	:	
GLP	:	No
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature: 24.5 degree C, loosely closed vessels
Reliability	:	(2) valid with restrictions

19.07.2001 (93)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
EC0	:	1.2
EC50	:	19
EC100	:	150
Method	:	other: DIN 38 412, part 11
Year	:	1982
GLP	:	no data
Test substance	:	no data
Remark	:	EC based on immobilisation
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature: 20 degree C; pH: 7.8 - 8.2; hardness: 16 degree Deutscher Haerte, open vessel, unfed
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

31.08.2001 (94)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
Analytical monitoring	:	No
EC0	:	3.5
EC50	:	14
Method	:	other: DIN 38412 L 11
Year	:	1989
GLP	:	no data

Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature: 24 - 26 degree C; pH: 7.8 - 8.2, closed system, fed
Reliability	:	(2) valid with restrictions
18.07.2001		(95)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	24 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
LC50	:	16
Method	:	
Year	:	1977
GLP	:	no data
Test substance	:	no data
Remark	:	LC0 : 6.4 mg/l LC100 : 115 mg/l
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature: 20 - 22 degree C; pH: 7.6 - 7.7; hardness: 16 degree Deutscher Haerte, open system, fed
Reliability	:	(2) valid with restrictions
19.07.2001		(96)

Type	:	
Species	:	Daphnia magna (Crustacea)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	
Method	:	
Year	:	1974
GLP	:	
Test substance	:	
Method	:	Daphnia magna, 2-3 weeks of age, were used for this study. At the start of each bioassay, appropriate concentrations of EDA, 0.0, 0.10, 0.19, 0.38, 0.58 and 1.04 mg/L were prepared and dispensed into 150-ml Griffin beakers. The pH of each test solution was adjusted to between 7.0-7.5. A medicine dropper was used to transfer 15 Daphnia into each test container. A final volume of 100-110 ml was used throughout the testing program. Controls, which contained only Daphnia in dilution water, were included in every bioassays. Adult mortalities were recorded on a daily basis. Births and newborn mortalities observed during the experiment were noted but not enumerated.
Remark	:	This study was conducted prior to standarized protocols with Daphnia. The Daphnia were 2-3 weeks of age at the start of the study whereas the standard protocol requires 1 day old animals. Additionally, the study was conducted for 96 hours which is much longer than the standardized time of 48 hours. Thus this study does not follow currently acceptable testing protocols and cannot be compared with other studies.
	:	

Result Mortality was as follows:

Conc (mg/L)	Cumulative mortality 24 hr	48 hr	72 hr	96 hr
0.0	0	0	0	0
0.10	0	0	0	0
0.19	0	0	0	0
0.38	0	0	0	0
0.58	0	0	0	1
1.04	0	3	5	10

The starting population consisted of 15 Daphnia for each concentration.

The 48 hour LC50 is greater than 1.04 mg/L.
The 96 hour LC50 was calculated as 0.88 mg/L.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable

19.07.2001 (76)

4.3 Toxicity to aquatic plants e.g. algae

Species : Scenedesmus subspicatus (Algae)
Endpoint : biomass
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no
EC10 : 55
EC50 : > 100
Method : other: DIN 38 412, part 9; cell multiplication test, modified
Year : 1990
GLP : no data
Test substance : no data
Remark : Endpoint measured was biomass, considered more preferred method.
No additional information supplied.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint

30.08.2001 (97)

Species : Selenastrum capricornutum (Algae)
Endpoint : other: growth rate (EC50) and biomass (EbC50)
Exposure period : 72 hour(s)
Unit : mg/l
Analytical monitoring : no data
NOEC : 3.2
EC50 : 645
ECb50 : 71
Method : other: Annex V Directive 67/548/EEC
Year :
GLP : yes
Test substance : other TS: Delamine, purity: > 99 %
Remark : ECb50, biomass is considered more preferred method.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint
30.08.2001 (98)

Species : Chlorella pyrenoidosa (Algae)
Endpoint : biomass
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : no data
EC50 : 61
Method :
Year : 1985
GLP : no data
Test substance : no data
Remark : Endpoint measured was growth inhibition, considered more preferred method.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
30.08.2001 (91)

Species : Chlorella pyrenoidosa (Algae)
Endpoint : growth rate
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : no data
EC50 : 100
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 1985
GLP : no data
Test substance : no data
Method : Tests with the amines (presume this includes ethylenediamine) were carried out in triplicate in infuse bottles.

No additional information supplied.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.07.2001 (91)

Species : Scenedesmus quadricauda (Algae)
Endpoint : growth rate
Exposure period : 8 day
Unit : mg/l
Analytical monitoring : no data
TT : .85
Method : other: according to Bringmann
Year : 1977
GLP : no data
Test substance : no data
Remark : 3% inhibition compared with the mean control value; exposure period: 7 days; TT = toxicity threshold
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Neutralized solution; pH value: 7.0; closed vessels
Reliability : (2) valid with restrictions
19.07.2001 (99)

Species : Scenedesmus quadricauda (Algae)
Endpoint : growth rate
Exposure period : 8 day

Unit	:	mg/l
Analytical monitoring	:	no data
TT	:	3.2
Method	:	other: according to Bringmann
Year	:	1977
GLP	:	no data
Test substance	:	no data
Remark	:	3% inhibition compared to mean of control value; exposure period: 7 days; TT = toxicity threshold
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature 27 degree C; closed vessels, constant lighting, no adjustment of pH
Reliability	:	(2) valid with restrictions
19.07.2001		(99)

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	growth rate
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
EC10	:	> 100
EC50	:	> 100
Method	:	other: DIN 38 412, part 9; cell multiplication test, modified
Year	:	1990
GLP	:	no data
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
19.07.2001		(100)

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	
EC50	:	151
Method	:	other: Off J Eur Comm L133: 1988-05-30
Year	:	1994
GLP	:	no data
Test substance	:	other TS: >99% Pure
Method	:	S. capricornutum, strain ATCC 22662 was used. Minor modifications included the following: culture medium was modified by increasing the KH2PO4 concentration from 1.6 to 160 mg/L and the NaHCO3 concentration from 50 to 100 mg/L to improve the growth of algae and the buffer capacity of the medium. Growth was determined by spectrophotom etric measurement at 436 nm each 24 hr. The inhibition of growth at different concentrations after 96 hr was calculated on the basis of the area under the growth curve. The algae were cultured at 22C under constant light conditions of 6000 to 10,000 lx.
Result	:	The EC50 was 151 mg/L with a standard deviation of 21.4 for 3 datapoints.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
30.08.2001		(101)

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	
Exposure period	:	7 day
Unit	:	mg/l
Analytical monitoring	:	
EC0	:	> 100
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

19.07.2001 (76)

4.4 Toxicity to microorganisms e.g. bacteria

Type	:	aquatic
Species	:	activated sludge of a predominantly domestic sewage
Exposure period	:	1 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
EC50	:	1600
Method	:	other: Annex V Directive 67/548/EEC
Year	:	1989
GLP	:	yes
Test substance	:	other TS: Delamine, purity: > 99%
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	measured endpoint was the respiratory rate
Reliability	:	(1) valid without restriction

19.07.2001 (90)

Type	:	aquatic
Species	:	Chilomonas paramaecium (Protozoa)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
TT	:	103
Method	:	other: no data
Year	:	1980
GLP	:	no data
Test substance	:	other TS
Remark	:	TT = toxicity threshold
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature: 20 degree C; pH value: 6.9
Reliability	:	(2) valid with restrictions

19.07.2001 (102)

Type	:	aquatic
Species	:	Entosiphon sulcatum (Protozoa)
Exposure period	:	72 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
TT	:	1.8
Method	:	other: no data
Year	:	1978
GLP	:	no data
Test substance	:	no data
Remark	:	TT=toxicity threshold
Source	:	Union Carbide Benelux Antwerpen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Temperature: 25 degree C; pH value: 6.9
Reliability : (2) valid with restrictions
19.07.2001 (103)

Type : aquatic
Species : Microcystis aeruginosa (Bacteria)
Exposure period : 192 hour(s)
Unit : mg/l
Analytical monitoring : no data
TT : .08
Method : other: no data
Year : 1975
GLP : no data
Test substance : other TS
Remark : TT = toxicity threshold
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Temperature: 27 degree C; pH value: 7.0
Reliability : (2) valid with restrictions
19.07.2001 (104)

Type : aquatic
Species : Microcystis aeruginosa (Bacteria)
Exposure period : 192 hour(s)
Unit : mg/l
Analytical monitoring : no data
TT : .04
Method : other: no data
Year : 1975
GLP : no data
Test substance : other TS
Remark : TT = toxicity threshold
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Temperature: 27 degree; no adjustment of pH
Reliability : (4) not assignable
19.07.2001 (104)

Type : aquatic
Species : Photobacterium phosphoreum (Bacteria)
Exposure period : 15 minute(s)
Unit : mg/l
Analytical monitoring : no data
EC50 : 20.4
Method : other: Microtox-test
Year : 1985
GLP : no data
Test substance : no data
Remark : EC50: concentration which reduces the bacterial luminescence by 50 %
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.07.2001 (91)

Type : aquatic
Species : Pseudomonas fluorescens (Bacteria)
Exposure period : 24 hour(s)
Unit : mg/l

Analytical monitoring : no
EC0 : 100
Method : other: modified DEV, L 15
Year : 1973
GLP : no
Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.07.2001 (52)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 17 hour(s)
Unit : mg/l
Analytical monitoring : no data
EC50 : 29
Method : other: ISO/TC 147/SC 5/WG 1 Guideline
Year : 1989
GLP : yes
Test substance : other TS: Delamine, purity: > 99%
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : measured endpoint was growth rate of Pseudomonas putida
Reliability : (1) valid without restriction
19.07.2001 (90)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 16 hour(s)
Unit : mg/l
Analytical monitoring : no data
TT : .85
Method : other: no data
Year : 1977
GLP : no data
Test substance : other TS
Remark : TT = toxicity threshold
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Temperature 25 degree C; pH value: 7.0; neutralized solution
Reliability : (2) valid with restrictions
19.07.2001 (99)

Type : aquatic
Species : Pseudomonas putida (Bacteria)
Exposure period : 16 hour(s)
Unit : mg/l
Analytical monitoring : no data
TT : .5
Method : other: no data
Year : 1977
GLP : no data
Test substance : no data
Remark : TT = toxicity threshold
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Temperature: 25 degree C; test solution not neutralized:
alkaline pH value
Reliability : (2) valid with restrictions

19.07.2001 (99)

Type	:	aquatic
Species	:	Uronema parduzci (Protozoa)
Exposure period	:	20 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
TT	:	52
Method	:	other: no data
Year	:	1980
GLP	:	no data
Test substance	:	other TS
Remark	:	50% inhibition compared to mean of control value; TT = toxicity threshold
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Temperature 25 degree C; pH value: 6.9; neutral solution
Reliability	:	(2) valid with restrictions

19.07.2001 (105)

Type	:	aquatic
Species	:	other bacteria: Klaerschlammorganismen
Exposure period	:	
Unit	:	
Analytical monitoring	:	
Method	:	other: Warburg-Methodik (Deutsches Einheitsverfahren L2)
Year	:	1976
GLP	:	
Test substance	:	
Remark	:	Neutralized ethylene diamine showed no toxicity up to a concentration of about 2 g/l.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

19.07.2001 (106)

Type	:	aquatic
Species	:	other bacteria: nitrifying bacteria
Exposure period	:	2 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
EC50	:	3
Method	:	other: Akzo method
Year	:	
GLP	:	yes
Test substance	:	other TS: Delamine, purity: > 99%
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	measured endpoint was the respiratory rate
Reliability	:	(2) valid with restrictions

19.07.2001 (107)

Type	:	aquatic
Species	:	other bacteria: suspension of seed microorganisms
Exposure period	:	16 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
IC50	:	500 - 1000
Method	:	other: Definitive 16-Hour Bacterial Inhibition Test
Year	:	1980

GLP	:	no data
Test substance	:	
Remark	:	Alsop,G.M., Waggy, G.T., Conray,R.A.,"Bacterial Growth Inhibition Test," Journal Water Poll. Control Fed., Vol 52, No.10, October 1980.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

19.07.2001 (70)

Type	:	soil
Species	:	other bacteria: Nitrobacter, Nitrosomonas
Exposure period	:	3 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
MIC	:	3.2
Method	:	other: Screening test according to Blok
Year	:	1985
GLP	:	no data
Test substance	:	other TS
Remark	:	MIC = Minimum inhibiting concentration Test principle: Conversion of ammonia via nitrite into nitrate. Reaction can be observed using a pH-indicator mixture. After 1 to 3 h a change in colour can be observed at the lowest effect concentration (MIC) determined.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

19.07.2001 (91)

Type	:	
Species	:	Nitrosomonas sp. (Bacteria)
Exposure period	:	
Unit	:	
Analytical monitoring	:	
Method	:	
Year	:	1985
GLP	:	
Test substance	:	
Remark	:	Test conc. (mg/l) % Inhibition of NH3 Oxidation 100 50-75 10 41
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

19.07.2001 (108)

4.5.1 Chronic toxicity to fish

Species	:	Gasterosteus aculeatus (Fish, estuary, marine)
Endpoint	:	other: length and weight of young fish; hatching
Exposure period	:	28 day
Unit	:	mg/l
Analytical monitoring	:	no data
NOEC	:	> 10
Method	:	OECD Guide-line draft "Early Life Stage Test (ELS-Test)"

Year	:	1992
GLP	:	yes
Test substance	:	other TS: Delamine, purity: > 99%
Remark	:	draft OECD Guideline "Fish Early Life Stage" NOEC: limit test, one dose level. Unpublished report Akzo Research to Delamine (1992)
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	test was semi static with renewal 3 times a week.
Reliability	:	(1) valid without restriction

19.07.2001

4.5.2 Chronic toxicity to aquatic invertebrates

Species	:	Daphnia magna (Crustacea)
Endpoint	:	reproduction rate
Exposure period	:	21 day
Unit	:	mg/l
Analytical monitoring	:	no data
NOEC	:	2
Method	:	other: EEC Draft 4 (XI/68/86)
Year	:	1992
GLP	:	yes
Test substance	:	other TS: Delamine, purity: > 99%
Remark	:	reproduction rate: number of juveniles per parent animal.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	test was semi static with renewal 3 times a week.
Reliability	:	(1) valid without restriction

19.07.2001 (109)

Species	:	Daphnia magna (Crustacea)
Endpoint	:	reproduction rate
Exposure period	:	21 day
Unit	:	mg/l
Analytical monitoring	:	yes
NOEC	:	.16
Method	:	other: UBA-Verfahrensvorschlag (vorlaeufiger) "VerlaengerterToxizitaetstest bei Daphnia magna" (Bestimmung der NOEC fuerReproduktionsrate, Mortalitaet und den Zeitpunkt des ersten Auftretensvon Nachkommen; 21 d) (01.02.1984)
Year	:	1989
GLP	:	no data
Test substance	:	no data
Remark	:	nominal concentration
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	semi-static; temperature: 25 +- 1 degree C, 9 hours/d exposed to artificial lighting, closed vessels, fed; pH was 8.0 +- 0.2
Reliability	:	(2) valid with restrictions

16.11.2001 (95)

4.6.1 Toxicity to soil dwelling organisms

4.6.2 Toxicity to terrestrial plants

Species	:	other terrestrial plant: Lactuca sativa Ravel R2

Endpoint	:	
Exposure period	:	
Unit	:	
EC50	:	208
Method	:	OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year	:	1993
GLP	:	
Test substance	:	other TS: purity >= 95 %
Remark	:	Unit: mg/l nutrient solution (semi-static) (nominal concentration) Exposure period: 16 - 21 days Analytical monitoring (at start and end of test): RP-HPLC, HR-GC; detection by UV, FID, FCD and/or NPD log Kow: -2.04 Tested at RIVM (National Inst. of Public Health and Environ. Prot.) Bilthoven
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
07.02.2002		(110)
Species	:	other terrestrial plant: Lactuca sativa Ravel R2
Endpoint	:	
Exposure period	:	7 day
Unit	:	
EC50	:	> 1000
Method	:	OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year	:	1993
GLP	:	
Test substance	:	other TS: purity >= 95 %
Remark	:	Unit: ug/g soil (static) (nominal concentration) Analytical monitoring (at start and end of test): GC/FID and/or GC/ECD log Kow: -2.04 Tested at RIVM (National Inst. of Public Health and Environ. Prot.) Bilthoven
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
07.02.2002		(110)
Species	:	other terrestrial plant: Lactuca sativa Ravel R2
Endpoint	:	
Exposure period	:	14 day
Unit	:	
EC50	:	692
Method	:	OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year	:	1993
GLP	:	
Test substance	:	other TS: purity >= 95 %
Remark	:	Unit: ug/g soil (static) (nominal concentration) Analytical monitoring (at start and end of test): GC/FID and/or GC/ECD log Kow: -2.04 Tested at RIVM (National Inst. of Public Health and Environ. Prot.) Bilthoven
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
07.02.2002		(110)

4.6.3 Toxicity to other Non-Mamm. terrestrial species

4.7 Bbiological effects monitoring

4.8 Biotransformation and kinetics

4.9 Aadditional remarks

Remark	:	The South African clawed toad Xenopus laevis (waterfrog) embryos were treated at 22 +- 1 degree C in closed vessels for ten days without changing the solutions. Yolk plug embryos (of age 10 - 12) were exposed to various concentrations of ethylenediamine. The concentrations evaluated (0.1 - 10 mg/l) were neither toxic nor teratogenic. Five- to twelve-day-old tadpoles were tested in a similar manner. LC50 value (250 mg ethylenediamine/l) was determined at day ten post exposure.	
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
11.04.1994			(111)
Remark	:	For frog tadpoles of Rana bravipoda porosa a 3 h-LC50 value of 150 mg ethylenediamine/l and 6 h-, 12 h-, 24 h- and 48 h-LC50 values of 130 mg ethylenediamine/l was determined (no further details).	
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
28.04.1994			(112)

5.1.1 Acute oral toxicity

Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	= 637 mg/kg bw
Method	:	other: Acute Oral Toxicity
Year	:	1984
GLP	:	no data
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

24.07.2001 (113)

Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	= 1850 mg/kg bw
Method	:	other: Acute Oral Toxicity
Year	:	1983
GLP	:	no data
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

07.06.2001 (114)

Type	:	LD50
Species	:	rat
Strain	:	no data
Sex	:	no data
Number of animals	:	
Vehicle	:	water
Value	:	ca. 1050 mg/kg bw
Method	:	
Year	:	1951
GLP	:	no
Test substance	:	other TS: 70% solution in water
Remark	:	Rats were orally gavaged with 10% solution in water. Dose levels were 1000 and 2000 mg/kg, which corresponds to 700 and 1400 mg/kg, respectively. The number of animals used was not specified.
Result	:	All animals survived at 700 mg/kg EDA and all died at 1400 mg/kg EDA. Thus the LD50 is approximately 1050 mg/kg.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

30.08.2001 (115)

Type	:	LD50
Species	:	rat
Strain	:	Fischer 344

Sex	:	male/female
Number of animals	:	5
Vehicle	:	
Method	:	other: essentially follows OECD 401
Year	:	1982
GLP	:	
Test substance	:	other TS: used ethylenediamine dihydrochloride salt
Method	:	Groups of 5 animals/sex/dose group received a single dose of ethyelnediamine as the dihydrochloride salt at dosages of 200, 400, 800, 1200 or 1800 mg ethylenediamine/kg body weight.
Remark	:	The LD50 is approximately 1500 mg/kg.
Result	:	In the 1800 mg/kg group, 9 of 10 animals died. In the 1200 mg/kg group, 2 of 10 animals died. Sex of the dead animals was not specified. All other animals survived. Diarrhea, bluish appearing extremities and thin appearance were recorded as clinical signs in the 1200 mg/kg group. No gross lesions were noted at necropsy and histopathology was not performed.
Reliability	:	(2) valid with restrictions

19.06.2001 (116)

Type	:	LD50
Species	:	mouse
Strain	:	B6C3F1
Sex	:	male/female
Number of animals	:	5
Vehicle	:	
Method	:	other: essentially follows OECD 401
Year	:	1982
GLP	:	
Test substance	:	other TS: ethylenediamine dihydrochloride
Method	:	Groups of 5 male and 5 female mice were dosed with a single dose of ethylenediamine dihydrochloride at doses of 200, 400, 800, 1200 or 1800 mg ethylenediamine/kg body weight. Surviving mice were sacrificed and necropsies performed at the end of a 14-day observation period.
Result	:	All animals from the 1200 and 1800 mg/kg groups died by the third day of the study. In addition, 3 male and 4 female mice in the 800 mg/kg dose group died during the 14-day observation period. All other mice survived until the scheduled sacrifice. The only clinical sign was moribundity prior to early death in the three highest dose groups. There were no gross lesions noted at necropsy.
Conclusion	:	The oral LD50 in mice is between 400 and 800 mg/kg.
Reliability	:	(2) valid with restrictions

19.06.2001 (117)

Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	= 1160 mg/kg bw
Method	:	other: Acute Oral Toxicity
Year	:	1951
GLP	:	no data
Test substance	:	no data
Remark	:	95 % conf. lmts.: 980 - 1370 mg/kg

Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
07.06.2001		(118) (119)
Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	= 2700 mg/kg bw
Method	:	other: Acute Oral Toxicity
Year	:	1975
GLP	:	no data
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
07.06.2001		(120)
Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	= 3250 mg/kg bw
Method	:	other: Acute Oral Toxicity
Year	:	1983
GLP	:	no data
Test substance	:	other TS: Ethylenediamine dihydrochloride
Method	:	The EDA-2HCl crystals were purified by repeated methanol washing. Elemental analyses and infrared spectroscopy revealed that the EDA-2HCl sample was pure with little or no impurities. Nonfasted animals were maintained on a standard laboratory diet and water ad libitum except during periods of treatment. Dosage levels differing by a factor of 2 in a geometric series were employed. LD50s were calculated by the moving average method (Thompson, 1947) using tables by Weil (1952). The detailed procedures for the peroral intubation were outlined in a previous publication by Smyth et al., (1962). Smyth, H.F. Jr., Carpenter, C.P., Weil, C.S., Pozzani, U.C. and Striegel, J.A. (1962). Range-finding toxicity data: List VI. Am. Ind. Hyg Assoc. J. 23:95-107.
Remark	:	95 % conf. lmts.: 2360 - 4470 mg/kg
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
07.06.2001		(121)
Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	

Number of animals :
Vehicle :
Value : 1.12
Method : other
Year : 1976
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : ml/kg
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.05.1994 (122)

Type : LD50
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Value : .71
Method : other
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : ml/kg
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.05.1994 (123)

Type : LD50
Species : Rat
Strain :
Sex :
Number of animals :
Vehicle :
Value : 1850 mg/kg bw
Method : other
Year : 1948
GLP : No
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.05.1994 (124)

Type : LD50
Species : Rat
Strain :
Sex :
Number of animals :
Vehicle :
Value : 866 mg/kg bw
Method : other: BASF-test
Year : 1979
GLP : No
Test substance : as prescribed by 1.1 - 1.4
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.05.1994 (125)

Type : LD50
Species : Rat

Strain :
Sex :
Number of animals :
Vehicle :
Value : 1170 mg/kg bw
Method : other: BASF-test
Year : 1957
GLP : no
Test substance : other TS
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : Ethylendiamin 90%ig, als Hydrochlorid
11.05.1994 (126)

Type : LD50
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Value : ca. 1800 mg/kg bw
Method : other: BASF-test
Year : 1952
GLP : no
Test substance : other TS
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : Ethylendiamin, 70%ig.
11.05.1994 (127)

Type : LD50
Species : rat
Strain : no data
Sex : no data
Number of animals :
Vehicle : water
Value : 1000 - 2000 mg/kg bw
Method :
Year : 1951
GLP : no
Test substance : other TS: Approximately 70% in water.
Remark : Rats were orally gavaged with a 10% aqueous solution at dose levels of 1000 and 2000 mg/kg.
Result : No animals died at 1000 mg/kg while all animals died at 2000 mg/kg.
13.11.2000 (128)

Type : LD50
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Value : = 1800 mg/kg bw
Method : other: Acute Oral Toxicity
Year : 1975
GLP : no data
Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

08.04.1994 (120)

Type : LD50
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Value : = 1620 mg/kg bw
Method : other: Acute Oral Toxicity
Year : 1983
GLP : no data
Test substance : other TS: Ethylenediamine dihydrochloride
Remark : 95 % conf. lmts.: 1200 - 2190 mg/kg
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.03.1994 (129)

Type : LD50
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Value : = 1770 mg/kg bw
Method : other: Acute Oral Toxicity
Year : 1983
GLP : no data
Test substance : other TS: Ethylenediamine dihydrochloride
Remark : 95 % conf. lmts.: 1280 - 2430 mg/kg
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.03.1994 (129)

Type : other
Species : rabbit
Strain :
Sex :
Number of animals :
Vehicle :
Method : other: BASF-test
Year : 1957
GLP : no
Test substance : other TS
Remark : An oral dose of 450 or 900 mg/kg bw of ethylendiamine (base) was lethal to rabbits within 2-4 days. No mortality was noted at a dose of 180 mg/kg bw.

When the compound was given as hydrochloride, a dose of 900 mg/kg bw was lethal while no mortality was observed at 450 and 180 mg/kg bw.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.01.2001 (130)

Type : other
Species : cat
Strain :
Sex :
Number of animals :

Vehicle	:	
Method	:	other: BASF-test
Year	:	1957
GLP	:	no
Test substance	:	other TS
Remark	:	An oral dose of 450 mg/kg bw was lethal in one out of two animals. No mortality was observed at 180 and 90 mg/kg bw. When given as Hydrochloride no mortality was noted at all dose levels (90, 180 and 450 mg/kg bw).
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

19.01.2001 (130)

Type	:	LD50
Species	:	guinea pig
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	= 470 mg/kg bw
Method	:	other: Acute Oral Toxicity
Year	:	1941
GLP	:	no data
Test substance	:	no data
Remark	:	95 % conf. lmts.: 400 - 540 mg/kg
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

09.02.1994 (118)

5.1.2 Acute inhalation toxicity

Type	:	LC50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Exposure time	:	8 hour(s)
Value	:	> 29 mg/l
Method	:	other: Acute Inhalation Toxicity
Year	:	1983
GLP	:	no data
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

19.07.2001 (114)

Type	:	LC50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Exposure time	:	8 hour(s)
Value	:	> 2.5 mg/l
Method	:	other: Acute Inhalation Toxicity
Year	:	1948
GLP	:	no data

Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.07.2001 (131)

Type : LC50
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 8 hour(s)
Value : > 5 mg/l
Method : other: Acute Inhalation Toxicity
Year : 1951
GLP : no data
Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.07.2001 (119)

Type : LC50
Species : guinea pig
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 8 hour(s)
Value : > 2.5 mg/l
Method : other: Acute Inhalation Toxicity
Year : 1948
GLP : no data
Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.07.2001 (131)

Type : other
Species : laboratory animal
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 4 hour(s)
Method : other: BASF-test
Year : 1952
GLP : no
Test substance : other TS
Remark : 10 mice, 4 rats, 1 rabbit and 1 cat were exposed to vapors generated once at the beginning of the exposure time at concentrations of 10 and 20 mg/l, and gradually decreasing in concentration over the exposure time of 4 hours. Two mice died within 24 hours when exposed to an initial concentration of 10 mg/l, all other animals did not show any toxic effects. When 10 mice, 4 rats, 1 rabbit and 1 cat were exposed to 20 mg/l (initial test concentration) of the test compound, the rabbit and one mice died, while there were no

findings in rats and the cat.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Ethylendiamin, 70%ig
Reliability : (2) valid with restrictions
19.07.2001 (132)

Type : other
Species : laboratory animal
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 6 hour(s)
Method : other: BASF-test
Year : 1952
GLP : no
Test substance : other TS
Remark : One cat, one rabbit, one guinea pig, 4 rats and 10 mice were exposed to 8 mg/l (continuous vapor exposure for 6 hours) the cat, rabbit, the rats and 6 mice died during the observation period.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Ethylendiamin, 70%ig
Reliability : (2) valid with restrictions
19.07.2001 (127)

Type : other: IRT
Species : laboratory animal
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 6 hour(s)
Method : other: BASF-test
Year : 1957
GLP : no
Test substance : other TS
Remark : Irritation of the mucous membranes and a mild dispnea was noted in 4 rabbits, cats and guinea pigs exposed to a saturated atmosphere (about 8,000 ppm) at 250C. Bronchopneumonia was noted in one rabbit and one guinea pig who died 4 resp. 9 days after exposure.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Ethylendiamin 90%ig
Reliability : (2) valid with restrictions
19.07.2001 (130)

Type : other: IRT
Species : laboratory animal
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 6 hour(s)
Method : other: BASF-test
Year : 1952
GLP : no

Test substance	:	other TS
Remark	:	No mortality was noted when one cat, one rabbit, 4 rats and 10 mice were exposed to saturated ethylenediamine vapors (about 5-6 mg/l) for 6 hours.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Ethylendiamin, 70%ig

19.01.2001 (127)

5.1.3 Acute dermal toxicity

Type	:	LD50
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	= 560 mg/kg bw
Method	:	other: Acute Dermal Toxicity
Year	:	1983
GLP	:	no data
Test substance	:	no data
Remark	:	Exposure period: 24 h
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

19.06.2001 (114)

Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	ca. 1000 mg/kg bw
Method	:	other: BASF-test
Year	:	1980
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

19.07.2001 (133)

Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	ca. 1000 mg/kg bw
Method	:	other: nach Noakes D.N. and Sanderson D.M., Brit.J.Industr.Med., 26, 59, (1969)
Year	:	1978
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
19.07.2001 (134)

Type : LD50
Species : rabbit
Strain :
Sex :
Number of animals :
Vehicle :
Value : > 6400 mg/kg bw
Method : other: Acute Dermal Toxicity
Year : 1983
GLP : no data
Test substance : other TS: Ethylenediamine dihydrochloride
Remark : Exposure period: 24 h
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.07.2001 (129)

Type : LD50
Species : rabbit
Strain :
Sex :
Number of animals :
Vehicle :
Value : = .63
Method : other
Year : 1976
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Remark : Male albino rabbits, 3 to 5 months of age, are immobilized during 24-hour contact period with the compound retained under impervious sheeting on the clipped intact skin of the trunk. Thereafter, excess fluid is removed to prevent ingestion. Maximum dosage that can be retained is 16to 20ml/kg.
ml/kg
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.07.2001 (135)

Type : LD50
Species : rabbit
Strain :
Sex :
Number of animals :
Vehicle :
Value : 550 mg/kg bw
Method : other: acute Dermal Toxicity
Year : 1951
GLP : no
Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
19.07.2001 (136)

Type : LD50

Species	:	guinea pig
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	= 655 mg/kg bw
Method	:	other: Acute Dermal Toxicity
Year	:	1951
GLP	:	no data
Test substance	:	no data
Remark	:	95 % conf. lmts.: 574 - 735 mg/kg; exposure period: 24 h
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

19.07.2001 (119)

5.1.4 Acute toxicity, other routes

Type	:	LD50
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Route of admin.	:	s.c.
Exposure time	:	
Value	:	= 424.2 mg/kg bw
Method	:	other: Acute Subcutaneous Toxicity
Year	:	1954
GLP	:	no data
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

19.07.2001 (137)

Type	:	LD50
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Route of admin.	:	s.c.
Exposure time	:	
Value	:	= 1500 mg/kg bw
Method	:	other: Acute Subcutaneous Toxicity
Year	:	1974
GLP	:	no data
Test substance	:	other TS: Ethylenediamine dihydrochloride
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable

19.07.2001 (138)

Type	:	LD50
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	

Vehicle	:	
Route of admin.	:	s.c.
Exposure time	:	
Value	:	ca. 360 mg/kg bw
Method	:	other: BASF-test
Year	:	
GLP	:	no
Test substance	:	other TS
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Ethylendiamin 90%ig, als Hydrochlorid
Reliability	:	(4) not assignable
19.07.2001		(130)

Type	:	LD50
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Route of admin.	:	s.c.
Exposure time	:	
Value	:	ca. 450 mg/kg bw
Method	:	other: BASF-test
Year	:	1952
GLP	:	no
Test substance	:	other TS
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Ethylendiamin, 70%ig
Reliability	:	(4) not assignable
20.07.2001		(139)

Type	:	other
Species	:	rabbit
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Route of admin.	:	i.v.
Exposure time	:	
Method	:	other: BASF-test
Year	:	1957
GLP	:	no
Test substance	:	other TS
Remark	:	90 mg/kg bw Ethylenediamine (base) were lethal after i.v. application, while a dose of 45 mg/kg bw caused no mortality. The hydrochloride was lethal at doses of 360 and 270 mg/kg bw in all animals and mortality was also diagnosed at 180 mg/kg bw while no mortality was noted at 90 mg/kg bw.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable
20.07.2001		(130)

5.2.1 skin irritation

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
PDII	:	
Result	:	
EC classification	:	
Method	:	other
Year	:	1951
GLP	:	no
Test substance	:	other TS: Approximately 70% in water.
Remark	:	Rabbit(s) were treated with neat material for 1 to 12 minutes. A 1% aqueous solution was applied to the ear and abdomen for 10 applications.
Result	:	Neat material resulted in minimal irritation after 1 and 3 minutes but necrosis within 6-12 minutes. Ten applications of a 1% aqueous solution resulted in slight irritation to the ear and abdomen.
Reliability	:	(2) valid with restrictions

19.06.2001 (128)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	3 minute(s)
Number of animals	:	1
PDII	:	
Result	:	
EC classification	:	
Method	:	other
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Undiluted material was applied to intact skin for 10 and 30 seconds and 3 minutes on one rabbit.. The animal was observed immediately after and one and six days after application.
Result	:	Slight irritation was observed following 10 seconds exposure of undiluted material on intact skin. Extensive redness was observed after 30 seconds exposure of undiluted material on intact skin. Extensive redness and slight necrosis was observed after 3 minutes. Extensive scab formation was observed.
Reliability	:	(2) valid with restrictions

19.06.2001 (140)

Species	:	rabbit
Concentration	:	
Exposure	:	Occlusive
Exposure time	:	
Number of animals	:	
PDII	:	
Result	:	
EC classification	:	
Method	:	

Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Aqueous solutions of 0.1, 1 or 10% was each tested on a single animal. The abdomen of the rabbit was shaved prior to initiating the study. Ten applications of 0.1 ml of test material were applied over an 11 day period to the ear and 0.5 ml of test material were applied to intact skin on the abdomen. Three consecutive daily applications of 0.5 ml were applied to abraded skin. The animals were observed for at least one week after the last application.
Result	:	10% solution caused moderate necrosis after a single application. Dermal NOEL: 0.1% solution No irritation was observed to the ear after 10 applications of a 10% solution. Slight irritation and moderate necrosis were observed to intact and abraded skin after a single application of a 10% solution. No further applications were made. Slight irritation and edema was observed after several applications of a 1% solution to intact skin but subsided after the last application. Abraded skin was normal after 3 applications. Slight scab appeared several days after the last application. No irritation was observed to the ear and intact skin after 10 applications and to abraded skin after 3 applications of a 0.1% solution.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

19.06.2001 (141)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
PDII	:	
Result	:	irritating
EC classification	:	corrosive (causes burns)
Method	:	other: Patch Test
Year	:	1951
GLP	:	no data
Test substance	:	no data
Remark	:	Application period: 24 h; 0.01 ml undiluted sample causes dermal necrosis; 10 % solution in acetone gives no reaction more than edema; primary skin irritation score: 6 (maximum possible: 10)
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

20.07.2001 (119)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
PDII	:	
Result	:	not irritating
EC classification	:	corrosive (causes burns)

Method : other: Skin Irritation
Year : 1983
GLP : no data
Test substance : other TS: 40 % aqueous solution of ethylenediamine dihydrochloride
Remark : Uncovered 24-h application
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.07.2001 (129)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
PDII :
Result : irritating
EC classification : corrosive (causes burns)
Method : other: Skin Irritation
Year : 1983
GLP : no data
Test substance : no data
Remark : Uncovered 24-h application of 0.01 ml/animal
(= 8.92 mg/animal) causes severe irritation.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.07.2001 (114)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
PDII :
Result : corrosive
EC classification : corrosive (causes burns)
Method : other
Year : 1976
GLP : no
Test substance : other TS
Remark : Ethylendiamin is applied in 0.01 ml amounts to clipped, uncovered intact skin of 5 rabbit bellies undiluted and as 10% in distilled water.
Necrosis on 2 of 2 rabbits from undiluted matrial. Moderate capillary injection on 1 rabbit. No irritation on 4 of 5 from the 10% dilution.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : Ethylenediamine undiluted and as 10% in distilled water.
Reliability : (2) valid with restrictions
20.07.2001 (142)

Species : rabbit
Concentration :
Exposure :
Exposure time :
Number of animals :
PDII :
Result : corrosive

EC classification	:	
Method	:	other: BASF-test
Year	:	1960
GLP	:	no
Test substance	:	other TS
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Ethylendiamin rein, ca. 90%ig
Reliability	:	(2) valid with restrictions

20.07.2001 (143)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
PDII	:	
Result	:	corrosive
EC classification	:	
Method	:	other: BASF-test
Year	:	1952
GLP	:	no
Test substance	:	other TS: 0.5-70% aqueous solutions
Remark	:	Ethylenediamine was irritant to caustic at concentrations above 10%. A 10 or 20% concentration of the hydrochloride salt was not irritant.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	The concentrations of ethylenediamine tested ranged from 0.5% to 70%. The hydropchloride was tested at concentrations of 10 and 20%.
Reliability	:	(2) valid with restrictions

20.07.2001 (127)

Species	:	rat
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
PDII	:	
Result	:	corrosive
EC classification	:	corrosive (causes burns)
Method	:	other: Patch Test
Year	:	1987
GLP	:	no data
Test substance	:	other TS: Aqueous [1,2-14C]ethylenediamine
Remark	:	Occlusive application of 408, 1020, or 2040 ug/cm2 for a 24-h period on approx. 10 % area of the clipped and intact back of male Wistar rats (= 0.2 ml of 10 %, 25 % or 50 % aqueous solution on an 7 x 7 cm area) causes epidermal necrosis at the intermediate and high dose level: Cell necrosis within basal and spinous cell layers which often extended into the hair-follicle infundibula; polymorpho-nuclear-cell infiltrates within the superficial dermis and often also within the necrotic epidermis; epidermal spongiosus and epidermal/dermal separation. Autoradiographic examination of the application site revealed the presence of radiolabel associated with the stratum corneum and hair shafts similar in all three treatment groups.
Source	:	Union Carbide Benelux Antwerpen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.07.2001 (144)

5.2.2 Eye irritation

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure Time	:	
Comment	:	
Number of animals	:	
Result	:	
EC classification	:	
Method	:	
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	One rabbit was treated with neat material while one rabbit each was treated with a 1 or 10% solution. Two drops of test material is placed on the right eye. This eye is washed within 30 seconds for 2 minutes in a flowing stream of water. The left eye is then treated with two drops of test material but the eye is unwashed. Within 2-3 minutes of treating the left eye, each eye is examined for conjunctival and corneal response. Similar observations are made of both eyes at 1, 24 and 48 hours and 6-8 days after treatment. Both eyes are stained with fluorescein (5% water solution) at 1, 24 and 48 hours and 6-8 days. This necessitates washing of both eyes to remove the excess stain.
Result	:	With the neat material, severe conjunctival irritation was observed immediately and 24 hours after dosing. This became more severe after 48 hours. The cornea was cloudy after one hour and was opaque after 48 hours. There was no apparent difference between the washed and unwashed eye. With 10% solution, slight conjunctival irritation was observed immediately after dosing. This progressed within one hour to severe in the unwashed eye and moderate in the washed eye. After 7 days the conjunctival irritation was slight in the unwashed eye and normal in the washed eye. The cornea was slightly cloudy in both eyes after one hour. This progressed to cloudy in the unwashed eye after 24 hours. The cornea was slightly cloudy in the unwashed eye after 7 days. The cornea of the washed eye was less affected and appeared normal within 48 hours. With the 1% solution, the conjunctiva and cornea appeared normal in the washed and unwashed eye after 1 and 24 hours.
Conclusion	:	Severe irritation with corneal injury.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

19.06.2001 (141)

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure Time	:	

Comment	:	
Number of animals	:	
Result	:	corrosive
EC classification	:	risk of serious damage to eyes
Method	:	other: Eye Irritation
Year	:	1983
GLP	:	no data
Test substance	:	no data
Remark	:	Ethylenediamine causes severe eye injury (no further data given).
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

20.07.2001 (114)

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure Time	:	
Comment	:	
Number of animals	:	
Result	:	corrosive
EC classification	:	risk of serious damage to eyes
Method	:	other: Eye Irritation
Year	:	1951
GLP	:	no data
Test substance	:	no data
Remark	:	5 ul undiluted sample causes severe eye injury read 18 - 24 h after instillation by necrosis on 63 - 87 % of cornea; primary eye irritation score: 8 (maximum possible: 10).
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

20.07.2001 (119)

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure Time	:	
Comment	:	
Number of animals	:	
Result	:	slightly irritating
EC classification	:	risk of serious damage to eyes
Method	:	other: Eye Irritation
Year	:	1983
GLP	:	no data
Test substance	:	other TS: 40 % aqueous solution of ethylenediamine dihydrochloride
Remark	:	Instillation volume: 0.5 ml
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

20.07.2001 (129)

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure Time	:	
Comment	:	
Number of animals	:	
Result	:	

EC classification	:	
Method	:	other
Year	:	1976
GLP	:	
Test substance	:	
Remark	:	Moderate to severe injury, with iritis, marked edema, purulence, injection, moderate hemorrhage, and necrosis of the lids following administration of 0.005 ml undiluted Ethylendiamine per eye or of 0.5 ml of 5% in distilled water. No injury was observed following instillation of 0.5 mf of 1% in distilled water. Single installation of 0.005 ml undiluted and 0.5 ml of 5 and 1 % dilutions are made into conjunctival sac of 5 rabbits. Reading immediately unstained and after fluorescein at 24 hours.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
20.07.2001		(145)

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure Time	:	
Comment	:	
Number of animals	:	
Result	:	irritating
EC classification	:	
Method	:	other: BASF-test
Year	:	1978
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
20.07.2001		(134)

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure Time	:	
Comment	:	
Number of animals	:	
Result	:	irritating
EC classification	:	
Method	:	other: BASF-test
Year	:	1952
GLP	:	no
Test substance	:	other TS
Remark	:	Ethylenediamine caused severe eye damage, while the hydrochloride was not irritant.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Ethylenediamine was tested at concentrations of 1, 10 and 70%. The hydrochloride was tested as a 10% concentration.
Reliability	:	(2) valid with restrictions
20.07.2001		(127)

Species	:	rabbit
Concentration	:	

Dose	:	
Exposure Time	:	
Comment	:	
Number of animals	:	
Result	:	irritating
EC classification	:	
Method	:	other: BASF-test
Year	:	1952
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Remark: The test substance caused severe eye damage.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

20.07.2001 (146)

Species	:	rabbit
Concentration	:	
Dose	:	
Exposure Time	:	
Comment	:	
Number of animals	:	
Result	:	
EC classification	:	
Method	:	
Year	:	1951
GLP	:	no
Test substance	:	other TS: Approximately 70% in water.
Remark	:	Rabbit(s) were treated with neat material or a 1% solution. One drop of liquid was placed on the eye and the eye examined several days after dosing.
Result	:	Neat material resulted in severe irritation with permanent loss of vision. A 1% solution produced slight, transitory corneal damage and very slight conjunctivitis. The treated eye was normal within 2 days. Washing the eye of rabbits treated with a 1% solution had a pronounced beneficial effect on the eye.
Conclusion	:	Neat material resulted in severe irritation with permanent loss of vision

13.11.2000 (128)

5.3 Sensitization

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	Induction .3 % intracutaneous Induction 7.5 % occlusive epicutaneous Challenge 2 % occlusive epicutaneous
Number of animals	:	10
Vehicle	:	physiol. saline
Result	:	sensitizing
Classification	:	sensitizing
Method	:	other: Skin Sensitization
Year	:	1981
GLP	:	no data
Test substance	:	no data
Remark	:	Mean patch test reaction score for erythema/edema: 2.95

(calculated from the sum of all patch test reactions considered positive at four challenges repeated at weekly intervals; maximum possible score: 3).

Result : 90% of the guinea pigs responded with a positive response. Substance considered to be a strong sensitizer.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (147)

Type : other: Draize test
Species : guinea pig
Concentration : Induction .5 % intracutaneous
Challenge .2 % intracutaneous
Challenge 10 % open epicutaneous
Number of animals : 10
Vehicle : physiol. saline
Result : sensitizing
Classification : sensitizing
Method : other: Skin Sensitization
Year : 1981
GLP : no data
Test substance : no data
Remark : 50 % of the animals were sensitized only after repeated induction treatment and a second challenge.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (147)

Type : other: Single injection adjuvant test
Species : guinea pig
Concentration : Induction .3 % intracutaneous
Challenge 2.5 % occlusive epicutaneous
Number of animals : 10
Vehicle : physiol. saline
Result : sensitizing
Classification : sensitizing
Method : other: Skin Sensitization
Year : 1981
GLP : no data
Test substance : no data
Result : 100% of the guinea pigs responded positive in the SIAT test. Substance was considered a strong responder.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
24.07.2001 (147)

Type : other: Repeated insult patch test
Species : guinea pig
Number of animals :
Vehicle :
Result : sensitizing
Classification : sensitizing
Method : other: Skin Sensitization
Year : 1980

GLP	:	no data
Test substance	:	other TS: 10 % EDA diluted in a solvent consisting 9:1 dipropylene glycol methylether (Dowanol DPM):polyoxyethylene sorbitan monooleate (Tween 80)
Method	:	The repeated insult patch test used a modified Maguire method. Aliquots of 0.1 ml were applied topically to the clipped and depilated backs of the guinea pigs 4 times in 10 days. At the time of the third application, 0.2 ml of Freund's adjuvant was injected intradermally at 1 point adjacent to the application site. After a 2-week rest period, all guinea pigs were challenged on the clipped flanks. Guinea pigs which initially received EDA were challenged with EDA on one flank and Na3EDTA on the other. For challenging, the test materials were applied topically as 0.1 ml aliquots for 1 application. At 24 and 48 hours following the final application, the flanks of each guinea pig were graded for hyperemia and edema, to determine if a sensitization response had occurred. A test material was considered to be a positive skin sensitizer if at least 3 of 10 guinea pigs tested exhibit slight erythema on the challenge application site.
Result	:	All guinea pigs (10 of 10) treated with EDA were sensitized. The application sites of all EDA - treated guinea pigs displayed slight to marked erythema and slight edema.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.07.2001 (148)

Type	:	Guinea pig maximization test
Species	:	guinea pig
Number of animals	:	
Vehicle	:	
Result	:	sensitizing
Classification	:	sensitizing
Method	:	other: skin sensitization
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Evidence of cross-sensitization to diethylenetriamine-high purity, triethylenetetramine, aminoethylethanolamine and piperazine.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

19.06.2001 (149) (150)

Type	:	Guinea pig maximization test
Species	:	guinea pig
Number of animals	:	10
Vehicle	:	
Result	:	ambiguous
Classification	:	
Method	:	other: Magnusson, B. and Klingman, A.M. (1970). Identification of contact allergens; Development of a standard procedure for identifying contact allergens. In Allergic contact dermatitis in the Guinea pig; Identification of Cont
Year	:	1982

GLP :
Test substance :
Method : A range finding study was conducted to determine a subirritating concentration for EDA. The following concentrations of ethylenediamine were applied as an occluded patch (2 x 2 cm) for 24 hours to the flank of each of two animals: 5, 10, 15, 25 and 50% (weight/volume). Skin test sites were evaluated for erythema and edema at 0, 24 and 48 hours after bandage removal.

During the Guinea Pig Maximization Test, guinea pigs were dosed ip with 5% EDA in saline. On test day 8, a filter paper patch was saturated with a 15% solution of EDA and applied to the shoulder region, over the injection sites for 48 hours. During the challenge phase, a 10% EDA solution was applied to the left flank of all animals for 24 hours. During the second challenge phase performed 8 days after the first challenge phase, a 5% solution was used.

The first challenge sites were evaluated 24 and 48 hours after removal of the patches. Three hours prior to the first reading, the test site was shaved with an electric razor. For the second challenge, evaluations were also performed at patch removal.

Result : In the range finding study, there was no evidence of erythema or edema at 0, 24 or 48 hours following patch removal for animals topically treated with 5, 10 or 15 percent. Animals treated with 25 or 50% EDA solutions had necrosis and eschar formation on the entire skin test site 24 or 48 hours after treatment. Based on these results, the maximum nonirritating concentration of the chemical which could be used was 15 percent. Since the threshold for irritation may vary from animal to animal, a conservative dosage level of 10% EDA was chosen for the challenge dosage in the Guinea Pig Maximization Test.

Severe ulcerations were found during the induction phase on all animals injected with the test chemical at the 5 percent concentration. These lesions ranged in size from 0.5-2 cm in diameter and required approximately two weeks to heal. Eschar formation was extensive at the site of the injection during the topical induction phase of the study. By study termination, the injection sites were considered normal except for areas of alopecia over the injeciton site. However, these animals appeared healthy during the study.

In eight of ten animals challenged with 10% EDA, necrosis and eschar formation occurred on the challenge site 24 hours following removal of the patch. Mild redness was observed at the edge of the eschar formation or necrosis. The two animals without necrosis or eschar formation also exhibited mild redness at the challenge site. At the 48-hour evaluation period, the redness was absent in all animals or the skin of the treatment site could not be evaluated due to necrosis or eschar formation. The mean skin evaluation scores of 0.8 and 0.0 obtained at the 24- and 48-hour evaluation periods, respectively, were not representative of the typical response found in sensitized animals. The skin lesions which occurred in the sensitized animals required approximately one week to completely heal.

A similar degree of erythema was noted in the controls. Additionally, an area of necrotic skin measuring 0.3 cm in diameter occurred on the challenge site at 24 and 48 hours. The mean score for erythema was 0.2 and 0.1 at the 24- and 48-hour evaluation periods, respectively.

Since the first challenge phase burned the skin, a second challenge phase was performed at 5% EDA. After the 24-hour application, one of ten animals had intense redness and swelling, while six of the remaining nine animals in this group had moderate diffuse redness; scattered mild redness occurred on three of ten animals. At the 24-hour evaluation period, no evaluation could be made in three of ten animals due to necrosis or yellow discoloration of the treatment site. Scattered mild redness occurred in four of the remaining seven animals; scores for erythema were zero for three animals. At the 40-hour evaluation period, no evaluation could be made for the challenge site in two of ten animals, while no erythema occurred in the remaining eight animals in this group. The mean skin evaluation scores were 1.2, 0.4 and 0.1 in the controls and 1.8, 0.6 and 0.0 in the test chemical animals at 0, 243 and 48 hours following patch removal, respectively.

Use of the adjuvant injections administered during the induction phase of the study, reduced the threshold for irritation in the controls and treatment groups. Due to the nature of the response in the control and treatment groups, the allergic potential of ethylenediamine could not be accurately evaluated.

Reliability : (2) valid with restrictions
20.07.2001 (151)

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : Sensitizing
Classification : Sensitizing
Method : other: Skin Sensitization
Year : 1979
GLP : no data
Test substance : no data
Remark : An attempt at oral or i.v. induction of unresponsiveness (tolerance) was unsuccessful with the test substance.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.07.2001 (152)

Type : Guinea pig maximization test
Species : guinea pig
Number of animals :
Vehicle :
Result : Sensitizing
Classification : Sensitizing
Method : other: Skin Sensitization
Year : 1978
GLP : no data

Test substance : other TS: commercial grade; vehicle: water
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.07.2001 (153)

Type : Maurer optimisation test
Species : guinea pig
Number of animals :
Vehicle :
Result : Sensitizing
Classification : Sensitizing
Method : other: Skin Sensitization
Year : 1979
GLP : no data
Test substance : no data
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.07.2001 (154)

Type : Mouse ear swelling test
Species : Mouse
Number of animals :
Vehicle :
Result : Sensitizing
Classification : Sensitizing
Method : other: Skin Sensitization
Year : 1986
GLP : no data
Test substance : other TS: vehicle: petrolatum
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.07.2001 (155)

Type : Mouse ear swelling test
Species : Mouse
Number of animals :
Vehicle :
Result : not sensitizing
Classification : Sensitizing
Method : other: Skin Sensitization
Year : 1990
GLP : no data
Test substance : other TS: vehicle: acetone
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.07.2001 (156)

Type : Skin painting test
Species : guinea pig
Number of animals :
Vehicle :
Result : not sensitizing
Classification :
Method : other: BASF-test
Year : 1960
GLP : No

Test substance	:	other TS
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Ethylendiamin rein, 90%ig
Reliability	:	(2) valid with restrictions
20.07.2001		(143)

Type	:	other: Buehler test
Species	:	guinea pig
Number of animals	:	
Vehicle	:	
Result	:	Sensitizing
Classification	:	Sensitizing
Method	:	other: Skin Sensitization
Year	:	1987
GLP	:	no data
Test substance	:	other TS: purity 99 %
Remark	:	Ethylenediamine solutions gave concentration-dependent scores of 0.8 - 2.5 in a vehicle of ethanol and of 0.6 - 2.8 in a vehicle of acetone/corn oil (maximum possible score: 3).
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
20.07.2001		(157)

Type	:	other: Buehler test
Species	:	guinea pig
Number of animals	:	
Vehicle	:	
Result	:	Sensitizing
Classification	:	Sensitizing
Method	:	other: Skin Sensitization
Year	:	1990
GLP	:	no data
Test substance	:	no data
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
20.07.2001		(158)

Type	:	other: Modified mouse ear swelling test and radioisotopic incorporation assay
Species	:	mouse
Number of animals	:	
Vehicle	:	
Result	:	not sensitizing
Classification	:	sensitizing
Method	:	other: Skin Sensitization
Year	:	1988
GLP	:	no data
Test substance	:	other TS: vehicle: acetone
Remark	:	Evaluation of both ear skin thickness and radiolabelled infiltration gave negative results.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
13.11.2000		(159)

5.4 Repeated dose toxicity

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	7 d
Frequency of treatment	:	daily
Post obs. period	:	none
Doses	:	m: 200, 630 or 1940 mg/kg bw/d (actual) f: 240, 820 or 2470 mg/kg bw/d (actual)
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 200 mg/kg bw
Method	:	other: Repeated Dose Toxicity
Year	:	1982
GLP	:	no data
Test substance	:	other TS: Ethylenediamine dihydrochloride
Method	:	Groups of 5 male and 5 female Fischer 344 rats were fed target concentrations of 0, 150, 500 or 1500 mg/kg/day of EDA.2HCl for 7 days. Parameters evaluated in the 7-day dietary study included diet and water consumption, body weight change, liver and kidney weights and mortality.
Remark	:	There were no deaths at any dose level. However one female rat at the high dose level was euthanized on day 6 when clinical signs of toxicity were evident - these signs included hyperactivity followed by collapse and greatly reduced respiratory rate, gross findings for this animal were massive gaseous distension of the entire gastro-intestinal tract and secondary respiratory embarrassment. High dose group: Significant reduction in body weight gain in males at termination. Female rats lost weight during the study. Absolute liver and kidney weights were significantly reduced. Relative kidney weight in female rats was significantly elevated. Middle dose group: Significant increase in relative kidney weights of female rats. All other parameters were comparable to control values. Low dose group: All parameters were comparable to control values.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

12.06.2002 (160) (121)

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	3 mo
Frequency of treatment	:	daily
Post obs. period	:	none
Doses	:	m: 50, 260 or 1040 mg/kg bw/d (actual) f: 50, 250 or 990 mg/kg bw/d (actual)
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 50 mg/kg bw

LOAEL	:	= 250 mg/kg bw
Method	:	other: Repeated Dose Toxicity
Year	:	1982
GLP	:	no data
Test substance	:	other TS: Ethylenediamine dihydrochloride
Method	:	Groups of 10 male and 10 female Fischer 344 rats were fed target concentrations of 0, 50, 250 or 1000 mg/kg/day of EDA.2HCl for 3 months. New concentrations of feed were prepared weekly, with the percentage of EDA.2HCl in the diet adjusted to maintain a constant dosage level in mg/kg for each sex according to the average body weight gain and diet consumption. Generally followed the spirit of OECD guideline #408, repeated dose oral toxicity study in rodents. Functional observational battery, grip strength and motor assessment were not conducted along with several clinical chemistry and hematology parameters.
Remark	:	No deaths and no clinical signs of toxicity in any dose group. High dose group: Diet and water consumption significantly reduced in the high dose female rats. Significant reduction in body weight gain of both sexes in the high dose group; significant reduction in absolute weights of liver and heart (both sexes), adrenal and brain (female), kidney and spleen (male) in the high dose group; increase of relative weight of brain (both sexes), spleen and heart (female) and testis in the high dose group. Significant elevation of alkaline phosphatase activity in males and females. Significant elevation of alanine aminotransferase activity in males and females of high dose groups. Increased mean corpuscular volumes in males and females. Significant increase of mean corpuscular hemoglobin and significant depression of hematocrit and hemoglobin values; significant depression of red blood cell counts, serum glucose level and urinary pH (from 6.0 to 5.0) and significant elevation of aspartate aminotransferase activity in both sexes of the high dose group; hepatocellular pleomorphism in 7/10 female and 2/10 male (control: 0/10 of each sex) in high dose group, hepatocellular degeneration and significant increased prevalence of tracheitis in male of the high dose group. Intermediate dose group: Water consumption significantly reduced in female rats. Significant elevation of alanine aminotransferase activity in males of intermediate dose groups. Increased mean corpuscular volumes in females. Low dose group: Water consumption significantly reduced in the middle dose female rats. Significant elevation of alkaline phosphatase activity in males.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

29.08.2001 (160) (129)

Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	oral feed
Exposure period	:	7 d

Frequency of treatment	:	daily
Post obs. period	:	none
Doses	:	m: 160, 630 or 2180 mg/kg bw/d (actual) f: 190, 770 or 2700 mg/kg bw/d (actual)
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 625 mg/kg bw
LOAEL	:	= 2500 mg/kg bw
Method	:	other: Repeated Dose Toxicity
Year	:	1982
GLP	:	no data
Test substance	:	other TS: Ethylenediamine dihydrochloride
Method	:	Groups of 5 male and 5 femlae B6C3F1 mice were fed target concentrations of 256, 625 or 2500 mg/kg/day for 7 days. Parameters evaluated in teh 7-day dietary study included diet and water consumption, body weight change, liver and kidney weights and mortality.
Remark	:	There were no deaths observed at any dose level. High dose group: Body weight gains were significantly reduced. The animals actually lost weight. Dietary consumption for male mice was significantly reduced. Absolute liver and kidney weights of male and female mice were significantly reduced while relative liver and kidney weights were slightly reduced. Middle dose group: All parameters were comparable to control values. Low dose group: All parameters were comparable to control values.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
29.08.2001		(160) (129)

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	12 treatments
Frequency of treatment	:	daily, 5 days/week
Post obs. period	:	
Doses	:	100, 200, 400, 800 and 1600 mg/kg ethylenediamine/kg body weight
Control group	:	yes, concurrent vehicle
NOAEL	:	= 100 mg/kg bw
LOAEL	:	= 200 mg/kg bw
Method	:	
Year	:	1982
GLP	:	
Test substance	:	other TS: ethylenediamine dihydrochloride
Method	:	Groups of 5 male and 5 female rats were dosed orally on weekdays only with 0, 100, 200, 400, 800 and 1600 mg ethylenediamine/kg body weight. The control group received distilled water. Animals received a total of 12 doses. Doses were administered on each of the 2 days immediately prior to necropsy. At the end of the study all survivors were euthanized and complete necropsies, with tissue collection, were performed.
Result	:	All rats in the 1600 mg/kg dose group died before the third dosing day. In addition, one male rat and two female rats from the 800 mg/kg dose group died before the scheduled

termination. Rats in the 1600 mg/kg dose group were reported to be inactive and weak and to have diarrhea prior to early death. All rats in the 800 mg/kg dose group were reported to have a rough haircoat and thin appearance. Those animals in the 800 mg/kg dose group that survived until termination also had pale eyes. A dose-related weight gain depression was observed in both sexes receiving 100 - 800 mg/kg. Female rats appeared to be less affected than males at the lower doses. There was a biologically significant depression in thymus to brain-and body weight ratios in the 800 mg/kg dose level animals and in liver-to-brain weight ratios for all animals dosed with ethylenediamine, when compared to controls. The only gross observation made at necropsy was that the 800 mg/kg dose level rats appeared thin. Renal lesions were observed microscopically in the 800 mg/kg dose level rats (dilation of tubular lumens, degeneration and regeneration of the tubular epithelium, necrosis of tubular epithelial cells); these lesions were seen to a lesser degree in the rats given the 400 mg/kg dose group. Very minimal evidence of renal tubular epithelial regeneration was seen in 2 rats in the 200 mg/kg dose group. Lymphoid depletion and/or necrosis was also present in all early death rats receiving the 800 mg/kg dose group. Mineralization of renal tubules was present in both dosed and control female rats.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
29.08.2001 (161) (116)

Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : 13-week
Frequency of treatment : daily, 5 days/week
Post obs. period :
Doses : 0, 100, 200, 400, 600 or 800 mg/kg
Control group : yes, concurrent vehicle
LOAEL : = 100 mg/kg bw
Method : other: Generally follows OECD guideline 408
Year : 1982
GLP : no data
Test substance : other TS: ethylenediamine dihydrochloride
Method : Groups of 10 male and 10 female rats were dosed orally with 0, 100, 200, 400, 600 or 800 mg/kg ethylenediamine/kg body weight on weekdays only. The control group received distilled water only. Dosage volumes were determined and adjusted weekly on the basis of the mean body weight of each dose group and sex. Individual body weights were collected weekly throughout the study. The rats were observed twice daily for moribunity/morbidity and all clinical signs and negative observations were recorded daily. Ophthalmoscopic exams were performed on all rats during weeks 6 and 12. All rats received a full necropsy with tissue collection. The eyes of all animals surviving to scheduled sacrifice were fixed in 3 percent glutaraldehyde. The weights of the intact body, liver, thymus, right kidney, heart, brain, lungs and right testicle were recorded at necropsy.
Result : Six male and one female rat from the 1600 mg/kg group died

during the in-life phase of the study. All animals in the lower dose groups survived to the end of the study. Animals in the two highest doses exhibited gasping, sneezing and squinting of both eyes shortly after dose administration. In some animals from the 600 and 800 mg/kg groups, there was a discoloration of the eye while others exhibited a purple color. Subsequently, rats from both dose groups developed white masses in their eyes. Bilateral pupil dilation was noted in all survivng rats receiving 600 or 800 mg/kg during week 11 or 12 of the study. All of these eye abnormalities appeared to be irreversible. Ophthalmoscopic examination revealed bilateral cataracts in 3 of 6 males and 7 of 10 females after receiving 800 mg/kg for 6 weeks. Hemorrhage in the posterior chamber of the eye and debris floating in the anterior chamber was also observed in two other rats from this group. Eight male and eight female rats in the 600 mg/kg group also had bilateral cataracts after 12 weeks. Retinal atrophy and posterior chamber hemorrhage were also observed in some animals.

Body weight gains were decreased in male and female rats administered 200 - 800 mg/kg. In males, the differential change in body weight ranged from -47% in the 800 mg/kg group to -20% in the 200 mg/kg group. In females, the differential change in body weight ranged from -50% in the 800 mg/kg group to -2.2% in the 200 mg/kg group. Body weight values of the low dose group were comparable to control values.
Liver, heart or lung to body weight ratios were unaffected in either sex. Increases in the right kidney, brain and right testicle (male only) to body weight ratios appeared to be the the result of lower body weights in the respective dose groups and not the result of any differences between actual organ wights of the dosed groups and controls. Thymus to body weight mean ratios of the dose group decreased as a function of increasing dose at 200 mg/kg in males and 600 mg/kg in females.

At necropsy, cloudy appearing lens were observed in most of the 600 mg/kg and all of the surviving 800 mg/kg rats. In addition, several of the female rats from the 600 and 800 mg/kg groups appeared to have smaller uterine horns and female rats from the 800 mg/kg group had small ovaries than controls.

Histopathologic changes were noted in the eyes, kidneys and uterus. Eye lesions were present to some degree in every dose group. In the more severe cases the retina was lacking all the normal layers while in less severe cases there was only rosetting and focal cellular losses. In many cases there were ghost-like cells near the lenticular surface of the lens, mineralized debris in the lens and a globular irregular appearance to the lens material. The iris was adherent to the anterior surface of the lens in most affected eyes. Renal tubular lesions were only observed in the 600 and 800 mg/kg groups. These lesions were characterized by degeneration, regeneration and occasional necrosis of the tubular epithelium especially at the corticomedullary junciton. Mineralization of renal tubules in the papillary ducts of Bellini was also observed.

Uterine lesions included atrophy of the myometrium and endometrium in the two highest doses. No ovarian lesions were seen in the rats examined microscopically. The thymus did not appear to be affected.

Conclusion : Ethylenediamine has a direct toxic effect on the renal tubular epithelium of rats. It does appear that some accommodation does occur however, because this lesion was more severe in the 14 day study at the same dose.

The uterine lesion could be attributed to a hypoplasia in the higher dose animals rather than an atrophy and is probably due to inanition in these rats.

The severe ocular lesions seen in the top doses could be due to a vascular lesion that caused protein leakage into the eye. The retinal atrophy, synechia and cataracts could be secondary to pressure from the fluid. However, focal or multifocal retinal atrophy and dysplasia were seen in the lowest doses with no indication of any exudation or intraoccular pressure increase.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
29.08.2001 (116)

Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 13-week study
Frequency of treatment : daily, 5 days/week
Post obs. period :
Doses : 25, 50, 100, 200 or 400 mg/kg.
Control group : yes, concurrent vehicle
LOAEL : = 400 mg/kg bw
Method : other: essentially follows OECD 408 guideline
Year : 1982
GLP : no data
Test substance : other TS: ethylenediamine dihydrochloride
Method : Groups of 10 male and 10 female mice received the chemical via oral gavage in distilled water at dose levels of 0, 25, 50, 100, 200 or 400 mg ethylenediamine/kg body weight. The vehicle control group received distilled water. Dosage volumes were determined and adjusted weekly on the basis of the mean body weight of each dose group and sex. Individual body weights were collected weekly throughout the study. The mice were observed twice daily for moribundity/mortality and all clinical signs and negative observations were recorded daily. All mice received a full necropsy with tissue collection. The eyes of all animals surviving to scheduled termination were fixed in 3 percent glutaraldehyde. The weights of the intact body, liver, thymus, right kidney, heart, brain, lungs and right testicle were recorded at necropsy.

Result : One male mouse in the 400 mg/kg group died during the 13-week subchronic study. This animal lost weight and had a hunched posture prior to death. One male mouse in the 200 mg/kg group died probably due to an error in gavaging technique. There was no apparent dose-response relationship in either sex with respect to body weight changes. Absolute

and relative organ weight changes were unaffected in any dose groups. There were no treatment-related gross lesions. Histopathologic changes were only observed in the kidneys of mice receiving 400 mg/kg and primarily in males. The kidney lesion was characterized by mild to moderate acute degeneration and/or necrosis of the renal tubular epithelium primarily at the corticomedullary junction. The effect was more marked in the male mouse that died. One high dose male mouse had a cataract in one eye which may or may not have been EDA related. The NOEL was 200 mg/kg.

Reliability : (2) valid with restrictions
29.08.2001 (117)

Species	:	rat
Sex	:	male/female
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	6 wk
Frequency of treatment	:	7 h/d, 5 d/wk
Post obs. period	:	none
Doses	:	59, 132, 225 or 484 ppm (147.5, 330.0, 562.5 or 1210.0 mg/m3)
Control group	:	yes, concurrent no treatment
NOAEL	:	ca. 59 ppm
Method	:	other: Repeated Dose Toxicity
Year	:	1954
GLP	:	no data
Test substance	:	no data
Remark	:	132 ppm: The death of 4/30 animals was attributed to lung infection (not substance-related); slight depilation; body weight gain and relative weights of liver and kidney were not affected; no substance-related macroscopic or histologic changes (5 organs examined). 225 ppm: The death of 16/30 was substance-related and another 10 death were considered not to be substance-related; the 4 rats which survived showed significantly lower weight gain and higher relative weights of liver and kidney; cloudy swelling of the liver and of the loop and convoluted tubules of the kidney; lung congestion was observed in exposed as well as in control rats in similar proportions. 484 ppm: All rats died within 20 days of initial exposure; depilation was first observed on the 6th day of exposure; cloudy swelling of the liver (in 23/28 animals), cloudy swelling and degeneration of convoluted tubules (in 7/28 animals); congestion of the lung (in 17/28 animals) and of the adrenal cortex (in 5/28 animals). 15 rats/sex/concentration and control group
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
19.06.2001 (162)

Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	7 days
Frequency of treatment	:	daily

Post obs. period	:	no data
Doses	:	1250, 500, 200 mg/kg bw d
Control group	:	yes
NOAEL	:	ca. 200 mg/kg bw
Method	:	other: repeated dose toxicity
Year	:	1976
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	dietary inclusion Harlan-Wistar albino rat Inclusion of ethylenediamine in the diet for 7 days at 1250 and 500 mg/kg resulted in statistically significant reductions in body weight of both male and female rats, and dosage-related decreases in liver weights per se and as organ weight/body weight ratios. Kidney weight/body weight ratios were increased in both sexes in a dosage-related manner. There were no mortalities in either sex at any dosage level.Tubular nephrosis was found in nine out of ten rats at each of the two highest levels. Casts also were present in these animals. A few other sporadic lesions were found in both treated and control rats.
Result	:	Dietary inclusion Harlan-Wistar albino rat Inclusion of ethylenediamine in the diet for 7 days at 1250 and 500 mg/kg resulted in statistically significant reductions in body weight of both male and female rats, and dosage-related decreases in liver weights per se and as organ weight/body weight ratios. Kidney weight/body weight ratios were increased in both sexes in a dosage-related manner. There were no mortalities in either sex at any dosage level. Tubular nephrosis was found in nine out of ten rats at each of the two highest levels. Casts also were present in these animals. A few other sporadic lesions were found in both treated and control rats.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

07.06.2001 (163)

Species	:	mouse
Sex	:	female
Strain	:	CD-1
Route of admin.	:	gavage
Exposure period	:	8 d
Frequency of treatment	:	daily
Post obs. period	:	none
Doses	:	25, 50, 100, 200 or 400 mg/kg bw/d
Control group	:	yes, concurrent vehicle
NOAEL	:	< 25 mg/kg bw
Method	:	other: Repeated Dose Toxicity
Year	:	1983
GLP	:	no data
Test substance	:	other TS: vehicle: distilled water
Remark	:	No deaths; reduction in body weight gain was observed in all dose groups and was dose-related (reaching 16 % in the high dose group at termination); clinical signs comprise piloerection and apathy in all dose groups, additional hyperactivity in 3rd intermediate and high dose groups and

only in the high dose group additional emaciated appearance, exophthalmia, lacrimation, swollen eyelids discolouration of four.
10 mice/dose and control group

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
07.06.2001 (164)

Species : mouse
Sex : female
Strain : CD-1
Route of admin. : gavage
Exposure period : 8 d
Frequency of treatment : daily
Post obs. period : none
Doses : 400, 600 or 800 mg/kg bw/d
Control group : no data specified
NOAEL : < 400 mg/kg bw
Method : other: Repeated Dose Toxicity
Year : 1983
GLP : no data
Test substance : other TS: vehicle: distilled water
Remark : Mortality: 1/16 in the low dose, 10/16 in the intermediate dose and 16/16 in the high dose group; dose-related increase in the incidence of the following clinical signs of toxicity: tremor, apathy, prostration, hypothermia, swollen adomen, and piloerection; additional gasping, ataxia, red stained perigenital area in the intermediate and high dose groups and only in the high dose group additional hyper-activity, dyspnoea; maximum tolerated dose = 400 mg/kg bw/day for 8 days.
16 pregnant mice/dose group

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
20.07.2001 (164)

Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : total of 12 doses
Frequency of treatment : daily, 5 days/week
Post obs. period :
Doses : 50, 100, 200, 400 or 600 mg ethylenediamine/kg body weight
Control group : yes, concurrent vehicle
Method :
Year : 1982
GLP :
Test substance : other TS: ethylenediamine dihydrochloride
Method : Groups of 5 male and 5 female mice were dosed via oral gavage daily on weekdays only, receiving a total of 12 doses. Ethylenediamine was administered as the dihydrochloride salt with distilled water as the vehicle and was dosed at 50, 100, 200, 400 or 600 mg ethylenediamine/kg of body weight. Doses were administered on each of the 3 days immediately prior to necropsy. At the end of the study

all survivors were euthanized and complete necropsies, with tissue collection, were performed.

Result	:	All 600 mg/kg group mice died by the fourth day of dosing. Three female mice in the 400 mg/kg dose group also died before the scheduled termination. Mice in the top dose exhibited inactivity and weakness from the first dose until death. The three 400 mg/kg female mice that died prior to the scheduled termination displayed weakness prior to death. All surviving ethylenediamine dosed male mice lost weight during the study but there was no apparent dose-response relationship. All female mice, except the 50 mg/kg group, gained weight. Absolute and relative organ weights were unaffected. There were no significant gross lesions observed at necropsy. Histopathologically, mice in the 100 - 400 mg/kg groups exhibited kidney tubular nephrosis, necrosis and regenerative processes. In the 100 and 200 mg/kg groups, there was very minimal evidence of tubular regeneration in the kidneys. In addition, lymphoid depletion and necrosis were observed in the splenic follicles in the 4oo mg/kg mice.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

20.07.2001 (165)

Species	:	rabbit
Sex	:	no data
Strain	:	no data
Route of admin.	:	oral unspecified
Exposure period	:	up to 18 days
Frequency of treatment	:	once/day
Post obs. period	:	none
Doses	:	90; 180 mg/kg
Control group	:	no data specified
Method	:	other: BASF-test
Year	:	
GLP	:	no
Test substance	:	other TS
Result	:	Ethylenediamine (base) has been administerd to 2 animals/dose at concentrations of 90 or 180 mg/kg bw. The high concentration was lethal after 9 resp. 11 applications. Clinical symptoms described were, lack of appetite, diarrhea and convulsions in animals dying. The hydrochloride has been tested only at the high dose and both animals died after 2 resp. 6 applications.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Ethylendiamin as base and as hydrochloride.
Reliability	:	(4) not assignable

20.07.2001 (130)

Species	:	rabbit
Sex	:	no data
Strain	:	no data
Route of admin.	:	oral unspecified
Exposure period	:	up to 10 days
Frequency of treatment	:	once a day
Post obs. period	:	none
Doses	:	1000; 500; 100 mg/kg

Control group	:	no
Method	:	other: BASF-test
Year	:	
GLP	:	no
Test substance	:	other TS
Result	:	One animal per dose level was tested. A single application of 1000 mg/kg bw was not lethal, however an additional dose of 500 mg/kg bw caused lethality in that animal. After 10 applications Ethylenediamine was completely lethal at doses of 100 and 500 mg/kg bw.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Ethylendiamin, 70%ig
Reliability	:	(2) valid with restrictions

20.07.2001 (127)

Species	:	cat
Sex	:	no data
Strain	:	no data
Route of admin.	:	gavage
Exposure period	:	10 days
Frequency of treatment	:	one day
Post obs. period	:	none
Doses	:	100 mg/kg
Control group	:	no
Method	:	other: BASF-test
Year	:	1952
GLP	:	no
Test substance	:	other TS
Result	:	Only one cat was tested. Vomiting occurred including parts of the test substance. Clinical symptoms obs erved were loss of appetite, diarrhoea, sedation, reduction of body weight. Urine tests were positive for proteins. No macroscopic pathological findings could be observed. Vomiting occurred at higher doses of 500 and 1,000 mg/kg bw, so that no further test substance application has been performed.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Ethylendiamin, 70%ig
Reliability	:	(4) not assignable

20.07.2001 (127)

Species	:	cat
Sex	:	no data
Strain	:	no data
Route of admin.	:	i.m.
Exposure period	:	10days
Frequency of treatment	:	every day
Post obs. period	:	none
Doses	:	100 mg/kg
Control group	:	no
Method	:	other: BASF-test
Year	:	1952
GLP	:	no
Test substance	:	other TS
Result	:	Only one cat was tested. Locals signs of irritation were noted at the injection site. Clinical symptoms observed where diarrhoea and body weight reduction. Urinalysis was

positive for the protein and the reduction test. Heinz bodies were increased in the blood after 10 applications.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : Ethylendiamin, 70%ig
Reliability : (4) not assignable
20.07.2001 (127)

Species : cat
Sex : no data
Strain : no data
Route of admin. : oral unspecified
Exposure period : up to 50 days
Frequency of treatment : once a day
Post obs. period : none
Doses : 90 mg/kg
Control group :
Method : other: BASF-test
Year : 1957
GLP : no
Test substance : other TS
Result : Two animals received ethylenediamine as base (50 exposures) and another two as hydrochloride salt (20 resp. 40 exposures). There was no mortality. Clinical symptoms observed were loss of appetite, diarrhoea, vomiting. There was no effect on haematological parameters and liver function.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : Ethylendiamin als Base und als Hydrochlorid
19.01.2001 (130)

5.5 Genetic toxicity 'in vitro'

Type : Ames test
System of testing : Salmonella typhimurium TA 100, TA 1535
Concentration : <= 6667 ug/plate
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method : other: Preincubation Assay
Year : 1983
GLP : no data
Test substance : other TS: purity 99.8 %
Remark : Results are considered to be weakly positive.
Result : Ethylenediamine

	TA100			TA1535		
Dose	NA	Rat Liver	Hamster Liver	NA	Rat Liver	Hamster Liver
0	122+3.3	130+13.3	98+2.4	19+1.0	19+6.7	15+0.9
30	126+5.8	135+6.7	133+24	19+3.8	9+0.9	11+3.5
100	117+8.4	116+9.3	109+8.4	22+1.5	10+4.7	13+0.0
300	111+4.8	142+5.6	119+7.5	23+2.0	18+2.4	17+1.0
1000	173+7.8	185+7.1	131+16.1	22+3.2	28+1.5	26+1.0
3000	158+1.5s	149+12.2s	185+11.8s	Toxic	29+4.9s	Toxic

Pos
Control 1995+78 1256+5.8 3659+20. 1305+40.0 82+5.5 143+18

0 115+5.6 117+11.6 109+4.9 19+1.0 9+1.2 13+1.0
30 118+8.4 103+1.8 112+10.7 19+3.8 15+2.6 8+1.0
100 126+12.5 88+8.4 111+6.1 22+1. 15+5.1 12+0.3
300 130+4.5 133+2.4 114+12.6 23+2.0 13+1.7 10+0.3
1000 156+5.5 153+2.0 146+7.1 22+3.2 28+1.9 19+3.5
3000 155+19.7s 164+4.9s 160+4.2s Toxic 29+4.8s 20+2 s

Pos
Control1864+48.3 1264+86.8 2739+115 1305+40 81+3.3 123+8.8

Standard deviations were occasionally rounded off to whole numbers due to spacing needs.

Studies conducted at Microbiological Associates, Bethesda Md, formerly EG&G Mason Research Institute.

Ethylenediamine

Dose	TA100 NA	TA100 Rat Liver	TA100 Hamster Liver	TA1535 NA	TA1535 Rat Liver	TA1535 Hamster Liver
0	112+10.7	107+4.6	112+ 5.0	11+2.3	9+2.1	7+1.5
33.3	125+2.1		145+3.4	18+1.8	8+0.7	
100	110+2.7	127+12.5	151+9.8	17+1.2	12+1.3	5+1.5
333.3	127+9.2	142+4.6	149+2.8	18+3.7	16+0.9	9+2.0
1000	102+4.5	148+4.2	178+8.3	22+4.7	23+2.4	16+1.2
3333	159+10.0	159+5.8	148+7.4s	47+4.5	43+4.7	15+3 s
6666.6		219+6.7				
6666.7				78+3.5		

Pos
Control 281+4.9 633+31.8 1464+84.3 170+3.9 246+19 333+16

0 98+10.1 86+3.8 134+4.0 18+0.6 8+1.9 8+1.9
33.3 123+7.6 6+1.2
100 136+8.5 131+15.3 135+7.2 9+1.8 5+1.7 11+2.8
333.3 138+6.2 166+4.1 151+4.6 12+2.2 9+1.8 9+1.8
1000 122+9.9 168+10.3 145+14.0 18+1.8 19+2.5 21+1.5
3333.3 168+10.3 166+2.1s 174+17.4 38+1.7 29+5.1s 47+2.5
6666.6 206+3.8 221+9.0 34+8.4 82+2 p

Pos
Control 217+3.5 571+39.1 1741+54.0 126+5.6 266+8.7 400+25

Standard deviations were occasionally rounded off to whole numbers due to spacing needs.
Studies conducted at Microbial Genetics Department, SRI International, Menlo Park, CA
s Slight clearing of background lawn growth
p precipitate

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Attached doc. : Haworth Ames results.doc
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
14.08.2001 (166)

Type : Ames test

System of testing : Salmonella typhimurium TA 98, TA 1537
Concentration : <= 3333 ug/plate
Cycotoxic conc. :
Metabolic activation : with and without
Result : negative
Method : other: Preincubation Assay
Year : 1983
GLP : no data
Test substance : other TS: purity 99.8 %
Remark : Results are considered to be weakly positive.
Result :

Ethylenediamine

Dose	TA98 NA	TA98 Rat Liver	TA98 Hamster Liver	TA1537 NA	TA1537 Rat Liver	TA1537 Hamster Liver
0	14+4.0	28+3.5	27+1.5	4+1.2	11+0.7	10+4.1
30	16+2.6	31+1.7	23+1.8	5+1.0	7+2.2	9+2.0
100	19+2.3	27+2.9	28+2.9	4+0.7	7+2.7	8+2.0
300	16+1.2	33+7.0	23+5.4	8+1.2	9+1.5	9+2.6
1000	22+2.7	38+4.7	26+2.0	10+1.5	9+0.3	8+1.5
3000	toxic	toxic	11+0.7s	Toxic	Toxic	Toxic
Pos Control	1399+44	1120+28	2974+112	65+3.8	69+8.0	358+16
0	19+1.8	22+2.9	20+1.5	9+1.2	17+11.4	6+1.2
30	23+0.9	24+3.5	27+2.3	8+1.8	9+0.6	6+0.3
100	26+1.8	20+1.0	20+1.8	9+0.9	8+1.0	6+0.7
300	22+1.8	24+1.2	16+3.7	8+3.6	11+1.5	4+0.7
1000	21+1.5	27+1.5	23+2.2	7+1.0	8+1.9	8+1.3
3000	43+28.0s	15+2.3s	20+4.3s	8+1.2s	Toxic	13+1.0s
Pos Control	1564+29	1322+36	2748+127	192+65	55+2.6	255+5.8

Standard deviations were occasionally rounded off to whole numbers due to spacing needs.
Studies conducted at Microbiological Associates, Bethesda Md, formerly EG&G Mason Research Institute.

Ethylenediamine

Dose	TA98 NA	TA98 Rat Liver	TA98 Hamster Liver	TA1537 NA	TA1537 Rat Liver	TA1537 Hamster Liver
0	24+2.4	31+3.6	32+4.1	4+1.0	7+1.3	5+0.7
33.3	28+1.8	31+6.9	29+5.0	8+0.7	4+0.6	6+0.6
100	25+4.0	29+0.9	35+2.4	5+0.7	4+0.3	4+0.7
333.3	26+2.6	27+0.9	32+1.0	6+1.8	4+1.5	6+1.7
1000	17+1.7	28+1.5	32+8.6	4+0.0	5+1.2	6+0.3
3333	21+2.2	7+1.2s	12+0.3s	7+2.3	5+1.5s	4+0.7s
Pos Control	438+3.5	448+22	1196+47.3	122+40	142+14.4	251+3.8

Standard deviations were occasionally rounded off to whole numbers due to spacing needs.
Studies conducted at Microbial Genetics Department, SRI International, Menlo Park, CA
s Slight clearing of background lawn growth

Source : Union Carbide Benelux Antwerpen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (166)

Type : Ames test
System of testing : Strains TA98, TA100, TA1535 and TA1538
Concentration : 0, 0.1, 1.0, 2.0, 4.0, 6.0 10 ul/plate
Cycotoxic conc. :
Metabolic activation : with and without
Result :
Method : other: Ames, B.N. et al.., (1975). Methods for detecting carcinogens and mutagens with the Salmonella mammalian-microsome mutagenicity assay. Mutation Res. 31:347-364
Year : 1979
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Result :

Ethylenediamine - Dow sample

	TA1535		TA100	
ul/plate	-S9	S9	-S9	S9
0	19+0.7	19+5.0	61+8.3	48+9.3
0.1	26+5.5	40+19.8	71+8.5	39+0.6
1.0	23+7.8	29+2.8	104+12.9	60+8.0
2.0	29+2.1	42+8.5	121+4.6	106+11.1
4.0	47+6.7	63+1.4	153+1.5	136+26.9
6.0	26+6.1	79+0.7	141+5.7	157+19.2
10.0	Toxic	47+2.8	117+3.5	168+16.3
Pos Control	88+36.1	196+0.0	180+6.4	611+87.7

	TA1538		TA98	
ul/plate	-S9	S9	-S9	S9
0	11+1.0	46+8.1	11+2.1	42+2.1
0.1	12+3.6	42+11.8	12+0.6	29+7.8
1.0	7+2.3	39+4.5	8+2.1	39+5.8
2.0	6+1.2	34+6.7	13+1.2	33+6.1
4.0	6+3.0	25+7.0	14+3.5	29+7.8
6.0	Toxic	Toxic	16+6.8	17+3.3
10.0	Toxic	Toxic	18+9.9	11+0.6
Pos Control	405+8.5	303+80.6	432+43.1	387+2.8

NA = Non activated. A = S-9 Activated

Ethylenediamine - Union Carbide sample

	TA1535		TA100	
ul/plate	-S9	S9	-S9	S9
0	19+0.7	19+5.0	61+8.3	48+9.3
0.1	25+3.2	30+15.2	69+11.6	51+4.2
1.0	24+3.8	23+7.8	87+10.6	60+14.0
2.0	24+4.9	25+1.4	99+8.5	68+9.6
4.0	13+2.6	18+1.5	109+18.1	Toxic
6.0	12+7.9	21+4.0	116+5.9	Toxic
10.0	Toxic	Toxic	Toxic	Toxic
Pos Control	88+36.1	196+0	180+6.4	611+87.7

	TA1538		TA98	
ul/plate	-S9	S9	-S9	S9
0	11+1.0	46+8.1	11+2.1	42+2.1
0.1	6+2.6	14+4.7	19+3.6	35+4.2
1.0	7+1.0	38+2.6	12+1.2	32+4.2
2.0	4+2.1	45+5.9	14+1.0	24+2.3
4.0	5+1.0	31+13.1	15+3.0	25+6.7
6.0	Toxic	Toxic	22+5.5	13+5.5
10.0	Toxic	Toxic	Toxic	Toxic
Pos Control	405+8.5	303+80.6	432+43.1	387+9.8

Strains TA100 and TA1535 were positive with metabolic activation. All other tests were negative.

Attached doc. : Mueller Ames results.doc
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
24.07.2001 (167)

Type : Ames test
System of testing :
Concentration : 90, 900, 4500 and 9000 ug/plate
Cycotoxic conc. :
Metabolic activation : with and without
Result : negative
Method : other: Ames, B.N. et al., (1975). Methods for detecting carcinogens and mutagens with the Salmonella/mammalian microsome mutagenicity assay. Mutation Res. 31:347-364.
Year : 1979
GLP : no
Test substance : other TS: distilled sample of EDA
Result :

Ethylenediamine - Dow Sample

	TA98		TA100		TA1535	
Dose/plate ug	NA	A	NA	A	NA	A
0	23+5	56+12	122+17	184+16	12+5	19+2
90	20+4	71+12	85+7	142+21	13+2	47+13
900	20+3	73+12	106+9	177+17	9+4	32+15
4500	Toxic	39+12	Toxic	218+22	3+2	21+4
9000	2+0.6	Toxic	2+1	Toxic	4+4	Toxic
Pos Control	160+243	1601+363	1744+95	834+792	1217+103	143+116
0	28+2	58+6	ND	ND	ND	ND
2250	15+6	47+19	ND	ND	ND	ND
4500	Toxic	32+3	ND	ND	ND	ND
6750	Toxic	Toxic	ND	ND	ND	ND
9000	Toxic	Toxic	ND	ND	ND	ND
Pos Control	2606+116	2212+276	ND	ND	ND	ND

Ethylenediamine - Dow Sample (cont.)

	TA1537		TA1538	
dose/plate ug	NA	A	NA	A
0	5+1	23+5	9+3	44+8
90	7+2		24+5	11+2	53+3
900	8+4		25+0.6	9+5	45+14
4500	Toxic		Toxic	Toxic	17+9
9000	4+2		Toxic	5+3	Toxic

Pos Control 1203+120 597+106 1652+126 1703+182

0	9+2	23+5	6+6	43+2
2250	10+5	20+13	5+0	23+2
4500	Toxic	9+3	Toxic	23+6
6750	Toxic	Toxic	Toxic	Toxic
9000	2.5+0.7	Toxic	Toxic	Toxic

Pos Control 895+69 475+220 1929+142 1246+334

NA = Non activated. A = S-9 Activated ND = Not Determined.

Ethylenediamine - Union Carbide Sample

	TA98		TA100		TA1535	
Dose/plate ug	NA	A	NA	A	NA	A
0	25+0	57+8	107+29	114+10	11+4	23+3
90	22+6	56+14	133+13	158+2	16+1	28+13
900	23+4	54+9	143+9	181+6	Toxic	26+8
4500	Toxic	Toxic	Toxic	Toxic	1.3+1.5	Toxic
9000	Toxic	Toxic	Toxic	Toxic	Toxic	Toxic

Pos Control 2049+38 683+112 1943+237 764+86 1247+142 152+80

0	28+2	58+6	ND	ND	ND	ND
2250	Toxic	36+8	ND	ND	ND	ND
4500	7+10	69+92	ND	ND	ND	ND
6750	Toxic	Toxic	ND	ND	ND	ND
9000	Toxic	8+8	ND	ND	ND	ND

Pos Control 2606+116 2212+276 ND ND ND ND

Ethylenediamine - Union Carbide Sample (cont.)

	TA1537		TA1538	
Dose/plate ug	NA	A	NA	A
0	6+2	17+3	11+5	49+14
90	9+4	24+6	12+5	45+10
900	8+4	20+6	Toxic	44+6
4500	Toxic	Toxic	7+8	Toxic
9000	Toxic	Toxic	Toxic	10+7

Pos Control 1306+197 703+49 2148+79 2137+206

0	9+2	23+5	6+6	43+2
2250	7+1	16+2	Toxic	39+4
4500	Toxic	9+3	Toxic	15+3
6750	Toxic	Toxic	Toxic	Toxic
9000	Toxic	Toxic	5+3	Toxic

Pos Control 895+69 475+220 1929+142 1246+334
Negative at all dose levels in both the nonactivated and activated assays.

Attached doc. : Domoradzki Ames results.doc
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
24.07.2001 (168)

Type : Ames test

System of testing : Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration : <= 5000 ug/plate
Cycotoxic conc. :
Metabolic activation : with and without
Result :
Method : other: plate incorporation assay
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Remark : metabolic activity: S-9
Result : Ambiguous in strain TA100 with metabolic activation. Negative in all other strains.

Ethylenediamine
without activation

Dose mg/plate	TA98	TA100	TA1535	TA1537	TA1538
0	26+3.5	113+19.7	19+2.5	6+1.0	8+2.5
0.01	23+9.6	112+7.0	21+5.7	6+3.8	7+1.7
0.03	25+8.4	119+13.9	17+10.5	5+1.5	10+5.0
0.1	28+4.8	136+26.3	27+1.5	6+2.0	9+4.7
0.3	32+7.8	152+5.9	35+10.4	7+3.2	11+4.5
1	Toxic	Toxic/s	22 Toxic	Toxic	Toxic
Pos Control	1140+63.5	2554+115	2369+117	269+53.3	1470+102.4

Ethylenediamine
with activation

Dose mg/plate	TA98	TA100	TA1535	TA1537	TA1538
0	34+7.4	114+4.6	6+1.2	5+0.6	28+1.7
0.1	36+5.8	119+21.4	11+5.2	4+0.6	25+8.1
0.3	30+2.3	128+9.6	8+3.1	6+3.6	27+6.4
1	27+6.4	121+9.2	8+2.0	7+4.0	17+4.0
3	29+4.2T	214+0.7S	15+7.5	9+4.0	20+8.5
5	16+9.1T	212+32.7	17+9.3	7+1.0	8+1.4S
Pos Control	1226+249.5	818+172.5	32+8.7	49+7.6	106+15.5

Ethylenediamine (repeat)
with activation

Dose mg/plate	TA100	TA1535
0	92+10.8	13+3.2
1	135+10.0	11+4.4
3	165+10.1	16+3.2
5	161+22.9	12+3.5S
Pos Control	940+152.0	42+7.4

Ethylenediamine (repeat)
with activation

Dose mg/plate	TA100	TA1535
0	116+14.0	16+4.4
1	139+5.3	9+2.5
2	148+15.3	12+2.5
3	157+28.5	16+1.2
4	193+17.9	16+6.6
5	201+25.0	16+3.6
6	149 S	14+2.1
Pos Control	1564+108.8	114+26.2

T-Toxic
S-Sparse growth of background lawn

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
14.02.2002 (169)

Type : HGPRT assay
System of testing : Chinese hamster ovary cells
Concentration : <= 897 ug/ml
Cycotoxic conc. :
Metabolic activation : with and without
Result : negative
Method : other: 6-Thioguanine Resistance Assay
Year : 1983
GLP : no data
Test substance : other TS: purity 99.9 %
Method : The range of concentrations for testing was determined by preliminary studies on the cytotoxicity of EDA. Because EDA is highly alkaline and significantly altered the pH of the medium, cultures exposed to high EDA concentrations were equilibrated with a 10 CO2:90% air mixture during exposure to EDA to attempt to buffer the alkalinity, and thus test the highest possible concentrations.
Cells were treated with the control and test material for 5 hours both with and without metabolic activation. S9 liver homogenate from male, Sprague-Dawley rats treated with Aroclor 1254 was purchased from Litton Bionetics and the metabolic activation mixture was prepared immediately prior to use. The surviviing fraction was determined after an expression period of at least 7 days following subculture at 2-3 day intervals in F12D5 medium. For each experiment, mutants were selected by plating a total of 1 x 10e6 cells in 5-100 mm culture dishes with F12D5 medium supplemented with 2 ug/ml (12 uM) thioguanine. Colonies were stained and counted either manually or with an Artek 880 colony counter.

Data were analyzed for significant differences from the concurrent solvent control values by transformation of the mutant frequency values using the procedure of Box and Cox (1964) and statistical comparison to the solvent control values with either Student's or Cochrans's t test (Irr and Snee, 1979; Snedecor and Cochran, 1967). Variances of historical control data were used for statistical comparisons for concurrent controls with zero mutants. The

spontaneous mutation frequency in our laboratory has ranged from 0 to 18 mutants/10e6 clonable cells (mean = 3.8 x 10e-6). A test result was considered a positive effect of the test chemical whenever the frequency of mutants corrected for colony-forming ability was statistically different from the concurrent control value at a minimum of 2 consecutive doses and/or there was evidence of a dose-related effect of treatment.

Result : None of the mutant frequencies for EDA-treated cells were statistically different from concurrent controls and the frequency of mutants for all doses of EDA was within the historical range of variation observed in the spontaneous mutation frequency for this test by us and others. The relatively high doses up to 0.1% by volume (1.0 ul/ml) tested in this assay were attained only by equilibrating cultures with 10% CO2 in air to attempt to neutralize the alkaline effects of EDA upon the medium. Although this CO2 equilibration procedure resulted in greater variability in the survival determinations in the separate experiments, very steep dose-survival effects were noted consistently in all experiments with EDA within the 2-fold range of concentrations between 0.5 and 1.0 ul/ml (0.05 and 0.10% by volume). Variability evident in the survival and plating efficiency values was likely caused by small variations in the CO2 equilibration and by growth variations typical of CHO cells in this test system. The lack of mutagenic effects of EDA in the repeated tests indicated that these variations were not of sufficient magnitude to affect the sensitivity of the test.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

07.06.2001 (170)

Type : Sister chromatid exchange assay
System of testing : Chinese hamster ovary cells
Concentration : <= 448 ug/ml
Cycotoxic conc. :
Metabolic activation : with and without
Result : negative
Method : other: BrdUrd/Dye Technic
Year : 1983
GLP : no data
Test substance : other TS: purity 99.9 %
Method : Test material from Dow Chemical Company and Union Carbide Corporation were tested individually. The range of concentrations tested for each material was determined by preliminary cytotoxicity studies.

For the definitive studies, concentrations of 0.015, 0.031, 0.062, 0.125, 0.250 and 0.500 ul/ml were examined without metabolic activation. Concentrations of 0.031, 0.062, 0.125, 0.250 and 0.500 ul/ml were examined with metabolic activation. Cells were treated with the test agents for 5 hrs without metabolic activation and for 2 hrs with metabolic activation in the presence of 3 ug/ml bromodeoxyuridine in the medium. After treatment the test chemicals were removed by rinsing with phosphate-buffered saline (pH 7.2). Chromosomes were prepared by standard

procedures with at least three changes of 3:1 methanol:acetic acid fixative. A minimum of 15 cells/treatment were scored blindly. Test data were decoded only after completion of the study and results were evaluated for significant increases above concurrent solvent control values using Student's t test. A positive effect of the treatment was considered to be a reproducible, statistically significant effect and/or a dose-related increase in the frequently of SCE.

Result : No-dose-related increases in the frequency of SCE were produced following EDA exposure in the two separate tests both with and without a rat S9 metabolic activation system.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
07.06.2001 (171)

Type : Unscheduled DNA synthesis
System of testing : primary rat hepatocytes
Concentration : <= 897 ug/ml
Cycotoxic conc. :
Metabolic activation : without
Result : negative
Method : other: Autoradiographic Procedure and Liquid-Scintillation Counting
Year : 1983
GLP : no data
Test substance : other TS: purity 99.9 %
Method : Test material from Dow Chemical Company and Union Carbide Corporation were tested individually.

For the UDS scintillation spectrometry procedure, concentrations of 0.001, 0.010, 0.030, 0.100, 0.300 and 1.000 ul/ml of EDA were examined.

For the autoradiography procedure, concentrations of 1 x 10 (-8) - 1 x 10 (-1) M were examined.

Result : No dose-related or reproducible effects upon UDS levels were noted in exposures of hepatocytes over a 1000-fold range of EDA concentrations of two separate materials in the liquid scintillation assay. In the autoradiography assay, neither sample of EDA caused a significant increase in UDS over a wide concentration range.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
07.06.2001 (171)

Type : Ames test
System of testing : Salmonella typhimurium TA 100, TA 1535
Concentration : no data
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method : other: Plate Incorporation Assay
Year : 1978
GLP : no data
Test substance : no data
Remark : No additional information available in reference.

Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(4) not assignable
07.06.2001		(172)

Type	:	Ames test
System of testing	:	
Concentration	:	no data
Cycotoxic conc.	:	no data
Metabolic activation	:	no data
Result	:	
Method	:	
Year	:	1981
GLP	:	no data
Test substance	:	no data
Method	:	Only strain TA100 mentioned in abstract along with E. coli. No mention made whether study was conducted with or without metabolic activation.
Result	:	Ethylenediamine showed only slight activity in TA100. No data provided.
Reliability	:	(4) not assignable
07.06.2001		(173)

5.6 Genetic toxicity 'in vivo'

Type	:	Dominant lethal assay
Species	:	rat
Sex	:	male
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	23 wk
Doses	:	50, 150 or 500 mg/kg bw/d
Result	:	
Method	:	other: Rodent dominant lethal test
Year	:	1983
GLP	:	no data
Test substance	:	other TS: Ethylenedimaine dihydrochloride
Method	:	Four groups, consisting of 20 male rats/group, were fed 0, 50, 150 or 500 mg/kg/day for 23 weeks. These rats were removed from their dosage regimens and fed control diet 24 hours prior to mating with naive females. An additional group received a single intraperitoneal injection of 250 mg/kg/day of triethylenemelamine and served as a positive control. A mating regimen was followed sequentially for 3 consecutive weeks. Approximately 13 days after conception, the female rats were sacrificed and the uteri examined. The criteria examined included fertility, corpora lutea count, number of implantations/female, late fetal deaths/female and early fetal deaths/female.
Remark	:	Significant decrease in body weight gain in males of the high dose group. For EDA-treated animals, there were no statistically significant or dose-related increases in the number of dead implants or any other parameter. For the positive control animals, marked mutagenic responses were noted in the positive control animals. These included decreased number of viable implants/pregnant female, decreased number of litters with all fetuses viable, increased preimplantation loss, and an increased percentage of fetal deaths.
Result	:	negative

Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.07.2001 (171)

Type	:	Drosophila SLRL test
Species	:	Drosophila melanogaster
Sex	:	male
Strain	:	other: Canton-S
Route of admin.	:	oral feed
Exposure period	:	72 h
Doses	:	10000 or 20000 mg/kg feeding mixture
Result	:	
Method	:	other: SLRL Test
Year	:	1985
GLP	:	no data
Test substance	:	other TS: purity 99.8 %
Remark	:	Mortality: 2 % at 10000 mg/kg
Result	:	negative
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

07.06.2001 (174)

Type	:	Drosophila SLRL test
Species	:	Drosophila melanogaster
Sex	:	male
Strain	:	other: Canton-S
Route of admin.	:	other: injection
Exposure period	:	single injection
Doses	:	1500 mg/l
Result	:	
Method	:	other: SLRL Test
Year	:	1985
GLP	:	no data
Test substance	:	other TS: purity 99.8 %
Remark	:	Mortality: 21 %
Result	:	negative
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

07.06.2001 (175)

5.7 Carcinogenity

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	2 yr
Frequency of treatment	:	daily
Post. obs. period	:	none
Doses	:	m: 20, 100 or 350 mg/kg bw/d f: 20, 100 or360 mg/kg bw/d
Result	:	negative
Control group	:	yes, concurrent no treatment

Method : other: Carcinogenicity
Year : 1991
GLP : no data
Test substance : other TS: Ethylenediamine dihydrochloride
Remark : Groups of 100 male and 100 female Fischer 344 rats were fed diets containing 0, 0, 20, 100 or 350 mg/kg/day for 24 months. 10 rats/sex/dose and control group were scheduled for sacrifice at 6 and 12 month, 15 - 20 rats/sex/dose and control group were scheduled for sacrifice at 18 month.

Rats were approximately 43 days of age at start of study. Body weight ranges for males and females at the start of the study were 81-141 g and 60-112 g, respectively. The total number of days of exposure to dietary EDA.2HCl ranged from 733 to 741.

The body weight of each animal on the study was measured biweekly. Diet consumption was determined on the first ten cages/sex/group biweekly. Two weeks prior to the scheduled sacrifice, water consumption of the first ten cages/sex/group of animals was measured for a five-day period using bottles with stainless steel tips.

Urinalysis was performed on all rats scheduled for sacrifice approximately one week before the target date. Urine samples were collected in stainless steel metabolism cages over a period of approximately 20-hours, terminating at around 8 a.m. on the day of analysis. The measurements and observations included volume, pH, specific gravity, protein, glucose, ketones, occult blood, turbidity, color, microscopic appearance, bilirubin and urobilinogen.

For clinical chemistry and hematology, all the tests were conducted within one week prior to the sacrifice. Blood samples were obtained by retro-orbital sinus bleeding while the rats were under methoxyflurane anesthesia. Approximately 0.5 ml of blood was transferred to Vacutainers* containing K3-EDTA for hematologic evaluation. This evaluation consisted of red and white blood cell counts, differental white cell counts, measurement of hemoglobin and mean corpuscular volume, and calculations of hematocrit, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration. Approximately one additional ml of blood for clinical chemistry was collected in tubes without anticoagulant. All clinical chemistry parameters were evaluated on serum samples using the Centrifichem centrifugal analyzer. This evaluation included the measurement of serum concentrations of glucose, urea nitrogen, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total protein, albumin, creatinine, bilirubin (conjugated and total) and sorbital dehydrogenase.

On the days of scheduled sacrifice, rats were anesthetized with methoxyflurane. All rats were given a complete gross necropsy examination, and organ weights were recorded for the brain, liver, kidneys, spleen, heart, adrenals and testes. Approximately 50 tissues were fixed in 10% neutral buffered formalin. These tissues were processed for paraffin embedding, sectioned at approximately 5 microns,

and stained with hematoxylin and eosin.

Result : As shown in Tables 1 and 2, mortality for groups ingesting EDA were comparable to control values during the first 18 months of the study. After 22 months, mortality in males and females ingesting EDA were elevated from both control groups. In addition, the mortality rate in female rats ingesting 100 mg/kg/day was increased after 24 months.

Increases in water consumption were observed for both males and females from the high dose group at 12 and 18 month and for females from the high dose group at 24 month associated with increased urine volume and decreased urine specific gravity.

Significant reduction in body weight gain in male rats of the high dose group throughout the whole study course and in female rats of the high dose group from the 18th month until termination. Significant increase of body weight gain in female rats of the intermediate dose group from day 21 until the 21st month.

Significant reduction in the absolute weights of liver, kidney, spleen (male) and increase of the relative weights of liver, kidney, heart, brain (females) in rats of the high dose group. No substance-related changes in hematologic data, clinical chemistry values and urinalysis except a decrease in erythrocyte count, hemoglobin concentration, hematocrit (male) and serum albumin concentration (female) in rats of the high dose group. Significantly higher incidence of hepatocellular pleomorphism in female rats of the intermediate and the high dose group; rhinitis and tracheitis were seen with greater frequency in high dose males at 12, 18 and 24 months and in high dose females at 18 months; at 24 months, rhinitis persisted at a significantly greater frequency in high dose females while tracheitis did not; lower incidence of pituitary adenomas and testicular interstitial cell adenoma in the high dose group (incidence ratio: 2/4 in comparison to 25/26 and 12/15 in the control groups); all other tumor incidences did not differ significantly from control. The NOEL for chronic toxicity was 20 mg/kg/day. There was no evidence, under the conditions of this study, that chronic feeding of ethylenediamine dihydrochloride exhibited a carcinogenic effect in the Fischer 344 rat.

Table 1: Cumulative % Mortality of Male Rats after 18 Months

	Dose Level, mg/kg/day				
Month	Control-A	Control-B	20	100	350
18	5.6	5.9	2.5	6.2	12.0
19	9.7	7.3	2.5	7.7	13.4
20	16.4	14.1	5.8	12.9	20.0
21	21.4	17.6	10.9	21.6	29.8
22	26.4	24.4	15.9	33.8	44.5a,a
23	34.8	41.6	27.7	40.8	65.7a,a
24	46.5	67.4-a	54.6	61.7	88.6a,a
25	63.4	78.7	77.3	68.1	95.4a,a

a,a First letter denotes significantly different from control group A and second letter denotes same from control group B ($p<0.05$).

Table 2:Cumulative % Mortality of Female Rats after 18 Months

	Dose Level, mg/kg/day				
Month	Control-A	Control-B	20	100	350
18	2.1	2.4	6.2	4.6	3.2
19	6.2	3.7	7.7	6.0	7.4
20	7.9	7.1	9.4	12.6	10.6
21	9.6	10.3	17.8	15.9	20.3
22	11.3	12.0	21.1	19.2	25.2a,a
23	14.6	16.8	21.1	27.5	33.3a,a
24	18.0	21.7	26.1	39.0a,a	41.5a,a
25	30.4	24.9	29.4	56.0a,a	55.7a,a

a,a First letter denotes significantly different from control group A and second letter denotes same from control group B ($p<0.05$).

Table 3 Selected tumor incidences in rats fed EDA-2HCl

Dose mg/kg/day	Pituitary adenomas	Testes/interstitial cell adenomas
0 (A)	15/61	49/60
0 (B)	21/60	44/59
20	14/58	48/58
100	14/59	47/58
350	5/59*	7/60*

* Statistically significant as compared to both control groups ($P<0.01$).

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
14.02.2002 (176) (177)

Species : mouse
Sex : male
Strain : other: C3H/HeJ
Route of admin. : dermal
Exposure period : complete life span
Frequency of treatment : 3x/wk
Post. obs. period :
Doses : 25 ul of a 1 % aqueous solution/mouse/application
Result : negative
Control group : yes, concurrent vehicle
Method : other: Carcinogenicity
Year : 1984
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : Uncovered application onto the clipped back, starting at day 74 to 79 of age.

Treatment group singly housed: 50 mice
Control group singly housed: 50 mice received distilled water
Positive control group group housed 5/cage: 40 mice received 0.1% 3-methylcholanthrene in acetone.
Control group group housed 5/cage: 40 mice received water

The EDA and the negative control groups were housed

individually in stainless steel cages with wire mesh floors. The positive control and group housed control group were housed 5/cage under similar conditions. All mice were housed in the same room with controlled lighting. Ziegler Bros. NIH 07 pellets (Gardners, PA) and water from an automatic watering system were provided ad libitum. Mice were treated three times weekly for their complete life span with 25 ul per application of each substance. Substances were applied with an Eppendorf pipet to the back of each mouse from which the fur was clipped once weekly. All mice were examined daily, and the onset and progress of tumor growth were recorded monthly. Ten mice from the EDA and individually housed water control groups were scheduled for sacrifice at 18 months to evaluate their tissues for possible pathologic changes. Complete necropsies were performed on all mice. The dorsal skin from all animals plus all gross lesions were examined histologically after sectioning and staining with hematoxylin and eosin. In addition, all livers, kidneys and lungs from the 18 month sacrifice were fixed for histopathologic examination.

The doses of EDA were selected in preliminary 2-week studies in which various concentrations, 1 to 10%, were applied daily. The skin was closely observed for signs of irritation, and the mice were weighed several times to assess any effects on weight gain. Application of a 5% solution resulted in open sores on the skin of 80% of the treated mice. The 1% solution was the highest EDA concentration which resulted in neither gross skin irritation or reduced weight gain and was, therefore, chosen for the lifetime study.

Result : Mean survival time of the exposure group (598 days) was shorter than that of the control group (626 days); no treatment-related macroscopic or histopathologic findings; one mouse of the exposure group had a dermal fibrosis at application site and another one had a mammary adeno-carcinoma. One sebaceous adenoma of the skin of the thorax was noted in the control group individually housed. In the 3-methylcholanthrene group, 39 of 40 mice had skin tumors including 37 with confirmed squamous cell carcinomas.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : Purity 99.1%;
Impurities:
0.54 % pyrazine
0.08 % ammonia
0.03 % water
0.02 % monomethylamine
0.02 % ethylamine
0.02 % N-methyl-piperazine
0.02 % methylpyrazine
trace dimethylamine
trace ethanol
trace N-ethylpiperazine
trace ethylpyrazine

Test material from Dow Chemical Co. Freeport, TX.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

29.08.2001 (178)

5.8 Toxicity to reproduction

Type	:	Two generation study
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	for two generations
Frequency of treatment	:	daily
Premating exposure period		
Male	:	100 d
Female	:	100 d
Duration of test	:	weaning day 21 (F2 generation)
Doses	:	50, 150 or 500 mg/kg bw/d
Control group	:	yes, concurrent no treatment
NOAEL Parental	:	= 50 mg/kg bw
NOAEL F1 Offspr.	:	= 150 mg/kg bw
Method	:	other: Two Generation Reproduction Test
Year	:	1983
GLP	:	no data
Test substance	:	other TS: Ethylenediamine dihydrochloride
Remark	:	At each dose level 13 male and 26 female rats were mated in both F0 and F1 generation (control group: 26 male and 52 female rats each); continous treatment starting 100 days prior to cohabitation of F0 rats until weaning of F2 rats; complete necropsies were performed on 5 weanlings from both F1 and F2 generation at each dose group, on 10 adults/sex/ dose group of F1 generation and on 20 rats/sex of control group; necropsies were performed on all dead pups (including the examination for cleft palate); parameters examined included indices of fertility, days from first mating to parturition, gestation index, survival rate on lactation day 4, 14 and 21, pups born alive/litter, pup body weight (by litter) at lactation day 14 and individual pup body weight at weaning day 21.
Result	:	Significant reduction in parental body weight gain of female rats in the intermediate and high dose group of the F0 generation, in the high dose group of the F1 generation and of male rats in the high dose group of boths F0 and F1 generations; no substance-related parental deaths in the F0 or F1 generation; significant decrease of absolute liver weight in male rats of the high dose F1 generation; no macroscopic or histopathologic findings except a significant higher incidence of hepatocellular pleomorphism in both sexes of the high dose group of the F1 generation (6/10 male, 10/10 female; control: 0/20 each) and a significant decreased prevalence of kidney tubular mineralization in female rats of the high dose group of the F1 generation (0/10 female; control: 10/20). In conclusion there was no evidence of fertility impairment or embryotoxic effect at dose levels that show maternal or paternal toxicity.
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

19.06.2001 (179) (180)

5.9 Developmental toxicity/teratogenicity

Species	:	rat
Sex	:	female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	gestation day 6 - 15
Frequency of treatment	:	daily
Duration of test	:	cesarean section on gestation day 21
Doses	:	50, 250 or 1000 mg/kg bw/d
Control group	:	yes, concurrent no treatment
NOAEL Maternalt.	:	= 50 - mg/kg bw
Method	:	other: Teratogenicity
Year	:	1983
GLP	:	no data
Test substance	:	other TS: Ethylenediamine dihydrochloride
Method	:	Groups of 20 (40 controls) timed-pregnant rats on gestion days 6-15 were fed 0, 50, 250 or 1000 mg/kg/day of ethylenediamine dihydrochloride. On gestation day 21, the fetuses were delivered by cesarean section and the standard endpoints for teratogenicity were evaluated. One-half of each litter, chosen by a random-numbers chart, were subjected to visceral examination using the Staples technique (Staples, 1974).
Remark	:	The first artery to branch off of the aorta is the brachiocephalic which becomes the innominate after the left carotid branches off. The innominate then branches into the right subclavian and right carotid artery. When the authors stated it was missing, they really mean that the right and left carotid branch off of the brachiocephalic artery at the same time. Thus there is no innominate. However, this would not affect blood supply to areas served by these arteries.
Result	:	Significant reduction in maternal body weight gain in the intermediate dose group during gestation day 6 - 15 and in the high dose group during gestation day 6 - 21; significant decreased diet consumption in the intermediate and high dose group during gestation day 6 - 15; significant increased number of resorptions/litter and significant decreased mean fetal body weight and reduced fetal crown-rump length in the high dose group; significant higher incidence of a shortened mandible, edematous eye bulge, shortened or missing innominate artery, unossified sternebrae in fetuses of the high dose group.

	Number of pups affected Dosage level (mg/kg/day)			
	Control	50	250	1000
No. of litters	40	23	21	24
No. of pups	379	232	201	242
Pup body weight, males (g)	4.5+0.3	4.5+0.2	4.5+0.2	4.1+0.3
Pup body weight, females (g)	4.2+0.2	4.2+0.2	4.2+0.3	3.8+0.3
Fetal crown rump length, males (mm)	40+2	40+2	40+2	39+2
Fetal crown rump length, females (mm)	38+1	39+2	39+2	37+2

Slightly edematous eye bulge
F 0 0 0 4
L 0 0 0 4
Shortened mandible
F 0 0 0 18
L 0 0 0 4
Missing innominate artery
F 0 0 1 9
L 0 0 1 6
Shortened innominate artery
F 4 2 0 27
L 4 1 0 14

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Attached doc. : EDA teratology study#1.doc
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
14.02.2002 (181) (182)

Species : rat
Sex : female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : gestation day 6 - 15
Frequency of treatment : daily
Duration of test : cesarean section on gestation day 21
Doses : 1000 mg/kg bw/d
Control group : yes, concurrent vehicle
Method : other: Teratogenicity
Year : 1983
GLP : no data
Test substance : other TS: Ethylenediamine dihydrochloride
Remark : 10 pregnant rats/dose and control group
Result : Significant reduction in body weight gain and diet consumption on gestation days 6 through 15; decreased number of live fetuses/litter (5; control: 12); increased number of resorptions/dam (7; control: 0); no signs of teratogenicity.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
07.06.2001 (183) (182)

Species : mouse
Sex : female
Strain : CD-1
Route of admin. : gavage
Exposure period : gestation day 6 - 13
Frequency of treatment : daily
Duration of test : lactation day 3
Doses : 400 mg/kg bw/d
Control group : yes, concurrent vehicle
Method : other: Prescreening Test according to Chernoff and Kavlock
Year : 1982
GLP : no data
Test substance : other TS: vehicle: distilled water
Remark : 50 pregnant mice/dose and control group; examination of teratogenic effects was not done

Result	:	Maternal mortality: 1/50 (control:0/50); significant decrease of mean pup weight and pup weight gain over days 1 - 3 post partum; evaluation of potential developmental toxicity scores 13 points (maximum possible: points: 22).
Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
07.06.2001		(184) (185) (164)
Species	:	rabbit
Sex	:	
Strain	:	New Zealand white
Route of admin.	:	gavage
Exposure period	:	gestation days 6-19
Frequency of treatment	:	daily
Duration of test	:	cesarean section on gestation day 21
Doses	:	10, 40 or 80 mg/kg/day
Control group	:	yes, concurrent vehicle
Method	:	other: teratogenicity
Year	:	1991
GLP	:	no data
Test substance	:	other TS: ethylenediamine dihydrochloride
Remark	:	Artificially-inseminated New Zealand White rabbits (26/group) were administered ethylenediamine (0, 10, 40 or 80 mg/kg/day) by gavage on gestational days (gd) 6 through 19. In order to avoid the irritant/corrosive properties of the EDA base, the test chemical was administered as the dihydrochloride salt. The doses administered were equivalent to 0, 22, 89 or 178 of EDA 2HCl. At termination (gd 30), the uterus was removed and examined to determine pregnancy status and to evaluate the number of resorptions, and dead or live fetuses. Dead or live fetuses were weighed, and live fetuses examined for external, visceral and skeletal defects.
Result	:	There were no treatment-related maternal deaths in this study, and no characteristic clinical signs of toxicity in EDA-treated does. At scheduled necropsy, 19-22 pregnancies per group were confirmed. There were no statistically significant effects of EDA on maternal food intake, body weight, weight gain, liver or kidney weight (absolute or relative), or gravid uterine weight. Uterine examination on gd 30 revealed no adverse effects of EDA upon prenatal viability, litter size, fetal weight or fetal morphology. In conclusion, the maternal and developmental NOAEL for EDA in the New Zealand White rabbit exposed during major organogenesis is >=80 mg/kg/day. Higher doses were not evaluated in this study due to the observation of >=20% maternal mortality at >=100 mg/kg/day in a preliminary investigation (NTP, 1991).
Reliability	:	(2) valid with restrictions
07.06.2001		(186)
Species	:	rat
Sex	:	female
Strain	:	Fischer 344
Route of admin.	:	oral feed
Exposure period	:	gestation day 6 - 15

Frequency of treatment	:	daily
Duration of test	:	cesarean section on gestation day 21
Doses	:	1000 mg/kg bw/d
Control group	:	other: yes, concurrent no treatment and pair-fed
Method	:	other: Teratogenicity
Year	:	1983
GLP	:	no data
Test substance	:	other TS: Ethylenediamine dihydrochloride
Remark	:	To determine whether the arterial defects observed in the conventional teratology study were the result of reduced feed intake, a pair-feeding study was performed in which EDA.2HCl was fed on gestation days 6 through 15 at 1000 mg/kg/day. A pair-fed control group received the same amount of diet consumed by the EDA.2HCl-treated rats. An untreated control group was fed ad libitum. All groups contained 20 pregnant rats. On gestation day 21, the fetuses were delivered by cesarean section and the standard endpoints for teratogenicity were evaluated.
Result	:	Significant decrease in maternal body weight gain (during gestation day 6 - 21) and diet consumption (during gestation day 6 - 15); significant reduced mean body weight, mean crown-rump length and mean length of innominate artery of fetuses; in both treatment group and pair-fed control group 2 fetuses each with missing innominate artery.

	Number of pups affected Dosage level (mg/kg/day)		
	Control	Pair-fed control	1000
Fetal weight, males (g)	4.4+0.3	4.2+0.3	4.0+0.3
Fetal weight, females (g)	4.2+0.2	4.0+0.2	3.8+0.3
Fetal length, males (mm)	39+2	39+2	38+2
Fetal length, males (mm)	39+2	38+2	37+2
Missing innominate artery			
F	0	2	2
L	0	2	2
Shortened innominate artery, males(mm)	1.07+0.29	1.08+0.28	0.75+0.31
Shortened innominate artery, females(mm)	1.03+0.24	1.02+0.28	0.78+0.33

Source	:	Union Carbide Benelux Antwerpen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Attached doc.	:	EDA teratology study #2.doc
Reliability	:	(2) valid with restrictions

14.02.2002 (187) (182)

5.10 Other relevant information

Type	:	Immunotoxicity
Remark	:	Using an enzyme-linked immunosorbent assay developed to detect the predominant serum antibodies to ethylenediamine, it was shown that guinea pigs treated by patch application

did not produce the main allergic antibody IgG specific for ethylenediamine. However, intradermal administration of an ethylenediamine guinea pig serum albumin conjugate (EDA-GSA) to guinea pigs presensitized by patch application resulted in antibody production by 39 % and 86 % of the animals, at the initial and second dosing, respectively.
An in vitro blastogenesis assay, using peripheral blood lymphocytes from ethylenediamine sensitized guinea pigs, was developed to identify specific chemical allergens implicated in in vivo sensitization. Maximum tritriated thymidine incorporation by lymphocytes stimulated in vitro with EDA-GSA was observed on day 7. Optimal antigen concentration for maximum lymphocyte proliferation ranged from 5 to 50 ug/ml, the major variation being attributable to interanimal differences.
These results indicate that epicutaneous application of ethylendiamine in the guinea pig induces a type IV delayed hypersensitivity.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.07.2001 (157)

Type : other: antibody production
Remark : Ethylenediamine (EDA) was very irritating to the skin of guinea pigs injected intradermally with 50 microliters per site into 2 sites. Blood was collected on study day 20, 31 and 38 for determination of antibody production to EDA. Antibody production was determined by an enzyme-linked immunosorbent antibody (ELISA) assay.
There was no weight loss in either dose group during the study. Animals injected with EDA alone developed skin erosion, scars, abscess, and scabs at the injection sites. Animals injected with EDA-Affi-Gel(R) did not develop any ofthe skin lesions that the EDA injected animals developed. Although EDA was irritating, the production of antibody to EDA was not detected by the methodology employed in this study.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.07.2001 (188)

Type : Distribution
Method : Groups of 3-8 male Wistar rats were dosed with [14C]EDA-2HCl at 5, 50 or 500 mg/kg via the oral, tracheal or intravenous route and the fate of [14C]EDA and the other radiochemicals was followed for 24 or 48 hours.
Remark : Resorption of ethylenediamine from gastrointestinal as well as from respiration tract is rapid and almost complete:
In all cases, urinary excretion was the primary route of elimination accounting for 42 to 65% of the administered radioactivity. Depending on the route of administrion and/or the dosage, fecal excretion (5-32%) may become an important factor in the elimination of EDA and its metabolites. Six to 9% of the administered radioactivity was eliminated via expired air in the form of [14C]CO2. At the end of the 48-hour experimental period, in all the animals studied, a relatively large portion of the radioactivity (11-21%) remained in the various organs and the carcass. The radioactivity was distributed throughout the body although thyroid, bone marrow, liver and kidney contained relatively higher concentrations of radioactivity. Urinary metabolic profile by AG 50W catioon-exchange column chromatography

consisted of 3 to 4 radioactive peaks. Depending on the dosage level, 2 to 49% of the radioactivity was unchanged parent compound. N-acetylethylenediamine, a major metabolite, accounted for approximately half of the urinary radioactivity. The route of administration did not appear to change the metabolic profile. As the dosage increased from 5 to 50 to 500 mg/kg, there was a general pattern of accumulation of EDA with a corresponding decrease of metabolite(s) formation. Four pharmacokinetic parameters (bioavailability, total clearance, terminal half-life and area under the curve) were compared among the three dosing routes at the three dosage levels. There were no significant differences with respect to route in any of the parameters. Based on this investigation, there is evidence to suggest the equivalency of the fate of EDA in the rat following oral or endotracheal dosing particularly at relatively low dosage levels.

Table 1
Material balance study following single oral dosing to the rat

		Percent Administered Dose		
	Experimental Period	5 mg/kg	50 mg/kg	500 mg/kg
Urine	0-24	55.8+ 3.4	55.9+ 3.0	45.7+ 3.3
	24-48	1,4+ 0.1	1.5+ 0.2	2.5+ 0.4
Feces	0-24	4.5+ 2.7	13.8+ 1.0	16.2+ 2.5
	24-48	0.6+ 0.3	0.6+ 0.1	1.1+ 0.2
14CO2	0-24	7.8+ 1.6	4.8+ 0.4	5.9+ 0.4
	24-48	1.1+ 0.03	0.8+ 0.1	1.3+ 0.2
Cage Washing	0-24	3.8+ 1.8	2.8+ 1.2	3.0+ 0.8
	24-48	<0.1	0.1+ 0.01	0.4+ 0.1
Major organs		2.3+ 0.4	1.7+ 0.1	2.0+ 0.2
Carcass		12.2+ 1.0	9.4+ 0.1	10.8+ 0.3
Total Recovery		90.5+3.8	91.4+ 2.3	90.4+ 2.2

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : [1,2-14C]ethylenediamine dihydrochloride

Reliability : (2) valid with restrictions
20.07.2001 (160) (189)

Type : Distribution

Method : As part of a 2-year chronic toxicity study, the pharmacokinetics of ethylenediamine was studies in Fischer 344 rats of both sexes at day zero (naive animals), 6 months (controls and high dose animals), and 18 months (controls and high dose animals). A single dose of 50 mg [14C]EDA-2HCl/kg was given to each rat and the plasma kinetics was followed for a 24 hour period. Five pharmacokinetic parameters (absorption rate constant, terminal half-life, area under the curve, volume of distribution and [14C]CO2 production rate constant) were compared with respect to age, sex and chronic dosing.

Result : Following a single or repeated oral administration (up to 18 month) to Fischer 344 rats there were no ages-, sex-, and/or chronic dosing-related differences in absorption rate constant or terminal half-life for plasma elimination. However, significant age-related changes in area under the curve (AUC) were evident: The older rats had approximately two- to threefold higher AUC values than the younger ones(Table 1)); the volume of distribution in the older rats was between a fourth and a half of the value in the younger rat (Table 2). There was much more EDA present in the systemic circultion in the older rats than the younger rats. Similarly, the older rats had much smaller volumes of distribution on the basis of liters/kg body weight. This indicates that EDA is distributed through a proportionally smaller circulatory and tissue volume in the older rats.

Table 1
Comparison of Area under the Curve

	AUC (ug/ml hr)	
	Control	High level
Zero-day (male)	13.1+ 2.6	-
Zero-day (female)	16.9+ 2.6	-
6-month (male)	37.4+ 7.7	34.0+ 6.5
6-month (female)	41.0+11.2	41.2+15.0
18-month (male)	50.0+ 9.0	80.9+72.2
18-month (female)	41.3+ 6.4	48.5+12.9

Table 2
Comparison of Volume of Distribution

	Vd (liters/kg)	
	Control	High Level
Zero-day (male)	14.0+10.3	-
Zero-day (female)	12.6+ 3.1	-
6-month (male)	6.1+ 1.2	6.2+ 1.0
6-month (female)	6.8+ 2.5	5.9+ 0.8
18 month (male)	3.8+ 1.1	4.4+ 0.4
18 month (female)	6.4+ 0.6	4.5+ 1.2

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : ethylenediamine dihydrochloride,
[1,2-14C]ethylenediamine dihydrochloride
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.09.2001 (190)

Type : Distribution
Remark : Tissue distribution pattern in male Wistar rats was very similar following a single oral, intratracheal or i.v. administration of [1,2-14C]ethylenediamine dihydrochloride. The radioactivity was distributed thoughout the body although thyroid, bone marrow, liver and kidney contain relatively higher concentrations of radioactivity. Measurements of radioactivity in 26 tissues revealed a direct proportion to the dosage levels in all cases.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : [1,2-14C]ethylenediamine dihydrochloride
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
20.07.2001 (191)

Type : Distribution
Method : Male Wistar rats were exposed to aqueous 14C-ethylenediamine solutions (10, 25 or 50%) percutaneously over a 7 x 7 cm area on the back with occlusion for 24 hours. For each rat dosed, three types of studies were conducted: 1) plasma kinetics, 2) material balance and 3) histological evaluation, including autoradiography of the skin sample from the dosing area.
Remark : Following occlusive topical application of [1,2-14C]-ethylenediamine dihydrochloride to male Wistar rats terminal half-life for plasma elimination was 4.41 h +- 1.21 for a 25% solution and 4.94 h +- 0.57 for a 50% solution. The half life for the 10%

solution could not be determined because of analytical limitations.

Result : Adequate kinetic measurements were obtained only from the animals treated with 25 and 50% EDA, but not from the 10% treatment group, dut to analytical limitations. The uptake of 14C-EDA percutaneously by the rat was relatively slow in comparison with uptake following peroral or endotracheal administration. The absorption of EDA by the animals was estimated to be greater than 61, 55 and 12%, respectively, for the 50, 25 and 10% treatment groups. A large portion (11-32%) of the dose was left on/in the dosing area. Urinary excretion was the predominant route for the disposition of EDA. The recovery of the administered dose was low (70-83%), possibly due to volatilization of EDA from the skin during dosing and holding. Histologic examination of skin sections (dosing area) revealed a normal, intact epidermis in rats dosed with 10% EDA, but full-thickness epidermal necrosis in rats dosed with 25 or 50% EDA solutions. The damage of the epidermis apparently enhanced the penetration of EDA. Autoradiographic preparations revealed a concentration of the 14C-EDA radiolabel over the keratin layer and hair shafts.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
06.09.2001 (192)

Type : Distribution

Method : Male Swiss Webster mice, 6-7 weeks old, were given an intravenous dose of 50 mg/kg or an oral gavage dose of 5, 50 or 500 mg/kg {1,2-14C}-ethylenediamine dihydrochloride and its fate was followed for 48 hours.

Result : Ethylenediamine was readily absorbed from the gut (bioavailability, 87% measured at 50 mg/kg). Absorption was rapid as the EDA concentraton in plasma reached a maximum at about 1 hour after dosing. 14C-EDA-derived radioactivity was distributed throughout the body, with the liver and kidney attaining the highest concentration among the major organs. Urine was the major route of excretion, accounting for over half of the dose. About 4-13 and 8% of the dose was eliminated in the feces and as expired CO2, respectively. Excretion was quite rapid, with over 70% of the applied dose eliminated within 24 hours. The principle metabolite in the urine was N-acetylethylenediamine. There was some indication that the metabolism of EDA in the mouse might be saturated at 500 mg/kg, as the percentage of N-acetylethylenediamine excreted in the urine decreased markedly, with a concomitant shift to a higher proportion of unchanged EDA, when compared with the lower dosages.

Reliability : (2) valid with restrictions
10.09.2001 (193)

Type : Excretion

Remark : Absorbed [1,2-14C]ethylenediamine dihydrochloride is rapidly excreted from the rat: Following oral, i.v. or intratracheal administration, the total excretion amounted to between 70 % and approximately 80 % of the administered radioactivity during the first 24 h p.a. In all cases, urinary excretion was the primary route of elimination accounting for approximately 40 % to 60 % of administered radioactivity. The proportion of fecal excretion ranged between 4.5 % and more than 30 %; approximately 5 % to 8 % of the administered dose was transformed to CO2. In addition, the results indicate a possible saturation behaviour of elimination.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : [1,2-14C]ethylenediamine dihydrochloride
Reliability : (2) valid with restrictions
20.07.2001 (160) (189)

Type : Excretion
Remark : During occlusive dermal 24-h application of [1,2-14C]-ethylenediamine dihydrochloride total sum of urinary and fecal excretion amounted to approximately 7 % to nearly 40 % of the administered dose.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
10.09.2001 (144)

Type : Excretion
Remark : Following a single intraperitoneal injection of [14C]ethylenediamine (16 mg/kg bw) to male Lewis rat traces of N,N'-diacethylethylenediamine and hippuric acid have been identified as (additional) urinary excreted metabolites (at < 2 % or < 1 % of administered radioactivity, respectively). The metabolism of ethylenediamine is proposed to proceed by two main pathways: 1. Acetylation at one or both amino groups, and 2. deamination, giving the intermediate aminoacetaldehyde which is rapidly converted to glycine; this glycine is presumably the source of both CO2 and hippuric acid.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
10.09.2001 (194)

Type : Excretion
Remark : Following single oral, endotracheal or intravenous administration of [1,2-14C]ethylenediamine dihydrochloride to male Wistar rats in doses of 5, 50 or 500 mg/kg bw the following urinary elimination rates (as percentage of administered radioactivity) have been detected in dose-dependent ranges: Approximately 2 % (low dose group) to 49 % (high dose group) unchanged ethylenediamine, approximately 68 % to 40 % N-acethylethylenediamine and approximately 26 % to 10 % unknown metabolite. Thus, independent of the route of administration ethylenediamine metabolism showed saturation at high dose level: There is a general pattern of increased excretion of (unchanged) ethylenediamine with a corresponding decrease of the proportion of metabolites formed as the dosage increased.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : [1,2-14C]ethylenediamine dihydrochloride
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
10.09.2001 (160) (189)

Type : Excretion
Remark : Analysis of changes in ethylenediamine plasma levels in Wistar rats did not reveal any significances in pharmacokinetic parameters (e.g. clearance or terminal half-life) with respect to different routes of administration (oral, intratracheal, i.v.). At high dose level, however, ethylenediamine metabolism showed saturation behaviour.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
10.09.2001 (160) (189)

Type : Excretion
Method : Male Swiss Webster mice, 6-7 weeks old, were given an intravenous dose of 50 mg/kg or an oral gavage dose of 5, 50 or 500 mg/kg {1,2-14C}-ethylenediamine dihydrochloride and its fate was followed for 48 hours.
Result : Urine was the major route of excretion, accounting for over half of the dose. About 4-13 and 8% of the dose was eliminated in the feces and as expired CO2, respectively. Excretion was quite rapid, with over 70% of the applied dose eliminated within 24 hours.
Reliability : (2) valid with restrictions
20.07.2001 (193)

Type : Metabolism
Method : Male Swiss Webster mice, 6-7 weeks old, were given an intravenous dose of 50 mg/kg or an oral gavage dose of 5, 50 or 500 mg/kg {1,2-14C}-ethylenediamine dihydrochloride and its fate was followed for 48 hours.
Result : The principal metabolite in the urine was N-acetylethylenediamine. There was some indication that the metabolism of EDA in the mouse might be saturated at 500 mg/kg, as the percentage of N-acetylethylenediamine excreted in the urine decreased markedly, with the concomitant shift to a higher proportion of unchanged EDA, when compared with the lower dosages.
Reliability : (2) valid with restrictions
20.07.2001 (193)

Type : Biochemical or cellular interactions
Remark : A number of in vitro as well as in vivo studies provided indication of ethylenediamine having direct or indirect gamma-aminobutyric acid-like effects.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
20.07.2001 (195) (196) (197) (198) (199) (200) (201) (202) (203) (204) (205) (206) (207)

Type : Biochemical or cellular interactions
Remark : In rat small intestine ethylenediamine caused concentration-dependent relaxation. However, cross-desensitization of ethylenediamine and gamma-aminobutyric acid was not detected and ethylenediamine induced effect was not inhibited by tetrodotoxin (acetylcholine antagonist), propranolol (betablocker) or bicuculline (gamma-aminobutyric acid (GABA) antagonist), whereas a GABA-induced effect was inhibited by each of these substances. Ethylenediamine did not affect relaxations induced by muscle relaxants (histamine, bradykinin or papaverine). The results provided indication of ethylenediamine being a direct acting muscle relaxant with a mechanism that does not depend on a GABA-like effect.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
20.07.2001 (208) (209)

Type : Immunotoxicity
Remark : Complement inactivation by ethylenediamine in mouse serum was studied in relation to a possible adjuvant effect of the substance in a cell mediated immune response. Ethylenediamine caused a dose-dependent depletion of both alternative pathway and overall complement activity in vitro and showed also pronounced adjuvant effects in the delayed type hypersensitivity response of mice to sheep red blood cells. A significant correlation between momentary inhibition of alternative pathway activity and adjuvanticity was observed, suggesting a causative relationship between these two phenomena.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
20.07.2001 (210)

5.11 Experience with human exposure

Remark : Hypersensitivity (topically induced local or generalized): Ethylenediamine is one of the most frequently encountered contact sensitizers. Patterns of topically induced hypersensitivity reactions (of delayed type) include local as well as generalized contact dermatitis (eczematous type). First case reports on contact dermatitis appeared in the late fifties and concerned pharmacists handling aminophylline preparations. In the seventies ethylenediamine had been nominated the second or the fifth most common contact allergen. In most cases sensitizations are caused by topical preparations containing ethylenediamine as stabilizer (e.g. Mycolog in the USA, Tri-Adcortyl in Great Britain, Kenacomb in Australia, Assocort and Halciderm Combi ointment in Italy). Current topical creams do not appear to contain ethylenediamine. Cases of occupational sensitization are only rarely reported.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
19.06.2001 (211) (212) (213) (214) (215) (216) (217) (218) (219) (220) (221) (222) (223) (224) (225) (226) (227) (228) (229) (230) (231) (232) (233) (234)

Remark : Hypersensitivity (epidemiologic data):
Ethylenediamine has been inserted as one of the main causes of contact dermatitis in the 'standard patch test series of the International Contact Dermatitis Group' (ICDRG), and from 1967 to 1987 a number of cross-sectional studies have been carried out on different test populations consisting of between 89 and 3216 individuals in various counties (Poland, Canada, USA, Scotland, Sweden, Italy, Denmark, Germany). The reported data on positive patch test rates to ethylenediamine ranged from 0 to 17 % (sensitization index calculated as percentage of positive reacting individuals of the individual study population). More recently, the incidence observed in Germany appears to be lower than in North America. The incidence rate in three German populations ranges from 0.2-0.5%.
Source : Union Carbide Benelux Antwerpen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.07.2001 (212) (235) (236) (237) (238) (239) (240) (241) (242) (243) (244) (245) (246) (247) (229) (233)

Remark : At two Swedish factories handling ethylenediamine (a petrochemical plant producing ethylenediamine and a factory using it for producing ethylenediaminetetraacetic acid) workroom air was sampled (flow through of aqueous ethylenediamine solution through an electrolytic system: 750 ml/min): a concentration of 1000 ug/m3 air was detected after 3 hours (sampling site and year not specified). The samples were taken under a ventilation hood at a site for tanking.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.07.2001 (248)

Remark : Hypersensitivity (cross-reaction):
Ethylenediamine showes cross-sensitization with several other structurally related substances including the epoxy resign hardeners triethylenetetramine (one of the most common polyamines) and triethylenediamine, the antihistamines piperazine (as the most frequently encountered systemic cross-sensitizer to ethylenediamine), hydroxyzine, chlorpheniramine maleate, and the complexing agent ethylenediaminetetraacetic acid.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
20.07.2001 (249) (250) (251) (252) (241) (253) (244) (254) (229) (231) (233) (255)

Remark : Experimental study in irritation potential:
After sniffing of ethylenediamine vapours for periods of 5 to 10 seconds four test persons agreed that 100 ppm was inoffensive, that 200 ppm produced slight tingling sensation of the face and slight irritation of the nasal mucosa and that 400 ppm caused definitely intolerable irritation of the nasal mucosa.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
20.07.2001 (162)

Remark : Experimental study in irritation potential:
Gastric instillation of 201.17 mg ethylenediamine dihydrochloride caused a slight irritation of stomach mucosa that has been studied by examining the gastric transmural potential difference changes in nine test persons.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
20.07.2001 (256)

Remark : In vitro study in irritation potential:
As a predictive alternative in vitro method for examination of irritant effect to human eye, the 51Cr-release assay has been used to quantitate cytotoxicity in human corneal

endothelial cell culture system: The ED50 evaluated for cytotoxic effect of ethylenediamine in this system was 60.1 mg/ml with 95 % confidence limits of 17.4 - 204.3 mg/ml (= 1 mmol/ml, 95 conf. lmts.: 0.29 - 3.4 mmol/ml).

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
20.07.2001 (257)

Remark : Clinical case report of behavioural effects:
A 7-year-old boy with bronchial asthma who was twice treated with aminophyllin (consisting of 14.3 % ethylenediamine plus 85.7 % theophylline), each time reacted upon this with an aggressive behaviour which was completely abolished after stopping the medication and which did not appear after application of (pure) theophylline. Thus, it was suspected that this side effect could be due only to the ethylene-diamine.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
20.07.2001 (258)

Remark : Hypersensitivity (systematically induced generalized):
Systematically induced generalized hypersensitivity reaction may be produced by oral or parenteral administration of ethylenediamine containing aminophylline to previously sensitized individuals. Currently only Roxane Laboratories sells aminophylline as an oral solution (PDR, 2001). As result, patterns of delayed type reaction include eczematous dermatitis or exfoliative erythroderma. Occupational inhalation of ethylenediamine or aminophylline dust can provoke a late asthmatic broncho-spasmic reaction or rhinitis. Only one single case of reaction to ethylenediamine of immediate urtical type has been documented, indicating that this type of reaction is very rare.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
Flag : Critical study for SIDS endpoint
20.07.2001 (259) (260) (261) (262) (263) (264) (265) (266) (267) (268) (269) (270) (271) (272) (273) (227) (230) (274)

Remark : Retrospective study in smoking and occupational sensitisation:
The relationships between a history of allergy symptoms and smoking practice on respiratory sensitization to ethylene-diamine has been studied in 337 employees of a manufacturing plant in USA which have been working with ethylenediamine at some time during the period from 1974 to 1981. A subset of 38 individuals of these was identified by clinical and work history as having become sensitized to ethylenediamine showing symptoms like rhinitis, coughing and expiratory wheezing which cleared after removal from ethylenediamine work environment. The responses of a mailed questionnaire revealed correlation of histories of smoking and symptoms with latency (period between first exposure to ethylene-diamine and onset of respiratory symptoms):
Current smokers had the shortest latencies, averaging 7

month. Persons with any history of allergic symptoms, but who had never smoked, had mean latencies of 11.3 month. Persons with histories of asthma or hay fever symptoms had mean latencies of 16.2 month and 16.7 month, respectively. Symptom-free employees who had never smoked had the longest latencies, averaging 37.3 month.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
20.07.2001 (275)

Remark : Case-control study in parental occupation and childhood cancer risk:
In 1983 - 1984, a case-control study in parental occupation and childhood brain tumor risk has been conducted in USA. Cases (n = 110) were identified through the tumor registry of a pediatric hospital and matched controls (n = 193) through random digit dialing. Results of odds ratio estimation for risk elevation caused by postnatal or parental exposure to ethylenediamine accounted for 1.5 (95 % conf. lmts.: 0.6 - 3.9) or 0.6 (95 % conf. lmts.: 0.1 - 2.9), respectively. Thus, the study provided no indication of ethylenediamine being causally related to childhood brain tumors.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
20.07.2001 (276)

Remark : Toxicokinetics:
Plasma concentrations of ethylenediamine have been determined after the oral or intravenous administration of aminophylline (ethylenediamine + theophylline) to three healthy male volunteers (ages 22 - 26 years; body weight 65 - 95 kg) who received on separate occasions 3 x 100 mg aminophylline tablets (= 43 mg ethylenediamine) or 250 mg aminophylline i.v. (= 35 mg ethylenediamine). From the results the following mean values of pharmacokinetic parameters have been calculated: Following oral administration peak concentration was 0.30 ug/ml at 45 min p.a., elimination half-life was 60 min (monoexponential decrease), plasma clearance was 589 ml/min and bioavailability was 34 %; 3 h p.a. ethylenediamine was undetectable; during the first 24 h p.a. urinary excretion rates amounted to 3 % unchanged material and 45 % acetylated ethylenediamine (as percentage of the administered dose). Following i.v. administration plasma concentration exhibited a biphasic decline with an initial half-life of 7.2 min and a terminal half-life of 33 min, plasma clearance was 574 ml/min, volumes of distribution were 214 ml/kg bw (initial phase) and 133 ml/kg (terminal phase); 3 h p.a. ethylene-diamine was undetectable in this case, too; urinary excretion during the first 24 h amounted to 18 % unchanged material and 43 % acetylated ethylenediamine (as percentage of administered dose); from the results a 'first pass loss' of 57 % was deduced.

Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (4) not assignable
20.07.2001 (277) (278) (279) (280) (281)

Remark : Toxicokinetics:
Six healthy volunteers (4 male and 2 female; ages 21 - 47 years; body weight 51 - 84 kg) received Euphyllin (46.9 mg ethylenediamine, 175.7 mg theophylline, 13.3 mg sodium bisulphite, pH 9.14) by short intravenous infusion. From the plasma drug concentration-time curves examined for ethylene-diamine an elimination half-life of 114 +- 58 min, a volume of distribution of 374 +- 45 ml/kg bw and a plasma clearance of 609 ml/min (calculated on the basis of an average body weight assumed to account for 70 kg) were deduced.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
20.07.2001 (282)

Remark : Toxicokinetics:
Plasma concentration of ethylenediamine were determined in six healthy volunteers (5 male and 1 female; ages 20 - 28 years; body weight 48 - 95 kg) after a single dose and also after further four consecutive doses at 12-h intervals of a tablet containing 225 mg aminophylline in a sustained release matrix (Phyllocontin). Ethylenediamine concentration after a single dose reached a peak of 0.16 ug/ml at 1 h, and returned to baseline values in 5 - 7 h. After the fifth dose the plasma level and kinetics were not different from those obtained with the first dose indicating that ethylenediamine did not accumulate as a result of chronic administration of aminophylline in a form designed to give steady-state levels of theophylline.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
20.07.2001 (283)

Remark : Metabolism:
In the urine of a pulmonary emphysema patient receiving four oral administrations of Amsec (= 68.5 mg ethylenediamine) daily N-acetylethylenediamine has been identified as metabolite with a diurnal excretion of 53 mg/day.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
20.07.2001 (284)

Remark : Biochemical and cellular interactions:
[14C]Ethylenediamine was neither bound to human plasma protein nor to blood cells as was examined in in vitro investigations.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
20.07.2001 (278) (279)

Remark : Between 1989 and 1993 one worker has been taken to hospital suffering from necrotic changes on the exposed skin.
Source : Union Carbide Benelux Antwerpen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
20.07.2001 (285)

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7.1 End point summary

7.2 Hazard summary

7.3 Risk assessment