FOREWORD INTRODUCTION

2-DIETHYLAMINOETHANOL

CAS N°:100-37-8

SIDS Initial Assessment Report

For

SIAM 15

Boston, USA; 22-25 October 2002

1. Chemical Name:	2-Diethylaminoethanol
2. CAS Number:	100-37-8
3. Sponsor Country:	Germany Contact Point: BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit) Prof. Dr. Ulrich Schlottmann Postfach 12 06 29 D- 53048 Bonn-Bad Godesberg
4. Shared Partnership with:	BASF AG, Germany; Air Products and Chemicals Inc., USA; Atofina Chemicals Inc., USA; DOW Chemicals Company, USA; The Amines HPV Panel of the American Chemistry Council, USA
5. Roles/Responsibilities of the Partners:	
• Name of industry sponsor /consortium	BASF AG, Germany Contact person: Dr. Hubert Lendle GUP/CL - Z570 D-67056 Ludwigshafen
• Process used	see next page
6. Sponsorship History	
• How was the chemical or category brought into the HPV Chemicals Programme?	by ICCA-Initiative
7. Review Process Prior to the SIAM:	last literature search (update): 16 May 2002 (Human Health): databases medline, toxline; search profile CAS-No. and special search terms 04 January 2002 (Ecotoxicology): databases CA, biosis; search profile CAS-No. and special search terms
8. Quality check process:	As basis for the SIDS-Dossier the IUCLID was used. All data have been checked and validated by BUA
9. Date of Submission:	13 August 2002
10. Comments:	

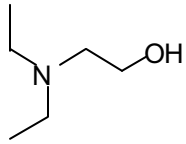
OECD/ICCA - The BUA* Peer Review Process

Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:

- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET
- Review of data and assessment of the quality of data
- Review of data evaluation
- Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications
- Review of key study description according robust summaries requirements; completeness and correctness is checked against original reports/publications
  (if original reports are missing: reliability (4), i.e. reliability not assignable)
- Review of validity of structure-activity relationships
- Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)
- In case of data gaps, review of testing plan or rationale for not testing

* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	100-37-8
Chemical Name	2-Diethylaminoethanol
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

2-Diethylaminoethanol was rapidly absorbed via the oral route. It is presumably absorbed by dermal and inhalation routes of administration. In the rat it was widely distributed to many tissues. It was primarily excreted unchanged via the urine in rats. Excretion via the feces was also observed in rats, but to a lesser extent. Urinary excretion was also reported in humans. The major metabolites in rats were reported to be diethylaminoacetic acid and diethyl-(2-hydroxyethyl)-amino-oxide.

The LD50 for the rat after oral administration was 1320 mg/kg bw. The main clinical signs described were apathy and dyspnea. After inhalation of vapors of 2diethylaminoethanol an LC50 of ca. 4600 mg/m^3/4 hour was estimated in rats using Haber's rule. Severe signs of irritation were observed, e.g. mucous membrane irritation and dyspnea. A dermal LD50 in guinea pigs was reported to be ca. 885 mg/kg bw.

2-Diethylaminoethanol was corrosive to the skin of rabbits; since the pH was measured to be 11.5 (100 g/l) at 20°C, the corrosive effects are not surprising. The potential for severe damage to the eyes can be expected based on the animal studies available and on the pH. 2-Diethylaminoethanol was not sensitizing to the skin in studies with guinea pigs.

Repeated exposure of rats to 2-diethylaminoethanol vapors (up to 365 mg/m^3) for 14 weeks caused local toxicity (irritation) at the site of contact, namely, the upper respiratory tract and the eyes; however, systemic toxicity was not observed (NOAEC, systemic toxicity, 365 mg/m^3 or 76 ppm). After inhalation exposure, the main symptom described was respiratory irritation which led to noises called rales and irritation of the eyes. The LOAEC for local toxicity (irritation) to the respiratory tract was 120 mg/m^3 (25 ppm) and the NOAEC for local toxicity was 53 mg/m^3 (10 ppm) based on histopathological effects in the nasal cavity. However, since an effect (rales) was seen at the lowest concentration a NOEC was not reached.

2-Diethylaminoethanol gave no evidence of *in vitro* mutagenic activity nor *in vivo* clastogenic potential.

Repeated exposure of rats to 2-diethylaminoethanol vapors (365 mg/m^3) for 14 weeks did not cause any adverse effects on the reproductive organs when administered by inhalation. In pregnant rats even the highest concentration tested of 486 mg/m^3, which already produced maternally toxic effects, did not lead to adverse developmental effects.

In a limited study, 2-diethylaminoethanol was not carcinogenic to rats when given by feed (tested up to ca. 50-400 mg/kg/d).

An odor threshold of 0.011 ppm (approx. 0.053 mg/mg^3) has been reported. In a laboratory worker short-time exposure to approx. 100 ppm (480 mg/m^3) 2-diethylaminoethanol caused nausea and vomiting. Subjects exposed to 2-diethylaminoethanol vapor by humidified air in office buildings complained about eye, nose and throat irritation, dizziness, nausea and vomiting. Also several cases of asthma were observed. However, these symptoms were more consistent with reactive airway dysfunction syndrome than with an allergic respiratory reaction. In one case

detectable amounts of 2-diethylaminoethanol were 0.05 and 0.04 mg/m^3.

Environment

2-diethylaminoethanol is a colourless – light yellowish organic liquid. The hygroscopic substance is miscible with water in all proportions, has a vapor pressure of about 1.8 hPa at 20 °C. The density is 0.885 g/cm³. Melting point and boiling point are – 68 °C and 162-163 °C (at 1013 hPa) respectively.

The distribution of the substance between the compartments of air, biota, sediment, soil and water was calculated according to Mackay Level I. The non-charged molecule distributes mainly to the water (99.1 %).

A soil adsorption coefficient (K_{OC}) of 5.98 was estimated for 2-diethylaminoethanol (DEAE). This Koc value suggests that this compound would be mobile in soil and adsorption to suspended solids would not be important. From the pKa-value of 9.87 it can be assumed that under environmental conditions the substance is available as a cation. Therefore, binding of the substance to the matrix of soils with high capacities for cation exchange (e.g. clay) cannot be excluded. However, no data was available for ionic-ionic interactions in soil. The calculated Henry's law constant ($3.16*10^{-4}$ Pa m³ mol^{-1} at 25 °C) and complete water solubility of 2-diethylaminoethanol suggest that volatilization from water would not be an important fate process. The substance has no considerable potential for bioaccumulation (logKow = 0.21, measured). The compound is readily biodegradable (OECD 301 A, 95% after 22 days 10d-window fulfilled). The EC20 (30 min) for activated sludge was determined to be >1000 mg/l. The photodegradation rate in the atmosphere is fast under environmental conditions (50% after 3.9 hours).

The following aquatic effect concentrations are available:

Leuciscus idus LC50 (96 h) = 147 mg/l (nominal concentration). The toxic effect may be (partly) due to the high pH of the non-neutralized test solutions, since the pH adjusted 1000 mg/l dose group tolerated the substance for 96 h without mortality.
Pimephales promelas LC50 (96 h) = 1780 mg/l (measured concentration, adjustment of pH)
Daphnia magna: EC50 (48 h) = 83.6 mg/l (nominal concentration) (toxicity due to pH effects cannot be excluded)
Daphnia magna EC50 (48 h) = 165 mg/l (nominal concentration, adjustment of pH)
Scenedesmus subspicatus: ErC50 = 44 mg/l, with a NOEC of 5 mg/l (corresponding values for biomass are 30 and 5 mg/l respectively; nominal concentration).

Using the aquatic toxic effect on the most sensitive species, *Scenedesmus subspicatus*, of 44 mg/l for the endpoint growth rate (30 mg/l endpoint biomass) a $PNEC_{aqua}$ of 44 µg/l is derived by applying an assessment factor of 1000. This factor is justified, because only short-term toxicity values were available.

The following terrestrial effect concentration was reported:

Chrysanthemum morifolium cultivar "Indianapolis white" EC50 (22 d) = 0.12 mg/l (in the nutrient solution; endpoint: chlorosis; nominal concentration). However, no PNECsoil can be derived from this result as no soil concentration is given.

Exposure

The production volume of this chemical at BASF, Germany, was more than 1000 tons in 2000. No information about the worldwide production volume is available.

The organic compound is used for the synthesis of pharmaceuticals and as a catalyst in the synthesis of polymers in the chemical industry. It is also used as a pH stabilizer. According to Swiss, Danish and Swedish Products Registers and the Hazardous Substances Data Bank, 2-diethylaminoethanol is contained in a large number of products. Some of them may be available to consumers.

Releases into the environment are likely to occur during the production and processing of 2-diethylaminoethanol as an intermediate, as well as from the use of the substance itself and use of products containing the substance.

Assuming worst case conditions, less than 9.5 kg of 2-diethylaminoethanol per day were released into the Rhine from an industrial site. During production and internal processing, less than 25 kg/a were emitted into the air from the same production site. From the reported use in consumer products, it can be concluded that most of the 2-diethylaminoethanol is released into wastewater, but part of it may also be released into the atmosphere.

RECOMMENDATION

The chemical is currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is currently of low priority for further work. Due to the corrosive potential, exposure to humans at the workplace and from consumer products has been regulated in the sponsor country. However, if this is not the case in other countries, further exposure assessment and, if necessary, risk assessment are recommended.

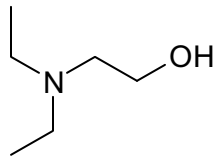
Environment: In addition to its use as chemical intermediate, European product registers indicate a wide dispersive use of 2-diethylaminoethanol. No information is available about the total production volume and about total environmental releases. However, the low aquatic toxicity, the low bioaccumulation potential and the ready biodegradability lead to the recommendation, that the chemical is currently of low priority for further work

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 100-37-8
IUPAC Name: 2-Diethylaminoethanol
Molecular Formula: $C_6H_{15}NO$
Structural Formula:



Synonyms: DEAE
ethanol, 2-(diethylamino)- (8CI, 9CI)
N,N -diethylethanolamine

1.2 Purity/Impurities/Additives

Substance type: organic

Physical status: liquid

Purity: ≥ 99.5 % (w/w)

1.3 Physico-Chemical properties

2-Diethylaminoethanol is a colorless – light yellowish organic flammable liquid with an amine-like odor (BASF AG, 2000). The hygroscopic substance is miscible with water in all proportions (BASF AG, 2000; Hazardous Substances Data Bank, 2001). The vapor pressure is about 1.8 hPa at 20 °C (BASF AG, 1984). A Henry´s law constant of $3.16*10^{-4}$ Pa*m^3/mol at 25 °C was calculated via HENRYWIN v3.00 (BASF AG, 2001a). The measured partition coefficient (log Kow) was 0.21 (BASF AG, 1987). The density was determined to be 0.885 g/cm³ (BASF AG, 1985). Melting point and boiling point of the substance are – 68 °C (BASF AG, 1985) and 162-163 °C (at 1013 hPa; Beilstein, 2001), respectively.

2 GENERAL INFORMATION ON EXPOSURE

2-Diethylaminoethanol is produced by the thermal reaction of diethylamine with ethylenoxide.

The production volume of 2-diethylaminoethanol at BASF AG, Germany, exceeded 1000 tons in 2000. No information is available about the worldwide production volume; however, it is produced by at least two companies in the USA and at least two companies in Europe.

The substance was not imported into the European Union in 2000.

The compound is used for the synthesis of drugs in the pharmaceutical industry and as a catalyst for the synthesis of polymers in the chemical industry. It is also used as a pH stabilizer. 2-Diethylaminoethanol is listed in the provisional list of monomers and additives notified to the European Commission as substances which may be used in the manufacture of plastics intended to come into contact with foodstuffs (Ref.-No 48370; European Commission, Directorate D, D3; Introduction of „Synoptic Document"; 2002).

Additional applications are cited in the European Product registers.

According to the current Swedish Register, there were 119 products on the Swedish market containing 2-diethylaminoethanol in a total amount of 216 t/a. The main uses are rust preventives, various paints, pigments, polishing agents, paper manufacturing chemicals, anti-shell agents etc. (Swedish Products Register, 23 September 2002).

The Danish Product Register cited overall 392 products. These were estimated to account for about 15 tons/a. The types of product listed were process regulators, coloring agents, corrosion inhibitors, surface-active agents, cleaning/washing agents, cutting fluids, paint, laquers and varnishes, surface treatment (Danish Product Register, 26 Feb 2002).

According to the Swiss Product register, there were 375 registrations on the Swiss market of products containing 2-diethylaminoethanol, predominantly paints, varnishes and lacquers (approx. 50 % of the registrations), glues/adhesives, cement, filler or sealing compounds (approx. 10 %), car polishes (approx. 10 %), technical oils (approx. 10 %) and other uses like wood stains and inks. Most of these uses were for professional applications. Approx. 60 products, i.e. about 16 % of the total product spectrum, were available to consumers. Paints, lacquer, household cleaners and polishes (shoe, leather, car) accounted for more than 75 % of these products (Swiss Product Register, 2001).

In the Norwegian Product Register 243 products containing a total quantity of 27 t are registered. Use categories are paints and inhibitors.

The following uses are listed in the Hazardous Substances Data Bank: the manufacture of emulsifying agents and special soaps, chemical intermediates for petroleum and gas processing chemicals as well as for paints and lacquers, cosmetics, pharmaceuticals, crop protection agents, flocculants, surface coatings, textiles and fibers, procaine, chloroquinone, anti-rust additives, plastics, paper and leather chemicals (Hazardous Substances Data Bank, 2001).

Releases into the environment are likely to occur during the production and processing of 2-diethylaminoethanol as an intermediate, as well as from the use of the substance itself and use of products containing the substance.

2-Diethylaminoethanol is measured in the influent and the effluent of the waste water treatment plant of BASF AG at regular intervals (24 h-mixing sample). Between the 1st of January 2001 and the 30th of June 2002 the concentration in the sewage as well as in the effluent was always found to be below the limit of quantitation (influent: 1 mg/l; effluent: 0.1 mg/l; BASF AG, 2002b). Additionally, the concentration in the effluent was always found to be below the limit of detection

(effluent: 0.025 mg/l) between the 1st and 30th of June in 2002. Based on the limit of detection and assuming worst case conditions, less than 9.5 kg of 2-diethylaminoethanol per day were released into the river Rhine in that period (BASF AG, 2002c).

In the 1970s 2-diethylaminoethanol was identified in an industrial effluent discharge in the USA (concentration: > 0.1 mg/L; Perry et al., 1978).

During production and internal processing at BASF AG, Ludwigshafen (Germany), less than 25 kg/a were emitted into the air in 2000 (BASF AG, 2002d).

Emission data from other production and processing sites was not available.

2.1 Environmental Exposure and Fate

For the uncharged molecule, modeling using Mackay, Level I indicates that water is the main target for environmental distribution (99.1 %; BASF AG, 2001b).

A soil adsorption coefficient (Koc) of 5.98 (log Koc = 0.78) was estimated for 2-diethylaminoethanol via PCKOCWIN (BASF AG, 2001c). The Koc value suggests that adsorption to suspended solids is not to be expected. From the pKa-value of 9.87 it can be assumed that under environmental conditions the substance is available as cation. Therefore, binding of the substance to the matrix of soils with high capacities for cation exchange (e.g. clay) cannot be excluded. However, no data was available for ionic-ionic interactions in soil. The calculation of the Henry´s law constant via HENRYWIN v3.00 yields a value of $3.16 * 10^{-4}$ Pa* m^3/mol at 25 °C (BASF AG, 2001a). This low value and the complete water solubility of 2-diethylaminoethanol suggests that volatilization from water would not be an important factor in the environmental distribution process. In addition, due to the protonation of the substance under environmental conditions, the volatility is further reduced. In the air rapid degradation can be expected according to the half life calculated via AOP v1.87 (50 % after 3.9 hours; BASF AG, 2001d). Due to the measured and calculated partition coefficients (log Kow 0.21 and log Kow 0.047; BASF AG, 1987 and BASF AG, 2002a) an accumulation in organisms is not to be expected.

2-Diethylaminoethanol is readily biodegradable according to the results obtained in a test conducted according to OECD 301 A (95 % degradation after 22 days, 10d-window fulfilled; BASF AG, 2002f). Using the model Simpletreat, an elimination in sewage treatment plants of 87 % can be estimated (no volatilization, no adsorption, biodegradation rate constant 1 h^{-1}). Based on the chemical structure of the substance hydrolysis is not likely to occur.

2.2 Human Exposure

Due to the information from European product registers, exposures to consumers and workers are likely. In the Swiss Product register, 375 products, among them 61 consumer products, containing 2-diethylaminoethanol are listed. The highest concentrations (up to 10 %) are reported for cleaning agents, surface treatment, car and floor care products (Swiss Product Register, 2001). According to the current Swedish Product Register, there were 108 products, among them 6 consumer products, on the Swedish market containing 2-diethylaminoethanol (Swedish Product Register, 2002). Concentrations in the range between 0 and 2 % may be found in paints, lacquers, varnishes and surface treatment products according to the Danish Product Register (Danish Product Register, 2002).

No data on human workplace exposure was available. 2-Diethylaminoethanol is produced by the thermal reaction of diethylamine with ethylenoxide in a closed system. There is no open handling of the product (BASF AG, 2002e). In the Safety Data Sheet of BASF AG, the workers should wear breathing protection if ventilation is inadequate and chemical resistant protective gloves and tightly

fitting safety goggles for personal protection. Body protection must be chosen depending on activity and possible exposure (BASF AG, 2000).

In Germany the current MAK value for 2-diethylaminoethanol is 5 ppm (24 mg/m^3) (DFG, 2002) and in the USA the current TLV value is 2 ppm (9,6 mg/m^3) (ACGIH, 2002).

The following indoor air monitoring data was reported:

2-Diethylaminoethanol was used as a corrosion inhibitor in an open steam humidification system at the H.F. Johnson Museum of Cornell University (USA). Analyses of air samples from the museum environment were taken in January of 1983. The chemical was detected in only 2 air samples of the 14 collected. The measured DEAE concentrations were 0.04 and 0.05 mg/m³. In addition residues of condensed 2-diethylaminoethanol were identified on samples of plastic materials in the museum at concentrations of 30 mg/m². Condensation accumulation was found to be directly related to the time of deposition for airborne concentrations (NIOSH, Health Hazard Evaluation Report, 1983; Volent P. and Baer N.S., 1985).

During the winter season 2-diethylaminoethanol was measured in the indoor air in a study room at Battelle Columbus Division (USA). The average room concentration of 2-diethylaminoethanol at an average relative humidity of 42 % was about 0.6 ppb (approx. $2.9*10^{-3}$ mg/m³) and at an average relative humidity of 61 % about 2.4 ppb (approx. 0.01 mg/m³). The primary fate of the amine that was introduced into the room air via steam humidification appeared to be condensation on surfaces (Edgerton et al., 1989).

This indoor concentration data is about 15 - 20 years old and may not be representative of, or comparable to, today's conditions. However, they indicate that inhalation is a possible route of exposure.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

2-Diethylaminoethanol has been reported to be readily absorbed via the gastrointestinal tract in humans and rats (Rosenberg et al, 1949; Schulte et al., 1972). On the basis of the physico-chemical properties of a saturated aqueous 2-diethylaminoethanol solution, a skin penetration rate of 3.44 mg/cm^2 per hour was estimated for human skin, and therefore, the resulting body burden from exposure to 5 ml/m^3 (the current MAK value) of 2-diethylaminoethalol by inhalation for 8 hours could potentially be increased by an additional three-fold factor via dermal absorption (Fiserova-Bergerova et al., 1990). However, this model was suspected to be too conservative and likely to overestimate percutaneous penetration (Guy and Russell, 1993). Absorption via inhalation has been mentioned (Toren, 1994), but the primary literature was not available for an assessment.

In a limited study with humans (Rosenberg et al, 1949), the plasma concentration peaked 3 hours after an oral administration of 5.6 g of 2-diethylaminoethanol-HCl, but was almost undetectable after 8 hours. About 25 % of the 2-diethylaminoethanol was excreted unchanged in the urine within 48 hours. Similar excretion results were observed after intravenous administration. In the same publication it was reported that 2-diethylaminoethanol-HCl given to dogs by intravenous infusion (71 mg/kg bw) , distributed rapidly. Three hours after infusion the level of 2-diethylaminoethanol was higher in the tissues examined (muscle, heart, brain, lung, liver and spleen) than in the plasma.

In a gavage study with rats (Schulte et al., 1972), ^{14}C-labeled-2-diethylaminoethanol-HCl was reported to be rapidly absorbed into the blood stream (with a dose of 68 mg/kg the maximum concentration in the blood was reached in 30 minutes and with 679 mg/kg it was reached within 1 hour). Elimination occurred primarily via the kidney. Elimination via exhalation and the feces played only minor role. The kinetics of urinary elimination was affected by the dose. In this regard, by 6 hours after the application of a 679 mg/kg bw dose 40 % was eliminated in the urine, and by 24 hours after application 58.5% was eliminated. When a 68 mg/kg dose was given, then after 6 and 24 hours 17.5 % and 37.4 % were excreted via the urine, respectively. In the experiment with 679 mg/kg 2-diethylaminoethanol, 90 % of the test substance had been eliminated via the urine 10 days after treatment. Some radioactivity was still detectable in the urine 40 days after treatment. 2-Diethylaminoethanol was predominantly (> 60 %) excreted unchanged over the first 96 hours. In the same period, the following metabolites were seen based on the recovery of radioactive compounds: 2-ethylaminoethanol (ca. 1 %), phosphoric acid-mono-(2-diethylaminoethylester) (2 - 8 %), diethylaminoacetic acid (ca. 10 %) and the N-oxide of 2-diethylaminoethanol (ca. 15 - 19 %). Incorporation into phospholipids was observed. In this study, autoradiography indicated that 2-diethylaminoethanol was widely distributed throughout the body after gavaging. 2-Diethylaminoethanol was concentrated in the liver, reaching a maximum at 7 hours, but thereafter, it decreased. Initially, the central nervous system showed very low levels of activity, but by day 7 it had increased. For the oral dose of 679 mg/kg the biological half-life was 19 hours and for the 67.9 mg/kg dose it was 36 hours.

In a separate study ^{14}C-labeled-2-diethylaminoethanol-HCl was given to rats by intravenous injection at doses of 2.9 µmol/rat (ca. 1.94 mg/kg bw) (Michelot et al., 1981). Cumulative excretion of 19.9 and 42.2 % of the radioactivity in the urine was observed after 24 and 48 hours, respectively. Additionally, 8.5 and 29.5 % of the radioactivity was excreted via the feces during the same time interval. Excretion via the bile was only measured over the first 6 hours, and was reported to be 5 %.

Since tertiary amines are poor substrates for monoamine oxidase, 2-diethylaminoethanol might presumably be metabolized by a P450 monoxygenase, or by a microsomal flavoprotein (reviewed in Cavender, 2001). Nitrosation would only be expected to occur very slowly in comparison to secondary amines (Mirvish, 1975).

Conclusion

2-Diethylaminoethanol was rapidly absorbed via the oral route. It is presumably absorbed by dermal and inhalation routes of administration. In the rat it was widely distributed to many tissues. It was primarily excreted unchanged via the urine in rats. Excretion via the feces was also observed in rats, but to a lesser extent. Urinary excretion was also reported in humans. The major metabolites in rats were reported to be diethylaminoacetic acid and diethyl-(2-hydroxyethyl)-amino-oxide.

3.1.2 Acute Toxicity

There were no studies available performed according to current guidelines, but studies were available which gave sufficient information to characterize the following endpoints.

Inhalation
LC_{50} rat (inhalation): ca. 4600 mg/m^3/4 hour; estimated by Haber's Rule from an Inhalation Hazard Test which used a highly enriched/saturated vapor exposure system at 20 °C, in which animals were exposed to 2-diethylaminoethanol vapor for 1, 3 and 8 hours (BASF AG, 1969). Clinical signs indicating severe irritation were noted, namely, attempts to escape, mucous membrane irritation, dyspnoea and gasping.

Dermal
In a non-guideline study with an exposure period of 4 days instead of 24 hours as prescribed by OECD Guideline 402, a dermal LD_{50} in guinea pigs was reported as ca. 885 mg/kg bw (Smyth and Carpenter, 1944). Normally, rats or rabbits are used for this endpoint, but the only available rabbit data was from secondary literature [LD_{50} rabbit (dermal): ca. 1100 mg/kg bw; from Smyth, 1964].

Oral
In a non-guideline study an LD_{50} in rats (oral) was determined to be ca. 1320 mg/kg bw (BASF AG, 1969). The clinical signs reported were described as apathy and dyspnea. This study was chosen as the key study since it was the one for which the most details are available. This LD50 is essentially the same as that reported by Smyth and Carpenter (1944). Higher values have been reported, but these were from tests conducted with the neutralized substance.

Conclusion

The LD_{50} for the rat after oral administration was 1320 mg/kg bw. The main clinical signs described were apathy and dyspnea. After inhalation of vapors of 2-diethylaminoethanol an LC_{50} of ca. 4600 mg/m^3/4 hour was estimated in rats using Haber's rule. Severe signs of irritation were observed, e.g. mucous membrane irritation and dyspnoea. A dermal LD_{50} in guinea pigs was reported to be ca. 885 mg/kg bw.

3.1.3 Corrosiveness and Irritation

In guideline studies (OECD 404) 2-diethylaminoethanol was corrosive to the skin of rabbits after both occlusive and semi-occlusive 4 hour applications (BASF AG, 1982 and Potokar et al., 1985).

Several studies were available that examined irritation to the eye. They are difficult to assess since they did not follow guideline conditions, but they demonstrate that 2-diethylaminoethanol has the potential of being severely irritating to the eyes, or could cause serious damage to the eyes (e.g. in

one study, 50 µl of the undiluted liquid was applied to the eye, and irreversible damage to corneal tissue was observed [staphyloma], as well as corrosion of the conjunctiva and eyelids; these finding were also not reversible after 8 days; BASF AG, 1969)

Conclusion

2-Diethylaminoethanol was corrosive to the skin of rabbits. Since its pH value was measured to be 11.5 (100 g/l) at 20 °C, these corrosive effects are not surprising. The potential for severe damage to occur to the eyes can be expected based on the animal studies available and on the pH.

3.1.4 Sensitisation

2-Diethylaminoethanol was tested for skin sensitization in guinea pigs using the method of Draize (TSCATS, 2/13/84) and the method of Magnusson and Kligman (Leung and Blaszcak, 1998; Nakamura et al., 1994) and was reported to be negative in all three studies. Taking all 3 studies into consideration, none of the 70 2-diethylaminoethanol-induced animals showed signs of sensitization when challenged with 2-diethylaminoethanol.

Conclusion

2-Diethylaminoethanol was not sensitizing to the skin of guinea pigs.

3.1.5 Repeated Dose Toxicity

A well documented 14 week inhalation study was available. In this study, 20 rats/dose/sex were exposed to 0, 11, 25 or 76 ppm (0, 0.053, 0.120 and 0.365 mg/l; or 0, 53, 120 and 365 mg/m3) of 2-diethylaminoethanol for 6 h/day, 5 days/week for 14 weeks using a whole body exposure method (Hinz et al., 1992; Exxon, 1990) and are comparable to ca. 13, 29 and 88 mg/kg bw per day doses assuming 100 % lung deposition and absorption. These concentrations were chosen based on a 2 week study. Half of the animals were terminated at the end of 14 week. Neurologic exams were preformed monthly using a modified Irwin Screen (Psychopharmacology, 13, 222-257, 1968) during the exposure period. The remaining animals were given a four week post-exposure recovery period prior to sacrifice. Full histological exams which included the gonads were conducted in the high dose group, but in the low and middle dose groups only the nasal cavity/turbinates (4 sections) were evaluated. No animals died as a result of exposure to 2-diethylaminoethanol. During exposure, dose-dependent transient signs of mild to moderate respiratory irritation (noises or rales) were noted. They usually cleared within one hour after exposure. In the high dose group, some animals continued to exhibit these signs overnight. Nasal discharge was observed at the beginning of the study, but this subsided as the study progressed. Corneal opacities were observed in control and 2-diethylaminoethanol-treated animals. According to the authors aging F344 rats are genetically predisposed toward developing corneal lesions. Prolonged exposure to an alkaline compound such as 2-diethylaminoethanol could have accelerated an underlying predisposition toward corneal dystrophy. Since the opacity was thought to be due to a calcium precipitate, this problem may have also been exacerbated by the high vitamin D diet which would increase calcium absorption. In this regard, all rats in the high dose group had corneal opacities after 1 month of exposure, and most rats in the middle group had developed them by 2 months. By the end of the study all rats were confirmed to have corneal opacity. No outstanding effects on blood chemistry, urinalysis or neurobehavioural parameters were observed. Through the first 7 weeks of exposure the high dose group had a slight, but statistically significant decrease in body weight gain as compared to controls. Subsequently, the rate of growth paralleled the other groups, but the initial decrement was never regained. Mean body weights of the high concentration group never decreased more than about 7 % from the controls. At week 14 there was a slight, but statistically significant increase in

the male liver and kidney weights in the high dose group (8.0 and 7.1 % resp.), but histologic changes were not associated with these findings. Histomorphologic changes in nerve tissues were not observed. The low dose group was free of exposure-related histologic changes in the nasal cavities and turbinates, but changes were noted in the middle and high dose groups sacrificed in the 14th week of exposure [45 % (50 % M, 40 % F) incidence in the middle and 95 % (90 % M, 100 % F) in the high concentration group]. These changes consisted of an increased incidence and severity of focal hyperplasias alone or in association with squamous metaplasia of the respiratory epithelium, and multi-focal mixed infiltrations of inflammatory cells in the nasal mucosa. These changes were most evident in the anterior sections of the nasoturbinates and on the lateral wall of the nasal cavity. In the high dose group hypertrophic goblet cells were seen in the nasal septum, along with a low incidence of focal necrosis and exudate in the lumen of the nasal cavity. The findings in the middle and high dose groups after the 4 week recovery period were similar to those seen in the 14 week rats, however, the incidence of focal hyperplasia with squamous metaplasia was decreased. The incidence of focal hyperplasia alone, infiltrations of inflammatory cells and goblet cell hypertrophy were comparable to what was noted at 14 weeks.

Summary: This study indicated that 2-diethylaminoethanol lacked systemic toxic properties, and the point of contact was the site of action, namely, the upper respiratory tract and the eyes. Since no systemic toxicological effects were observed, the No Observed [Adverse] Effect Concentration (NO[A]EC) for systemic toxicity was 0.365 mg/l (365 mg/m^3, 76 ppm), which was the highest dose tested. The NO[A]EC for local toxicity, based on the lack of an effect observed in the nasal cavity was 0.053 mg/l (53 mg/m^3 or 11 ppm, rounded off to 10 ppm). The noises or rales at this concentration can be considered an adaptive effect, but not an adverse effect, since no histological changes were observed at this concentration. However, since an effect was seen at the lowest concentration, a NOEC was not reached. The Lowest Observed [Adverse] Effect Concentration (LO[A]EC) was the first dose where nasal lesions were observed, namely, 0.12 mg/l (120 mg/m^3 or 25 ppm).

NO[A]EC, rat (inhalation) 14 weeks, systemic tox.: 0.365 mg/l (365 mg/m^3 or 76 ppm)

NO[A]EC, rat (inhalation) 14 weeks, local toxicity: 0.053 mg/l (53 mg/m^3 or 10 ppm)

LO[A]EC, rat (inhalation) 14 weeks, local toxicity: 0.12 mg/l (120 mg/m^3 or 25 ppm)

Several repeated dose toxicity studies were performed in the 1960's, but their quality was limited in part due to a lack of detail or poor design. In one of these studies (TSCATS, 8/02/90), rats were fed 2-diethylaminoethanol-HCl at doses of 200, 500 and 1000 (10,000) ppm of the free base (i.e. ca. 11, 25, 50-400 mg/kg bw/day, respectively) for 2 years. The high dose group was progressively increased to 10,000 ppm (ca. 400 mg/kg/d). For 2-diethylaminoethanol treatment 35 rats/sex/group were used, and in the control there were 60 rats/sex/group. Males were reported to have low incidences of testicular atrophy, namely 0/34 (0 %), 3/18 (17 %), 2/17 (12 %) and 4/15 (27 %) in the control, 200 ppm, 500 ppm and 1000 (10,000) ppm dose groups, respectively. The atrophy sometimes occurred bilaterally. This finding was considered insignificant for the following reasons:

1) It was not dose-dependent;

2) Similar findings were not seen in 6 month old males (a more appropriate time point to assess the induction of gonadal lesions), and only one case was seen in 12 month old males (200 ppm dose group) from the same study;

3) It is not an unusual finding in aging rats (Glaister, 1986);

4) Anorexia was also reported in this study, but data on individual animal weight was not given except at the final sacrifice. Thus, anorexia could have been a / the causative factor for testicular atrophy. Furthermore, in the last 12 weeks of the study, the high dose male body

weight was on average 8.6% lower that the controls, and the terminal body weight of this group was significantly (11 %, $p < 0.05$) lower than controls;

5) And finally, the historical control data for testicular atrophy in Charles River albino rats was not available, but based on a comment by the sponsor, similar incidences were reported in control animals. No historical control data from the 1960s was available. But, in a study conducted nearly 35 years later, it was reported that the incidence of testicular atrophy found in control 31 week old Charles River CrJ: (SD) rats was 20 % (Sugimoto et al., 2000). According to Charles River, the type of rat used in the 1960s was probably a Sprague-Dawley (personal communication, P.A. Mirley, 24 June 2002).

Thus, the testicular finding in this study with 2 year old Charles River albino rats is not surprising. The lack of a finding in the 34 control males in this could most likely be a result of the randomness of the group assignments.

Another study was conducted with dogs in the 1960s in which 2-diethylaminoethanol-HCl was given via feed at doses of ca. 20, 40, 200 (80) and 400 mg 2-diethylaminoethanol/kg/day, [i.e. 500, 1000, 5000 (2000) and 10000 ppm] (TSCATS, 8/02/90). According to the report, "weakness, tremors, convulsions and ataxia" were observed, however, this occurred at doses where animals were dying, namely at 5000(2000) and 10000 ppm. In a lower dose (1000 ppm based on the free base) "tremors and/or shaking of the head from side to side" were described. This data is difficult to assess due to the limited nature of the report. Furthermore, in the 2 year study in rats already mentioned, no such findings were seen in rats treated with similar doses. Cerebellar changes were observed in all males and one female of the 5000 (2000) ppm dose group.

In another study with rats, they were given 2-diethylaminoethanol neutralized with HCl via drinking water for up to six months at doses resulting in 2-diethylaminoethanol levels of ca. 150 and 300 mg/kg bw/day (Cornish, 1965). No significant adverse changes were observed, although a slight increase in kidney weight was described in both 2-diethylaminoethanol-treated groups, and decreased body weight was seen in the high dose group.

Conclusion

Repeated exposure of rats to 2-diethylaminoethanol vapors (up to 0.365 mg/l) for 14 weeks caused local toxicity (irritation) at the site of contact, namely, the upper respiratory tract and the eyes; however, systemic toxicity was not observed (NOAEC, systemic toxicity, 0.365 mg/l; i.e. 365 mg/m^3 or 76 ppm). After inhalation exposure, the main finding described was respiratory irritation which led to noises called rales and irritation of the eyes. The LOAEC for local toxicity (irritation) to the respiratory tract was 0.120 mg/l (120 mg/m^3 or 25 ppm). The NOAEC for local toxicity was 0.053 mg/l (53 mg/m^3 or 10 ppm) based on a lack of histopathological effects in the nasal cavity at this dose. However, since an effect (rales) was seen at the lowest concentration a NOEC was not reached.

3.1.6 Mutagenicity

In vitro Studies

2-Diethylaminoethanol was tested at doses of up to 5000 µg/plate in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538, both with and without metabolic activation using guideline and non-guideline conditions and consistently yielded negative results (BASF AG, 1989; Life Science Research, 1991a; Zeiger et al, 1987). In a guideline assay using the HPRT locus of V79 Chinese hamster cells, no evidence for mutagenic activity was seen when tested up to 3500 µg/ml (Life Science Research, 1991b). It was also negative in a DNA damage test using *E. coli* which used doses up to 3500 µg/ml (Life Science Research, 1991c).

In vivo Studies

In a detailed and well conducted study 2-diethylaminoethanol was tested for its ability to induce micronuclei in bone marrow erythrocytes in mice using doses up to 500 mg/kg bw under guideline conditions and was found to be negative (Life Science Research, 1991d). The report also indicates that the highest dose tested was adequate since animals showed a hunched posture, piloerection, rales, irregular respiration, a swollen abdomen and one animal was sacrificed *in extremis*. Data from the preliminary test indicated that the test substance can reach the bone marrow.

Conclusion

2-Diethylaminoethanol gave no evidence of *in vitro* mutagenic activity or *in vivo* clastogenic potential.

3.1.7 Carcinogenicity

In a study from the 1960's (TSCATS, 8/02/90) which does not meet the guidelines for carcinogenicity studies of today (see below), rats received 2-diethylaminoethanol-HCl at dietary concentrations of 200, 500 and 1000 (10,000) ppm of the free base (ca. 11, 25, 50-400 mg/kg bw/day, respectively) for two years. The high dose group was progressively increased to 10,000 ppm (ca. 400 mg/kg/d). For the 2-diethylaminoethanol treated groups 35 rats/sex/group were used, and the control group consisted of 60 rats/sex. Ten animals/sex from controls and the high dose group were examined histologically at the end of the 2 years. The following tumors were seen in the fourty animals which were examined completely: pituitary adenomas in 9 animals each in the control and high dose group group; mammary gland fibromas, adenomes or fibroadenomes in 8 control and 4 high dose group females; miscellaneous tumors which included one ganglioneuroma, one pheochromocytoma and two renal embryomas in the control group; adrenal cortical adenomas in one control and three high dose group females; and one pancreatic duct adenoma, one hepatoma and three granulosa cell tumors in the high dose group. Regarding the limitations of the study, in the 1960s international guidelines for cancer studies were not available. Even so, the following limitations should be noted: the number of animals was low, a maximum tolerated dose was not achieved and the rational for the doses chosen was not given.

Conclusion

2-Diethylaminoethanol was not carcinogenic to rats by feed in a limited 2-year study from the 1960s. While this data is limited, the lack of a carcinogenic effect of 2-diethylaminoethanol is supported by the negative data for genotoxicity.

3.1.8 Toxicity for Reproduction

Studies specifically designed to assess reproductive toxicity were not available for an assessment. However, an investigation of changes in the weight and/or morphology of the reproductive organs in a repeated dose toxicity studies can also be used to assess reproductive toxicity. Typically, a 28 day or 90 day study can be used for such an assessment (ECETOC, 2002). Several repeated dose studies were available for 2-diethylaminoethanol (see section 3.2.4); however, the best documented and most appropriate study was a 14 week repeated dose toxicity study which performed gonadal examinations.

In a range finding study for the 14 week inhalation study detailed in section 3.2.4, rats were exposed to 301 ppm (1.44 mg/l or 1440 mg/m^3) of 2-diethylaminoethanol for 9 days, 6 h/day over a 2 week period (Hinz et al., 1992). At this concentration animals lost weight throughout the study

and a high rate of mortality occurred. In addition, undersized spleens, thymuses and gonads were reported in the surviving animals. This effect on the gonads should be considered as the result of secondary toxicity, given that mortality also occurred at this dose. In the main study (see section 3.2.4 for details), i.e. the 14 week inhalation study, the testes were weighed prior to fixation and epididymides, testes and ovaries were prepared and stained for histopathological assessment. No signs of gonadal toxicity were observed in either sex (Hinz et al., 1992). Since no effects on the gonads were noted at the highest concentration tested in the 14 week study (the two lower concentrations were not examined), the NO[A]EC for gonadal toxicity was the highest concentration tested, i.e. 0.365 mg/l (365 mg/m^3, i.e. 76 ppm, or ca. 88 mg/kg/day assuming 100 % lung deposition and absorption).

In an older 2 year feed study in rats (see section 3.2.4 for details) a low incidence of gonadal degeneration was reported, but only (with one exception) in 2 year old males with an incidence of 0/34 (0 %), 3/18 (17 %), 2/17 (12 %) and 4/15 (27 %) in the 0, 200, 500 and 1000 (10,000) ppm dose groups (TSCATS, 8/02/90). Unilateral and bilateral cases were seen. Since testicular atrophy is not an unusual finding in aging rats (Glaister 1986), and since there was not a clear dose-dependency in their occurrence, these results were not considered to be substance-related. Furthermore, during the time frame where the model is suitable for detecting testicular toxicity, no changes were observed (see also discussion in section 3.2.4).

Conclusion

Based on the results of a well-documented 14 week animal study, the inhalation of 365 mg/m^3 (76 ppm) 2-diethylaminoethanol did not cause any adverse effects on the reproductive organs in rats. This data suggests that 2-diethylaminoethanol does not cause any adverse effects on the reproductive system under the conditions tested.

3.1.9 Developmental Toxicity/Teratogenicity

In a guideline-like study, pregnant rats were exposed to vapors of 2-diethylaminoethanol at concentrations of 0, 33, 66 and 100 ppm (i.e. 0.160, 0.320 and 0.486 mg/l; or 0, 160, 320 and 486 mg/m^3) for 6 h/day on gestational days (GD) 6 - 15, and then the dams were sacrificed on GD 21 (Exxon, 1991; Leung and Murphy, 1998). These concentrations are comparable to ca. 38, 76 and 116 mg/kg bw per day doses, assuming 100 % lung deposition and absorption. The doses were chosen based on toxicity observed in a range finding study. No deaths were observed in the study. Maternal toxicity was seen in the high dose group and included reduced body weight (6 %) on GD day 15 and reduced body weight gain (52 %) during the entire exposure period (GD 6 - 15). Dry rales were observed in up to one third of the animals over GD 11 to 21 in the high dose group. Decreased body weight gain was also observed in the middle dose group during GD 12 to 15. Statistically significant ($p < 0.01$) decreases in maternal food consumption were observed during the exposure period in the middle and high dose group and during the post-exposure period in the high dose group. No treatment-related effects were observed in gestational parameters, including pre- and post-implantation loss or sex ratio. Mean fetal body weights in the treated groups were similar to control. There was no increase in the incidence of total malformations (external, visceral, or skeletal) or individually by category. The incidence of a single developmental variation (hypoplastic bones of the forepaw) was significantly decreased in the high dose group when compared to control. A statistically significant ($p < 0.05$) increasing dose-trend in the incidence of advanced ossification of the hindpaw was reported (9.7, 9.8, 12.6, 16.9 % control to high concentration group), but it was not significant when analyzed on a per fetus or per litter basis. Since this increased incidence of advanced hindpaw ossification was higher than expected in both treated and control groups compared to the laboratories' historical control range (0 - 2.3 %), this finding was not considered treatment-related or biologically relevant.

The no-observed-adverse-effect concentration (NO[A]EC) for maternal toxicity was 33 ppm and for developmental toxicity the NO[A]EC was 100 ppm.

NO[A]EC, rats, maternal toxicity: 0.160 mg/l (160 mg/m^3; 33 ppm)

NO[A]EC, rats, developmental toxicity: 0.486 mg/l (486 mg/m^3; 100 ppm)

In an embryotoxicity screening study 2-diethylaminoethanol was administered by gavage to 5 pregnant female Crl:CD(SD)Br rats/dose at doses of 0, 10, 30, 100 and 250 mg/kg bw on days 0 to 11 of gestation (TSCATS, 11/12/97). The dams were sacrificed on day 12 of gestation. The only treatment-related clinical finding in the study was rales at the 250 mg/kg bw dose, indicating that a highly irritating dose was achieved. No internal findings were seen macroscopically. Body weights, body weight gain, food consumption and liver and kidney weights were not effected by treatment. No treatment-related microscopic findings were seen in the liver and kidneys of the 250 mg/kg dose group. In the 250 mg/kg bw dose group post implantation loss was increased by 16.6 % (S.D. 20.90), and the number of viable embryos was decreased by 15 % (83.4 % in the 250 mg/kg group versus 98.6 % in controls). The increase in postimplantation loss and the decrease in live litter size in this group was predominantly due to one female with nine early resorptions (52.9 %). Intrauterine parameters were unaffected by treatment in the 10, 30 and 100 mg/kg dose groups. According to the report, the NOEL was 100 mg/kg bw for maternal toxicity and embryotoxicity. The basis for this was the observation of rales in 2/5 dams of the 250 mg/kg dose and the lack of this finding in the 100 mg/kg dose. Thus, the LOEL for the dams was 250 mg/kg bw. However, it is not clear if a true maternally toxic dose was achieved on the basis of rales. Histologic examinations were limited to the kidneys and liver. Due to the low number of animals in the study, the assignment of clear substance-related embryotoxic effect at 250 mg/kg bw is also difficult since the increase in postimplantation loss and the decrease in live litter size was due to one animal with 9 resorptions.

Conclusion:

In pregnant rats even the highest concentration tested of 0.486 mg/l (486 mg/m^3 or 100 ppm), which already produced maternally toxic effects, did not lead to adverse developmental effects.

3.1.10 Experience with human exposure

An odor threshold of 0.011 ppm has been reported (Amoore and Hautala, 1983). A laboratory worker was briefly exposed (approx. 30 sec.) to approx. 100 ppm 2-diethylaminoethanol, which caused nausea and vomiting. No irritation of eyes or throat was noted. (Cornish, 1965). Subjects exposed to 2-diethylaminoethanol vapor by humidified air in office buildings complained about eye, nose and throat irritation, dizziness, nausea and vomiting. Also, several cases of asthma were observed (Fannick et al, 1983, Hills and Lushniak, 1989, Gadon et al., 1994); however, the symptoms were more consistent with a reactive airway dysfunction syndrome than with an allergic respiratory reaction. Detectable amounts of 2-diethylaminoethanol were 0.05 and 0.04 mg/m^3. Since 2-diethylaminoethanol has a low vapor pressure and was detected on surfaces, skin contact with surfaces was a possible route of absorption (Fannick et al., 1983).

3.2 Initial Assessment for Human Health

2-Diethylaminoethanol was rapidly absorbed orally. It is presumably absorbed by dermal and inhalation routes of administration. In the rat it was widely distributed to many tissues. It was primarily excreted unchanged via the urine in rats. Excretion via the feces was also observed in rats, but to a lesser extent. Urinary excretion was also reported in humans. The major metabolites in rats were reported to be diethylaminoacetic acid and diethyl-(2-hydroxyethyl)-amino-oxide.

2-Diethylaminoethanol had the following acute toxic effects in mammals:

LD50 rat (oral): 1320 mg/kg bw. The clinical signs reported were described as apathy and dyspnea.

LC50 rat (inhalation): ca. 4600 mg/m^3/4 hour (estimated by Haber's rule). Severe signs of irritation were observed, e.g. mucous membrane irritation and dyspnoea.

LD50 guinea pig (dermal): ca. 885 mg/kg bw [LD50 rabbit (dermal): ca. 1100 mg/kg bw, only available as a secondary citation]

2-Diethylaminoethanol was corrosive to the skin of rabbits. Since the pH was measured to be 11.5 (100 g/l) at 20°C, the corrosive effects are not surprising. The potential for severe damage to the eyes can be expected based on the animal studies available and on the pH.

2-Diethylaminoethanol was not sensitizing to the skin in studies with guinea pigs.

Repeated exposure to 2-diethylaminoethanol vapors up to 365 mg/m^3 for 14 weeks caused local toxicity (irritation) at the site of contact in rats, namely, in the upper respiratory tract and the eyes.

This study indicated that 2-diethylaminoethanol lacked systemic toxic properties up to 365 mg/m^3. Since no systemic toxicological effects were observed, the NO[A]EC for systemic toxicity was the highest dose tested, i.e. 0.365 mg/l (76 ppm, or 365 mg/m^3). The NO[A]EC for local toxicity, based on the lack of observed effects in the nasal cavity/turbinates, was 0.053 mg/l (11 ppm, rounded off to 10 ppm, or 53 mg/m^3). A NOEC could not be derived since respiratory noises (rales) were observed in all concentration groups.

2-Diethylaminoethanol gave no evidence for *in vitro* mutagenic activity or *in vivo* clastogenic potential.

Based on the results of a well-documented animal study, 2-diethylaminoethanol did not cause any adverse effects on the reproductive organs of rats when administered by inhalation at concentrations of up to 365 mg/m^3 (0. 365 mg/l or 76 ppm) for 14 weeks.

In pregnant rats even the highest concentration tested of 0.486 mg/l (486 mg/m^3 or 100 ppm), which already produced maternally toxic effects, did not lead to adverse developmental effects.

2-Diethylaminoethanol was not carcinogenic to rats when given by feed for 2 years in a limited 1960's study (tested up to ca. 50 – 400 mg/kg/d). While this data is limited, the lack of a carcinogenic effect of 2-diethylaminoethanol is supported by the negative data for genotoxicity.

An odor threshold of 0.011 ppm (approx. 0.053 mg/m^3) has been reported. In a laboratory worker short-time exposure to approx. 100 ppm (480 mg/m^3) 2-diethylaminoethanol caused nausea and vomiting. Subjects exposed to 2-diethylaminoethanol vapor by humidified air in office buildings complained about eye, nose and throat irritation, dizziness, nausea and vomiting. Also several cases of asthma were observed; however, the symptoms were more consistent with a reactive airway dysfunction syndrome than with an allergic respiratory reaction. In one case detectable amounts of 2-diethylaminoethanol were 0.05 and 0.04 mg/m^3.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

The most sensitive studies available were considered to evaluate the aquatic toxicity of 2-diethylaminoethanol.

Acute Toxicity Test Results

Fish

In a study with *Leuciscus idus*, following the German DIN 38 412, 4 concentrations, from 100 - 1000 mg/l (nominal) plus control and pH adjusted 1000 mg/l group, were tested. An LC50 (96 h) of 147 mg/l (nominal; geometric mean of LC_0 at 100 mg/l and LC100 at 215 mg/l) was calculated. The toxic effect may be, in part, due to the high pH of the non-neutralized test solutions, since the pH adjusted 1000 mg/l concentration group tolerated the substance for 96 h without mortality (BASF AG, 1987). This assumption is also confirmed by the result of other fish tests. Geiger et al. (1986) found a LC50 (96 h) of 1780 mg/l (measured) for *Pimephales promelas* exposed in a flow-through system. The pH of the test solution was adjusted to that of lake water with HCl.

Invertebrates

A test following Directive 79/831/EEC, C2 with Daphnia magna with 7 nominal concentrations ranging from 7.8 – 1000 mg/l, resulted in an EC50 (48 h, immobilisation) of 83.6 mg/l (BASF AG, 1988a). As the pH value at the concentration at which immobilization of the daphnids occurred was in the range of 8.6 to 10.7 it cannot be excluded that the toxicity was in part due to pH effects. This fact could be confirmed by a further study with *Daphnia magna* (Atofina, 1993) where an EC50 (48 h) of 165 mg/l was found using pH adjusted test solutions.

Algae

Acute Toxicity to Scenedesmus subspicatus was determined in a study following DIN 38 412 part 9, with 7 nominal concentrations ranging from 2-320 mg/l. The E_rC_{50} for growth rate (72 h) was 44 mg/l and the NOEC 5 mg/l; corresponding values for the endpoint biomass were 30 mg/l and 5 mg/l respectively (BASF AG, 1988b). As the reported pH of the test solutions was in the range of 7 to 8.5 it can be concluded that the observed effects are due to the inherent toxicity of the test substance itself and not due to pH effects.

Chronic Toxicity Test Results

No chronic aquatic toxicity data are available.

Toxicity to Microorganisms

The EC_{20} (30 min) for inhibition of the respiration of activated sludge (domestic) was >1000 mg/l (nominal concentration; BASF AG, 1994b).

4.2 Terrestrial Effects

In a study with the terrestrial plant *Chrysanthemum morifolium* cultivar "Indianapolis white" an EC_{50} (22 d, nominal concentration) of 0.12 mg/l in the nutrient solution for the endpoint chlorosis was obtained (Horst et al., 1983).

4.3 Initial Assessment for the Environment

Distribution modeling predicts water to be the main target compartment for 2-diethylaminoethanol. The substance tends not to accumulate in biota (log Kow = 0.21, measured). The calculated log Koc of 0.78 suggests that adsorption to suspended solids is not to be expected. From the pKa-value of 9.87 it can be assumed that under environmental conditions the substance is available as cation. Therefore, binding of the substance to the matrix of soils with high capacities for cation exchange (e.g. clay) cannot be excluded. However, no data was available for ionic-ionic interactions in soil. 2-Diethylaminoethanol was readily biodegradable in a test conducted according to OECD 301 A with domestic sludge (95 % degradation after 22 days, 10d-window was fulfilled). Based on the chemical structure of the substance hydrolysis is not likely to occur. 2-Diethylaminoethanol entering the atmosphere is rapidly degraded by reaction with photochemically produced hydroxyl radicals ($t_{1/2}$ = 3.9 h).

The following aquatic effect concentrations are available:

Leuciscus idus LC50 (96 h) = 147 mg/l (nominal concentration).The toxic effect may be (partly) due to the high pH of the non-neutralized test solutions, since the pH adjusted 1000 mg/l dose group tolerated the substance for 96 h without mortality.

Pimephales promelas LC50 (96 h) = 1780 mg/l (measured concentration, adjustment of pH).

Daphnia magna: EC50 (48 h) = 83.6 mg/l (nominal concentration) (toxicity due to pH effects cannot be excluded).

Daphnia magna: EC50 (48 h) = 165 mg/l (nominal concentration, adjustment of pH)

Scenedesmus subspicatus: ErC50 (72 h) = 44 mg/l, EbC50 (72 h) = 30 mg/l, NOEC = 5 mg/l for both endpoints.

Compared to daphnia and fish, aquatic plants are most sensitive to 2-ethylaminoethanol.

Using the aquatic toxic effect on the most sensitive species, *Scenedesmus subspicatus*, for the endpoint growth rate, a $PNEC_{aqua}$ of 44 µg/l is derived by applying an assessment factor of 1000.

No PNECsoil can be derived from the available terrestrial study with *Chrysanthemum* as no soil concentration is given (EC50 (22 d) = 0.12 mg/l; chlorosis).

5 RECOMMENDATIONS

Human Health:

The chemical is currently of low priority for further work. Due to the corrosive potential, exposure to humans at the workplace and from consumer products has been regulated in the sponsor country. However, if this is not the case in other countries, further exposure assessment and, if necessary, risk assessment are recommended.

Environment:

The chemical is currently of low priority for further work. In addition to its use as chemical intermediate European product registers indicate a wide dispersive use of 2-diethylaminoethanol. No information is available about the total production volume and about total environmental releases. However, the low aquatic toxicity, the low bioaccumulation potential and the ready biodegradability lead to the recommendation that the chemical is currently of low priority for further work.

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ANNEX I

Details of the literature search used

The data bases searched are indicated below.

Toxicology: **Date of last literature search: June 24, 2002**

JETOC
RTECS
AGRICOLA
CABA
CANCERLIT
TOXCENTER
TOXLINE
JICST-EPLUS
LIFESCI
TOXLIT
EMBASE
ESBIOBASE
EMBAL
HEALSAFE
CSNB
MEDLINE
IRIS
ATSDR TOX. PROFILES
ATSDR TOX: FAQS
CHEMFINDER
CIVS
GESTIS
GINC
NICNAS
NTP

Ecology: Date of last literature search: 21June 2002

AQUASCI
BIOSIS
EMBASE
ESBIOBASE
LIFESCI
OCEAN
POLLUAB
SCISEARCH
TOXCENTER
TOXLINE
ULIDAT
DATALOG
CHEMFATE
BIODEG
AQUIRE
HSDB

I U C L I D Data Set

Existing Chemical ID: 100-37-8
CAS No. 100-37-8
EINECS Name 2-diethylaminoethanol
EC No. 202-845-2
Index number 603-048-00-6
Molecular Formula C6H15NO

Producer Related Part
Company: BASF AG
Creation date: 12-NOV-1992

Substance Related Part
Company: BASF AG
Creation date: 12-NOV-1992

Memo: master

Printing date: 07-MAR-2003
Revision date:
Date of last Update: **06-MAR-2003**

Number of Pages: **116**

Chapter (profile): Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile): Reliability: without reliability, 1, 2, 3, 4
Flags (profile): Flags: without flag, SIDS

1.0.1 Applicant and Company Information

Type: lead organisation
Name: BASF AG
Contact Person: Product Safety **Date:**
c/o Dr. Hubert Lendle
GUP/CL - Z570
Street: Carl-Bosch-Str.
Town: 67056 Ludwigshafen
Country: Germany
Phone: +49 621 60 44712
Telefax: +49 621 60 58043
Email: hubert.lendle@basf-ag.de
Homepage: www.basf.com

Flag: Critical study for SIDS endpoint
24-JUN-2002

Type: cooperating company
Name: Air products and Chemicals Inc.
Country: United States

Flag: Critical study for SIDS endpoint
24-JUN-2002

Type: cooperating company
Name: Atofina Chemicals Inc.
Country: United States

Flag: Critical study for SIDS endpoint
24-JUN-2002

Type: cooperating company
Name: DOW Chemical Company
Country: United States

Flag: Critical study for SIDS endpoint
24-JUN-2002

Type: other: cooperating organisation
Name: The Amines HPV Panel of the American Chemistry Council
Country: United States

Flag: Critical study for SIDS endpoint
24-JUN-2002

1.0.2 Location of Production Site, Importer or Formulator

1.0.3 Identity of Recipients

1.0.4 Details on Category/Template

1.1.0 Substance Identification

Mol. Formula: C6 H15 N O
Mol. Weight: 117.19 g/mol

Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002

1.1.1 General Substance Information

Substance type: organic
Physical status: liquid
Purity: >= 99.5 - % w/w
Colour: colourless - faint yellow
Odour: amine - like

Method: GC
Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (1)

1.1.2 Spectra

1.2 Synonyms and Tradenames

(2-Hydroxyethyl)diethylamine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

(Diethylamino)ethanol

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

beta.-(Diethylamino)ethanol

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

2-(Diethylamino)ethanol

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

2-(Diethylamino)ethyl alcohol

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

2-(N,N-Diethylamino)ethanol

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

2-Hydroxytriethylamine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

DEAE

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

Diethyl(2-hydroxyethyl)amine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

Diethylethanolamin

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

Diethylethanolamine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

Diethylmonoethanolamine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

Ethanol, 2-(diethylamino)- (8CI, 9CI)

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

MKS

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

N,N-Diethyl-2-aminoethanol

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

N,N-Diethyl-2-hydroxyethylamine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

N,N-Diethyl-N-(.beta.-hydroxyethyl)amine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

N,N-Diethylethanolamine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

N,N-Diethylmonoethanolamine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

N-(2-Hydroxyethyl)diethylamine

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

Pennad 150

Flag: non confidential, Critical study for SIDS endpoint
02-DEC-1992

1.3 Impurities

CAS-No: 7732-18-5
EC-No: 231-791-2
EINECS-Name: water
Mol. Formula: H2 O
Contents: <= .2 - % w/w

Method: DIN 51777
Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (1)

1.4 Additives

1.5 Total Quantity

Remark: Quantity produced

> 1000 t/a in Germany 2000
Flag: Critical study for SIDS endpoint
13-JAN-2003

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: (C) corrosive
Specific limits: no
R-Phrases: (10) Flammable
(34) Causes burns
(20/21/22) Harmful by inhalation, in contact with skin and if swallowed
S-Phrases: (25) Avoid contact with eyes
(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)

Flag: non confidential, Critical study for SIDS endpoint
23-OCT-2001 (2)

1.6.2 Classification

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

Flag: non confidential, Critical study for SIDS endpoint
23-OCT-2001 (2)

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

Flag: non confidential, Critical study for SIDS endpoint
23-OCT-2001 (2)

Classified: as in Directive 67/548/EEC
Class of danger: harmful
R-Phrases: (20/21/22) Harmful by inhalation, in contact with skin and if swallowed

Flag: non confidential, Critical study for SIDS endpoint
23-OCT-2001 (2)

1.6.3 Packaging

1.7 Use Pattern

Type: industrial
Category: Polymers industry

Remark: used as a catalyst in the synthesis of polymers
Flag: non confidential, Critical study for SIDS endpoint
05-OCT-2001

Type: use
Category: pH-regulating agents

Remark: pH stabilizer
Flag: non confidential, Critical study for SIDS endpoint
05-OCT-2001

Type: use
Category: Pharmaceuticals

Remark: used in the synthesis of drugs
Flag: non confidential, Critical study for SIDS endpoint
05-OCT-2001

1.7.1 Detailed Use Pattern

1.7.2 Methods of Manufacture

Orig. of Subst.: Synthesis
Type: Production

Remark: 2-diethylaminoethanol is produced by the thermal reaction of diethylamine with ethylenoxide.
Flag: non confidential, Critical study for SIDS endpoint
27-FEB-2003

1.8 Regulatory Measures

1.8.1 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value: 5 ml/m3

Flag: non confidential, Critical study for SIDS endpoint
05-AUG-2002 (3)

Type of limit: MAK (DE)
Limit value: 24 mg/m3

Remark: cutaneous resorption
Exceeding factor: 1
Flag: non confidential, Critical study for SIDS endpoint
05-AUG-2002 (3)

Type of limit: TLV (US)
Limit value: 9.6 mg/m3

Remark: equal to 2 ppm
Flag: non confidential, Critical study for SIDS endpoint
05-AUG-2002 (1)

1.8.2 Acceptable Residues Levels

1.8.3 Water Pollution

Classified by: other: VwVwS (Germany) of 17.05.1999, Annex 2
Labelled by: other: VwVwS (Germany) of 17.05.1999, Annex 2
Class of danger: 1 (weakly water polluting)

Remark: Identification number: 1288
Flag: non confidential, Critical study for SIDS endpoint
03-JUL-2002 (4)

1.8.4 Major Accident Hazards

1.8.5 Air Pollution

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

Flag: non confidential, Critical study for SIDS endpoint
23-FEB-2001 (1)

1.8.6 Listings e.g. Chemical Inventories

Type: EINECS
Additional Info: EINECS No. 202-845-2

Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (5)

Type: ENCS
Additional Info: ENCS No. 2-297X

Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (5)

Type: ECL
Additional Info: ECL Serial No. KE-20903

Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (5)

Type: other: SWISS
Additional Info: SWISS No. G-1873

Remark: SWISS classification:
Giftliste 1 (List of Toxic Substances 1), 31 May 1999
Toxic Category 4: Acute oral lethal dose of 500 - 2000 mg/kg.
Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (5)

Type: TSCA

Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (5)

Type: DSL

Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (5)

Type: AICS

Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (5)

Type: PICCS

Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (5)

1.9.1 Degradation/Transformation Products

1.9.2 Components

1.10 Source of Exposure

1.11 Additional Remarks

Memo: Hazardous reactions: Exothermic reaction with acids

Flag: non confidential, Critical study for SIDS endpoint
24-JUN-2002 (1)

1.12 Last Literature Search

Type of Search: External

Remark: date of last literature search:
- toxicology: 24 June 2002
- ecology/environment: 21 June 2002

Flag: Critical study for SIDS endpoint
02-JUL-2002

Type of Search: Internal and External
Chapters covered: 3, 4, 5
Date of Search: 13-NOV-2002

Remark: update 2003, no new data found
13-JAN-2003

Type of Search: Internal and External
Chapters covered: 5.10
Date of Search: 06-NOV-2002

06-FEB-2003

1.13 Reviews

2.1 Melting Point

Value: < -70 degree C

Reliability: (4) not assignable
Manufacturer/producer data without proof
09-MAY-2000 (1)

Value: = -68 degree C

Method: other: measured (test procedure according to an internal BASF standard, comparable to OECD 102)

Remark: reason for flagging this data: experimental derived data
Test substance: 2-diethylethanolamine, purity > 99.5 % (GC)
Reliability: (2) valid with restrictions
scientifically acceptable method
Flag: Critical study for SIDS endpoint
18-NOV-2002 (6) (7)

2.2 Boiling Point

Value: = 161.5 - 163 degree C

Reliability: (4) not assignable
Manufacturer/producer data without proof
09-MAY-2000 (1)

Value: = 162 - 163 degree C at 1013 hPa

Remark: reason for flagging this data: handbook (Beilstein) enjoys a good reputation
Test substance: CAS 100-37-8 (2-diethylaminoethanol), purity not indicated
Reliability: (2) valid with restrictions
data from reliable handbook
Flag: Critical study for SIDS endpoint
02-JUL-2002 (8)

Value: = 162.1 degree C at 1012.96 hPa
Decomposition: no

Method: other: measured using a twin ebulliometric apparatus
Year: 2002
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Water was used in the reference ebulliometer.
T is the condensation temperature of the sample. The pressure p was calculated considering the condensation temperature of the reference substance.
Test substance: N,N-Diethylethanolamine, purity >= 99.95 mol %
Reliability: (2) valid with restrictions
scientifically acceptable method
14-NOV-2002 (9)

Value: = 163 degree C at 1010 hPa

Test substance: CAS 100-37-8 (2-diethylaminoethanol), purity not indicated
Reliability: (4) not assignable
only secondary quotation
15-OCT-2001 (10)

2.3 Density

Value: = .88 - .89 g/cm³ at 20 degree C

Reliability: (4) not assignable
Manufacturer/producer data without proof
09-MAY-2000 (1)

Type: density
Value: = .885 g/cm³ at 20 degree C

Method: other: measured (test procedure according to an internal BASF standard)

Remark: reason for flagging this data: reliable data available on this parameter
Test substance: 2-diethylethanolamine, purity > 99.5 % (GC)
Reliability: (2) valid with restrictions
scientifically acceptable method
Flag: Critical study for SIDS endpoint
18-NOV-2002 (7)

Type: density
Value: = .8809 g/cm³ at 22.9 degree C

Method: other: measured using a high-pressure pycnometer
Year: 1992
GLP: no
Test substance: other TS

Remark: all measurements were done at atmospheric pressure in the present work
Test substance: N,N-Diethylethanolamine, purity 99 %
Reliability: (2) valid with restrictions
scientifically acceptable method
14-NOV-2002 (11)

Type: density
Value: = .8559 g/cm³ at 50 degree C

Method: other: comparable to OECD 109
Year: 2002
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: vibrating tube densimeter
Test substance: N,N-Diethylethanolamine, purity >= 99.95 mol %

Reliability: (2) valid with restrictions
scientifically acceptable method
18-NOV-2002 (9)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: ca. 1.8 hPa at 20 degree C

Method: other (measured): dynamic with nitrogen (test procedure according to an internal BASF standard, comparable to OECD 104)

Remark: reason for flagging this data: experimentally derived data

Result:

temperature (°C)	vapour pressure (hPa)
13.36	1.007
22.40	2.006
28.19	3.004
38.66	5.996
47.10	10.061
67.24	30.046
84.90	70.022
93.30	100.610
122.29	300.400
148.94	700.160
155.71	850.040
161.61	999.910

using the measured set of data and plotting the log of the vapour pressure (in Pascals) against the reciprocal of the temperature (in Kelvins) then drawing in the line of best fit, to give the equation y = -2505.4x + 10.801, were y = vapour pressure (Pa) and x = temperature (K) the vapour pressure at 25°C is ca. 2.5 hPa and at 20°C it is ca. 1.8 hPa

Test substance: 2-diethylethanolamine, purity 99.68 area%

Reliability: (2) valid with restrictions
scientifically acceptable method

Flag: Critical study for SIDS endpoint

18-NOV-2002 (12)

Value: = 1.9 hPa at 20 degree C

Reliability: (4) not assignable
Manufacturer/producer data without proof

09-MAY-2000 (1)

Value: = 2 hPa at 22.4 degree C

Method: other (measured): dynamic with argon (test procedure according to an internal BASF standard, comparable to OECD 104)

Remark: reason for flagging this data: experimentally derived data

Result:

temperature (°C)	vapour pressure (hPa)
22.40	2.00
35.63	5.00
46.93	10.00
59.28	20.00
77.61	50.00
93.43	100.0
111.11	200.0
138.07	500.0

	162.30 1011.5
Test substance:	2-diethylethanolamine, purity 99.7 % (GC)
Reliability:	(2) valid with restrictions scientifically acceptable method
Flag:	Critical study for SIDS endpoint
18-NOV-2002	(13)

Value:	= 20.022 hPa at 59.4 degree C
Decomposition:	no
Method:	other (measured): using a twin ebulliometric apparatus
Year:	2002
GLP:	no
Test substance:	as prescribed by 1.1 - 1.4

Result:

method	temperature (T/K)	vapour pressure (p/kPa)
d	332.500	2.0022
d	346.094	4.0031
d	352.159	5.3331
d	361.220	8.0029
d	368.003	10.6642
d	373.496	13.325
d	379.233	16.669
d	383.986	19.937
d	390.254	25.037
w	390.227	25.011
w	396.546	31.178
w	402.902	38.576
w	409.277	47.366
w	415.709	57.801
w	422.189	70.099
w	428.716	84.517
w	435.281	101.296

Water (w) or n-decane (d) refers to which material was used in the reference ebulliometer.
T is the condensation temperature of the sample. The pressure p was calculated from the condensation temperature of the reference substance.

Test substance:	N,N-Diethylethanolamine, purity >= 99.95 mol %
Reliability:	(2) valid with restrictions scientifically acceptable method
18-NOV-2002	(9)

2.5 Partition Coefficient

Partition Coeff.:	octanol-water
log Pow:	= .047
Method:	other (calculated): computer program KOWWIN v1.66
Remark:	reason for flagging this calculation: model accepted by the US-EPA
Reliability:	(2) valid with restrictions scientifically acceptable method
Flag:	Critical study for SIDS endpoint
23-JUL-2002	(14)

log Pow:	= .05 - .51

Method: other (calculated): different methods

Reliability: (2) valid with restrictions
Calculated value in accordance with generally accepted standard methods
28-FEB-2000 (15)

log Pow: = .21 at 23 degree C

Method: other (measured): following OECD 107
Year: 1987
GLP: no

Method: TS concentration was measured titrimetrically in both phases
Remark: reason for flagging this study: Inspite of using a non-buffered solution the result is comprehensible.
Result:

TS concentration (mol/L) (octanol)	(water)	Pow (1)	log Pow (mean)
0.0266	0.0139	1.628	0.21
0.0309	0.0187	1.655	

(1) = c(oct.)/c(H20)
Test substance: CAS Nr. 100-37-8 (2-diethylaminoethanol), purity 99.1 %
Reliability: (2) valid with restrictions
following guideline with restrictions
Flag: Critical study for SIDS endpoint
04-JUL-2002 (16)

log Pow: = .31 - .46

Reliability: (2) valid with restrictions
data from reliable handbook
03-JUL-2002 (17)

log Pow: = .333

Method: other (calculated): incremental method of Rekker (computer program from CompuDrug Ltd.)
Year: 1989

Reliability: (2) valid with restrictions
Scientifically acceptable method
09-OCT-2001 (18)

log Pow: = .401

Method: other (calculated): computer program CLOGP 3.3

Method: In the article calculated log Pow values were compared with experimentally derived values.
Test substance: CAS 100-37-8 (2-diethylaminoethanol), purity not indicated
Reliability: (2) valid with restrictions
Scientifically acceptable method
23-JUL-2002 (19) (20)

2.6.1 Solubility in different media

Value: at 20 degree C
pH value: 11.5
Conc.: 100 g/l at 20 degree C
Descr.: other: miscible in all proportions

Reliability: (4) not assignable
Manufacturer/producer data without proof.
02-JUL-2002 (1)

pH value: = 12
Conc.: 100 g/l at 20 degree C

Method: other: DIN 19 267

Remark: reason for flagging this data: experimentially derived data
Result: pH values at different concentrations of DEAE:

(wDEAE + (1-w) H20; w= mass proportion)

pH = 11.45 at 20 °C (w = 0.01)
pH = 11.86 at 20 °C (w = 0.05)
pH = 12.03 at 20 °C (w = 0.1)
pH = 12.36 at 20 °C (w = 0.3)
Reliability: (4) not assignable
Secondary quotation. Only test results are cited in the report BRU 85.219, BASF, Physikalisch-chemische Konstanten, 16.12.1985. Original reference (BASF, ZAM/C, J.-No. 306025) is not available
Flag: Critical study for SIDS endpoint
02-JUL-2002 (7)

Remark: reason for flagging this data: important information on this parameter
Result: soluble in all proportions
Test substance: CAS 100-37-8 (2-diethylaminoethanol), purity not indicated
Reliability: (4) not assignable
only secondary quotation
Flag: Critical study for SIDS endpoint
15-OCT-2001 (10)

2.6.2 Surface Tension

Test type: other: capillary method (test procedure according to an internal BASF standard)
Value: = 27.9 mN/m at 20 degree C

Remark: reason for flagging this data: experimentially derived data
Test substance: 2-diethylethanolamine, purity > 99.5 % (GC)
Reliability: (2) valid with restrictions
scientifically acceptable method
Flag: Critical study for SIDS endpoint
18-NOV-2002 (7)

2.7 Flash Point

Value: = 51.5 degree C
Type: closed cup

Method: other: DIN 51 755

Remark: reason for flagging this data: experimentially derived data
Reliability: (1) valid without restriction
National standard specification
Flag: Critical study for SIDS endpoint
09-OCT-2001 (21)

2.8 Auto Flammability

Value: 270 degree C

Method: other: DIN 51 794

Remark: Ignition temperature
reason for flagging this data: experimentially derived data
Reliability: (2) valid with restrictions
National standard specification
Flag: Critical study for SIDS endpoint
24-JUN-2002 (21)

2.9 Flammability

Result: flammable

Remark: reason for flagging this data: only statement available on this parameter
Reliability: (4) not assignable
Manufacturer/producer data without proof
Flag: Critical study for SIDS endpoint
09-OCT-2001 (1)

2.10 Explosive Properties

Result: not explosive

Remark: because of chemical structure
reason for flagging this data: only statement available on this parameter
Reliability: (2) valid with restrictions
Expert judgement
Flag: Critical study for SIDS endpoint
09-OCT-2001 (22)

2.11 Oxidizing Properties

Result: no oxidizing properties

Remark: because of chemical structure
reason for flagging this data: only statement available on this parameter

Reliability: (2) valid with restrictions
Expert judgement

Flag: Critical study for SIDS endpoint
09-OCT-2001 (22)

2.12 Dissociation Constant

Acid-base Const.: pKa = 9.87

Method: other
GLP: no data

Remark: reason for flagging this data: only information available on this parameter
Test substance: CAS 100-37-8 (2-diethylaminoethanol), purity not indicated
Reliability: (4) not assignable
only secondary quotion
Flag: Critical study for SIDS endpoint
10-OCT-2002 (23)

2.13 Viscosity

Value: = 4.6 mPa s (dynamic) at 25 degree C

Reliability: (4) not assignable
Manufacturer/producer data without proof
23-JUL-2002 (1)

Test type: Capillary Method
Value: = 4.496 mPa s (dynamic) at 22.2 degree C

Method: other: similar OECD 114
GLP: no
Test substance: other TS

Method: Kinematic viscosities were measured using calibrated Cannon-Ubbelohde capillary viscometer.
The measured kinematic viscosities were converted to absolute viscosity considering the measured densities
Test substance: N,N-Diethylethanolamine, purity 99 %
Reliability: (2) valid with restrictions
scientifically acceptable method
14-NOV-2002 (11)

2.14 Additional Remarks

Memo: Hygroscopic liquid

Remark: reason for flagging this information: important information on this parameter
Reliability: (4) not assignable
only secondary quotion
Flag: Critical study for SIDS endpoint
10-OCT-2002 (24)

Remark: reason for flagging this data: reliable data available on this parameter
Result: Explosive limits in air: 0.7 vol.% (39 °C) - 10.1 vol.% (92.5 °C)
Reliability: (2) valid with restrictions
test procedure according to internal standard
Flag: Critical study for SIDS endpoint
09-OCT-2001 (21)

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm³
Rate constant: = .0000000000985519 cm³/(molecule * sec)
Degradation: = 50 % after 3.9 hour(s)

Method: other (calculated): AOP v1.87

Remark: reason for flagging this data: only information available on this parameter; model accepted by the US-EPA
Reliability: (2) valid with restrictions
scientifically acceptable method
Flag: Critical study for SIDS endpoint
04-JUL-2002 (25)

3.1.2 Stability in Water

3.1.3 Stability in Soil

3.2.1 Monitoring Data (Environment)

Remark: reason for flagging this information: important information about measured DEAE in industrial effluent discharges even data were evaluated nearly 25 years ago and may not be representative of, or comparable to today´s situation.
Samples of 63 effluent and 22 intake waters were collected from a wide range of chemical manufacturers in areas across the United States. The samples were analyzed for organic compounds (among them DEAE) in an effort to identify previously unknown and potentially hazardous organic pollutants.
Each water sample was preconcentrated for analysis of organic compounds. All sample analyses involved a GC/MS/COMP system that used high-resolution glass capillary GC columns.
Result: - Over 570 compounds were tentatively identified.
- DEAE was analyzed in one sample (compound concentration: >100 µg/L)
Reliability: (2) valid with restrictions
acceptable publication which meets basic scientific principles
Flag: Critical study for SIDS endpoint
16-JUL-2002 (26)

Type of measurement: other

Remark: In 1980, N,N-diethylethanolamine has been detected qualitatively by gas chromatography-mass spectroscopy in the effluent of the publicly-owned treatment works at Decatur (Illinois) in which industrial wastes of different origin were discharged.
reason for non-flagging this information: the documentation is insufficient for assessment since the effluent concentration of DEAE is not reported

Reliability: (2) valid with restrictions
scientifically acceptable method
08-JUL-2002 (27)

Type of measurement: other

Remark: Emissions of volatile organic compounds (VOC) from different types of furniture coatings have been investigated by test chamber studies under dynamic conditions:
- test chamber: 1 m³ glass chamber (Salthammer T. and Marutzky R., Kammerverfahren zur Bestimmung der Emissionen organischer Substanzen aus Materialien. In: Bagda E. (ed.). Emissionen aus Beschichtungsstoffen und deren Einfluß auf die Innenraumluft, Renningen, Expert-Verlag, 75-94, 1995)
- temperature: 23 °C
- relative humidity: 45 %
- air exchange rate n: 1.0 h-1 (air velocities: 0.05 m/s - 0.
- loading factor a (surface to volume ratio): 1.0 m²/m³
- samples: 44 furniture samples manufactured under industrial conditions. Samples were placed in the test chamber immediately after production (samples 1-17) and after preconditioning for 20 days at 23°C and 45 % relative humidity (samples 18-44), respectively.

Reason for non flagging this study: the documentation is insufficient for assessment since the chamber concentration or emission rate of DEAE is not reported

Result: 2-diethylethanolamine was identified in 2 samples in the chamber air test, but no chamber concentrations c (µg/m³) or emission rate ER (µg/(h*m²)) are reported in the article

Reliability: (2) valid with restrictions
acceptable publication which meets basic scientific principles
25-JUL-2002 (28)

Type of measurement: other

Remark: DEAE has been used as a corrosion inhibitor since 1979 in the open steam humidification system of the H. F. Johnson Museum at Cornell University. Analysis of air samples from the museum environment were undertaken in January of 1983.
Reason for flagging this information: important information about measured indoor air concentration even data were evaluated nearly 20 years ago and may not be representative of, or comparable to today´s situation.

Result: 14 air samples were collected, 10 at a sampling rate of 0.2 l/min (detection limit: 0.4 mg/m³) and 4 at 1.5 l/min (detection limit: 0.04 mg/m³). DEAE was detected in only 2 air samples in concentrations of 0.05 and 0.04 mg/m³. Residues of condensed DEAE were identified on samples of plastic materials in the museum in concentrations of 30 mg/m². Condensation accumulation was found directly related to time of deposition for airborne concentrations of 0.05 mg/m³.

Reliability: (2) valid with restrictions
acceptable publications, which meet basic scientific principles

Flag: Critical study for SIDS endpoint
25-JUL-2002 (29) (30)

Type of measurement: other

Remark: - During the winter season, buildings are often humidified with steam which may come from a boiler system that is being treated with volatile neutralizing amines to prevent corrosion. In this study, a room at Battelle Columbus Division, in Columbus, OH, was selected as a typical steam-humidified room.
- The Battelle boiler system was treated with a mixture of cyclohexylamine (CAS-No. 108-91-8) and 2-diethylaminoethanol for corrosion control.
- The concentrations of both chemicals were measured in indoor air in the study room.
Reason for flagging this information: important information about measured indoor air concentration even data were evaluated nearly 15 years ago and may not be representative of, or comparable to today´s situation.

Result: - The concentration of DEAE (detection limit: 0.1 ppb) measured in indoor room air during normal operation of the boiler and humidification systems remained very low compared with any established health standards and did not present any hazard to health.
- The average room concentration of DEAE at the average of 42 % relative humidity was about 0.6 ppb (approx. 2.9*10-³ mg/m³).
- At 61 % relative humidity, the average DEAE-concentration was 2.4 ppb (approx. 0.01 mg/m³).
- During the final hour of the monitoring period when the humidifier was shut off, the concentration decayed to ~50 % of the steady-state value at 61 % relative humidity.
- When the humidifier was opened all the way at the end of the study, the concentration of the DEAE increased up to 8.2 ppb (approx. 0.034 mg/m³), the highest value recorded.
- At 61 % relative humidity, the removal rate was 14 µg/s for DEAE.
- The primary fate of the amine that was introduced into room air through steam humidification appears to be removal to surfaces.

Reliability: (2) valid with restrictions
acceptable, well documented study which meets basic scientific principles

Flag: Critical study for SIDS endpoint

25-JUL-2002 (31)

3.2.2 Field Studies

3.3.1 Transport between Environmental Compartments

Type: adsorption
Media: water - soil
Method: other: calculated: PCKOWWIN v1.63

Remark: reason for flagging this data: model accepted by the US-EPA
Result: KOC = 5.979; Log KOC = 0.7767
Reliability: (2) valid with restrictions
scientifically acceptable method
Flag: Critical study for SIDS endpoint

04-JUL-2002 (32)

Type: adsorption
Media: water - soil
Method: other: model calculation

Remark: A soil sorption coefficient Koc = 30.99 (log Koc = 1.49) was estimated on the basis of the regression derived equation (log Koc = 0.544 log Pow + 1.377; log Pow = 0.21)
Reliability: (2) valid with restrictions
scientifically acceptable method
02-JUL-2002 (33) (34)

Type: volatility
Media: water - air
Method: other: estimated value

Remark: a Henry´s law constant (H = 2.51E-4 (hPa*m3/mol)) was estimated on the basis of the equation H= p/S.
S = water-solubility. The water-solubility of 2-diethylaminoethanol is unlimited (S = 1E6 ppm (= 1 m3/m3) respectively S = 7.560372E3 mol/m3).
p = vapour pressure (p = 1.9 hPa)
Reliability: (2) valid with restrictions
scientifically acceptable method
09-OCT-2001 (35)

Type: volatility
Media: water - air
Method: other: calculated: HENRYWIN v3.00

Remark: reason for flagging this data: calculation based on standard calculation program
Result: Henry´s law constant:
H = 3.16E-4 Pa*m3/mol at 25 °C (bond method)
Reliability: (2) valid with restrictions
scientifically acceptable method
Flag: Critical study for SIDS endpoint
02-JUL-2002 (32)

3.3.2 Distribution

Media: air - biota - sediment(s) - soil - water
Method: Calculation according Mackay, Level I

Method: Level I, V 2.11
Remark: calculation is based on the following physical chemical properties of the substance:
H = 0.0251 Pa*m3/mol (20 °C); molecular weight: 117 g/mol;
vapour pressure: 190 Pa; melting point: -68 °C;
water-solubility: 8.8E5 g/m3; log Kow: 0.21
reason for flagging this data: only information available on this endpoint
Result: The calculation is for the uncharged molecule:

air: 0.88 %
water: 99.1 %
soil: 0.01 %
sediment: 0.01 %

Reliability: (2) valid with restrictions
scientifically acceptable method
Flag: Critical study for SIDS endpoint
23-JUL-2002 (32)

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 33 mg/l related to Test substance
20 mg/l related to DOC (Dissolved Organic Carbon)
Contact time: 22 day(s)
Degradation: 95 % after 22 day(s)
Result: readily biodegradable
Kinetic: 7 day(s) 5 %
10 day(s) 82 %
22 day(s) 95 %
Control Subst.: Aniline
Kinetic: 3 day(s) 2 %
5 93 %

Method: OECD Guide-line 301 A (new version) "Ready Biodegradability: DOC Die Away Test"
Year: 1992
GLP: yes
Test substance: other TS: N,N-Diethylethanolamin, purity: 99.5 % (area)

Remark: reason for flagging this study: only reliable test on ready biodegradability available
test device:
- 2 l Erlenmeyer flasks, liquid volume: 1000 ml

incubation:
- on a laboratory shaker, approx. 120 rpm
- temperature: 22 +- 2 °C

number of replicates:
- test substance (TS): 2
- reference substance (RS): 1
- blank (BC): 2
- inhibition control (IH): 1
- assay to examine physico chemical (abiotic) elimination (PC): 1
- adsorption control (AC): 1

inoculum:
- source: activated sludge, domestic (sludge from laboratory wastewater treatment plants fed with municipal sewage)

reference control:
- reference substance: aniline
- concentration: 20 mg/L related to DOC
- kinetic of reference substance: 3 day(s) 2 % DOC-elimin.
7 day(s) 89 % DOC-elimin.

14 day(s) 92 % DOC-elimin.
22 day(s) 96 % DOC-elimin.

inhibition control:
- substances: aniline + test substance
- concentration: aniline: 20 mg/L related to DOC
test subst.: 20 mg/L related to DOC
- kinetic of inhibition control: 3 day(s) 2 % DOC-elimin.
7 day(s) 49 % DOC-elimin.
14 day(s) 96 % DOC-elimin.
22 day(s) 101 % DOC-elimin.

assay to examine physico-chemical (abiotic) elimination:
- concentration: 20 mg/L related to DOC
- w/o inoculum, w mercury chloride to avoid microbial biodegradation
- kinetic of physico-chemical elimination:
1 day(s): -5 % DOC-elimin.
7 day(s): 8 % DOC-elimin.
14 day(s): 1 % DOC-elimin.
22 day(s): -4 % DOC-elimin.

adsorption control:
- concentration: 20 mg/L related to DOC
- w incoulum, w mercury chloride to avoid microbial biodegradation
- kinetic of adsorption control:
1 day (s): -3 % DOC-elimin.
5 day (s): 0 % DOC-elimin.

Result: - duration of the adaption phase (lag-phase): 7 days
- duration of the degradation phase (log-phase): 10 days
- physico-chemical (abiotic) elimination assay: <10 % (DOC) at the end of the test
- adsorption control: < 10 % (DOC) after 5 days
- inhibition assay: 100 % (DOC) after 22 days

Reliability: (1) valid without restriction
guideline study

Flag: Critical study for SIDS endpoint

07-NOV-2002 (36)

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 354 mg/l related to Test substance
200 mg/l related to DOC (Dissolved Organic Carbon)
Contact time: 14 day(s)
Degradation: = 96 % after 14 day(s)
Result: inherently biodegradable
Control Subst.: Diethylene glycol

Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: 1992
GLP: yes
Test substance: other TS: 2-diethylaminoethanol, purity 99.9 %

Method: Test mixture (total volume 1.5 L) containing test substance (354 mg/L <> 200 mg/L DOC), mineral medium and activated sludge from a laboratory wastewater treatment plant treating municipal wastewater (1 g/L) was incubated for 14 days.

The following controls were included:
- Inoculum blanc: control without test substance but with inoculum (1 flask)
- Positive control: diethylene glycol (200 mg/L DOC) with inoculum (1 flask)
- Abiotic control: control with test substance and mercury chloride but without inoculum (1 flask)

Aliquots were removed from the flasks on day 0 (0 and 3 h), 1, 2, 3, 6, 7, 9, 10, 13 and 14 and analyzed for DOC

Remark: Control substance: diethylene glycol. DOC-elimination after 9 days: 99 %
reason for flagging this data: test was performed with non adapted inoculum from municipal wwtp

Result:

time (day)	elimination (% DOC of day 0 values) TS with inoculum	Reference substance	abiotic control
0 (0 h)	0	0	0
0 (3 h)	-5	4	-6
1	-5	8	-4
2	-5	8	-4
3	-1	12	-3
6	-4	98	-6
7	8	100	6
9	38	99	0
10	97		3
13	98		-4
14	96		1

- The sigmoidal shape of the elimination curve is a strong indication on biodegradation
- Test substance was not adsorbed by the sludge
- Adaptation phase: approx. 8 days.
- Biodegradation phase: approx. 2-3 days

Reliability: (1) valid without restriction

GLP-study

Flag: Critical study for SIDS endpoint

23-JUL-2002 (37)

Type: aerobic
Inoculum: other: acclimated sewage sludge enrichment culture

Remark: Rothkopf and Bartha (1984) observed biodegradation of 2-diethylethanolamin. They measured cell growth. Test medium: 0.05 % test substance as C- and N-source. Incubation temperature: 28 °C. Max. protein yield: approximately 175 µl/ml. Conversion factor of 35 % protein yield/2-diethylethanolamin. 70 µg/mL were measured for the test substance in an adapted culture and after an incubation time of one week

Reliability: (2) valid with restrictions
acceptable publication which meets basic scientific principles

02-JUL-2002 (38)

Inoculum: other bacteria: industrial sludge from wwtp of BASF
Degradation: = 100 % after 11 day(s)

Method: other: Modified Zahn-Wellens Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: easily eliminated, mainly by biodegradation
Reliability: (2) valid with restrictions
comparable to guideline study with acceptable restrictions
09-OCT-2001 (39)

02-OCT-2002

3.6 BOD5, COD or BOD5/COD Ratio

Method:
Year:
Method:
Remark: - inoculum:
effluent from industrial wwtp (BASF AG, Ludwigshafen, Germany)

- result:
TOC = 571 mg/g
COD = 760 mg/g
BOD5 = 2 mg/g

BOD5*100/COD: < 1%

- method:
BODx-determination, DEV H DIN 38409, part 51, Deutsche Einheitsverfahren zur Wasser-, Abwasser- und Schlammuntersuchung (determination of biochemical oxygen demand)
Reliability: (2) valid with restrictions
test procedure according to guideline with acceptable restrictions
24-JUN-2002 (39)

Method:
Year:
Method:
Remark: - inoculum:
acclimated microbial seed: a mixed microbial culture capable of using 2-diethylaminoethanol as sole carbon and energy sources was isolated by an enrichment culture technique. Microbial seed for the BOD test was prepared from the culture growth (1E5-1E6 cells/ml) in mineral salts medium containing 100 µl/l chemical substance. The culture was diluted (1:1) with physiological saline and incubated on a shaker for 24 h prior to its use.

- method:
BOD technique according to American Public Health Association. Standard Methods for the Examination of Water and Wastewater. American Public Health Association, Washington, DC., 1980.
incubation: 20 days at 21 °C +-3 °C; 300 ml BOD bottle.
Result: ThBOD: 9.25 mmol/mmol chemical
BOD5 +- SD: 5.5+-0.24 mmol/mmol chemical

BOD5*100/ThBOD = 59.5 %

Reliability: (2) valid with restrictions
acceptable publication which meets basic scientific principles
23-JUL-2002 (40)

3.7 Bioaccumulation

Method: other: estimated value

Remark: Based on a measured log Pow of 0.21, the bioconcentration factor (BCF) for 2-diethylaminoethanol can be estimated to be 0.85 from the recommended regression-derived equation log BCF = 0.76*log Pow - 0.23.
reason for flagging this data: only data available on this endpoint

Reliability: (2) valid with restrictions
scientifically acceptable method

Flag: Critical study for SIDS endpoint
27-JUN-2002 (33) (35)

3.8 Additional Remarks

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
LC50: = 1780

Method: other
GLP: no data
Test substance: other TS: 2-diethylaminoethanol, Aldrich Chemical Co., purity > 99%

Remark: The TS was given in a solution in which the pH was adjusted to that of lake water with HCl.
Reliability: (1) valid without restriction
comparable to guideline study
Flag: Critical study for SIDS endpoint
01-JUL-2002 (41)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: = 100
LC50: 147

Method: other: German Industrial Standard DIN 38 412, Part 15
Year: 1982
GLP: no

Remark: Closely followed the German Industrial Standard Guideline Number DIN 38 412, Part 15 (June 1982) using a static exposure procedure.
The Golden Orfe (L. idus), golden variety was used.
Aeration: slight, with oil free air
Duration of housing and adaptation: about 5 weeks
Duration of adaptation: 3 days
Withdrawal of food before exposure: 1 day
Body length: 5.1 cm (4.8-5.7 range)
Body weight: 1.8 g (1.4-2.7 range)
Loading (g fish/l test water): 1.8
Test design: 10 fish were used per concentration, at concentrations of 0, 100, 215, 464 and 1000 mg/l, and a pH neutralized dose group of 1000 mg/l dose;

measured pH values:

concentration	pH				
(nominal, mg/L)	beginning	24 h	48 h	72 h	96 h
100	10	8.0	8.1	8.1	8.1
215	10.1	9.8			
464	10.5				
1000	10.8				
control	7.7	7.8	7.9	8.0	7.9
1000#	7.9	7.8	7.8	7.8	7.8

= test solution after pH-adjustment

The D.O. concentration ranged between 8.1 and 8.4 mg/l at the beginning of the experiment.
The doses used were chosen based on a range finding study. The product was added to the test water without any prior treatment. Subsequently, the fish were added to the water.
Test vessel: All-glass aquarium non-sealed (30 x 22 x 24 cm)
Dilution water chemistry: reconstituted freshwater was prepared from demineralized tap water that was resalted by the addition of 294.0 mg/l CaCl2.2H2O, 123.3 mg/l MgSO4.7H2O, 64.8 mg/l NaHCO3 and 5.8 mg/l KCl. Test water had a total hardness of 2.5 mmol/l, an acid capacity of 0.8 mmol/l and a pH of about 7.8. The water temperature was 20 degrees centigrade +/- 1 degree. The controls were the test water without the test substance and the pH adjusted control mentioned above.
Reason for flagging this data: most sensitive study available on this endpoint
Statistical evaluation:
the number of doses tested did not allow for a Probit Analysis to be performed, since the data did not yield intermittent values between the LCO (~100 mg/L) and the LC100 (~215 mg/L). Therefore the geometric mean of the two concentrations was calculated: LC50 (96 h): 147 mg/L (nominal).

Result: The fish were found to respond to a positive control (chloroacetamide) with an LC50 of 32 mg/L after 48 hours.

None of the fish in the test died in the 100 mg/L dose group. All fish in the 215, 464 and 1000 mg/L dose groups died. Thus, the LC50 was >100 and <220 mg/L (nominal), respectively 147 mg/L using the geometric mean of the two concentrations.

Symptoms: apathy, tumbling.

The toxic effect may be due to the high pH of the test solutions: no adverse effects were observed, when testing a neutralized sample (1000 mg/L).

Test substance: CAS 100-37-8 (2-diethylaminoethanol), purity >99 %
Reliability: (1) valid without restriction
guideline study
Flag: Critical study for SIDS endpoint
06-MAR-2003 (42)

Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 1900

Method: other: not indicated
GLP: no data
Test substance: other TS

Method: The report consists of a QSAR study of the toxicity to the fathead minnow. In the report calculated results were compared with observed results

Reliability: (2) valid with restrictions
test method (observed 96 h LC50 to the fathead minnow (Pimephales promelas)) not specified, but original reference is well cited
09-OCT-2001 (19) (20)

Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mmol/l **Analytical monitoring:**
log LC50 : 1.18

Reliability: (4) not assignable
only secondary quotation
01-JUL-2002 (43)

Species: Pimephales promelas (Fish, fresh water)

Result: acute toxicity to the fathead minnow (Pimephales promelas): -log (LC50; 96 h): 1.82
Reliability: (4) not assignable
only secondary quotation
01-JUL-2002 (44)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** yes
EC50: = 165

Method: OECD Guide-line 202
Year: 1993
GLP: yes
Test substance: other TS: Diethylaminoethanol, MRD-93-591, Elf Atochem Product Code: 00129

Remark: reason for flagging this study: Although the complete test report is not available, the study can be regarded as valid, because the data for concentration-effect relationship were provided. The EC0 is not clearly deducible, but the EC50 is comprehensible.
Result: The study was performed under pH-adjusted conditions at 1.6, 8, 40, 200, 600 1000 mg/l 2-diethylaminethanol.

pH measurements:	day 0 (0h)	day 2 (48h)
control	7.3	6.0
1.6 mg/l	7.3	6.1
8 mg/l	7.3	6.1
40 mg/l	7.3	6.2
200 mg/l	7.3	6.3
600 mg/l	7.3	7.4
1000 mg/l	7.2	7.0

The number of immobile daphnids were recorded at 24 h and 48 h:

survival (n):	24 h	48 h
control	20	19
1.6 mg/l	18	18
8 mg/l	19	19
40 mg/l	20	19
200 mg/l	14	7
600 mg/l	0	0
1000 mg/l	0	0

Test material was stable in test solutions with day 2 measurements being >/=83 % of day 0 measurements.
All measured values were >/=88 % of nominal concentrations.
Endpoint calculated using nominal concentrations.
EC50 = 165 mg/L (95 % C.L. = 127-230 mg/L)

Test substance: CAS 100-37-8 (2-diethylaminoethanol)
Reliability: (2) valid with restrictions
guideline study, but EC0 not clearly deducible
Flag: Critical study for SIDS endpoint

05-AUG-2002 (45)

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC0: = 62.5
EC50: = 83.6
EC100: = 250

Method: other: Directive 79/831/EEC, C2
Year: 1984
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: reason for flagging this data: most sensitive study available on this endpoint
Result: results after 24 h:
EC0 = 62,5 mg/L
EC50 = 92,4 mg/L
EC100 = 250 mg/L
Test condition: water solubility: >500 mg/l at 293 K, O2-contents: > 2 mg/l, illumination: day/night rhythm (16:8 h), light intensity: 5 uE at a wave of 400-700 nm, test volume: 10 ml, volume/animals: 2 ml, number of animals/vessel: 5, total number of animals/conc.: 20, age of animals: 2-24 h, check of the study: visually after 0, 3, 6, 24 and 48 h, concentration range: 7,81 - 500 mg/L
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint

17-JUL-2002 (46)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: = 5
LOEC: = 10
EC10: = 16
EC50: = 44

Method: other: Closely followed German Industrial Standard Guideline DIN 38 412, Part 9 using a static exposure
Year: 1988
GLP: no

Remark: reason for flagging this data: only study available on this endpoint

Result: Endpoint: biomass
EbC10 (72 h) = 9.8 mg/L
EbC50 (72 h) = 30.0 mg/L
EbC90 (72 h) = 90.0 mg/L

Growth factor control: 16

Rises in pH of 1-2 units in the control treatments were probably associated with CO2 depletion from test media and do not invalidate the test, since in controls within 72 hours the minimum growth factor of 16 was achieved. In the highest test concentration a decrease in pH of 1.5 units was observed

Test condition: A stem culture of Scenedsmus subspicatus was cultivated in nutrient medium of pH 8,2 according to DIN 38412, Part 9.
The culture was reinoculated once a week.
Three days before test initiation a preculture was inoculated at a cell density of 10000 cells/mL.
Duration of the study test: 72 h;
test temperature: 20 °C ± 1 °C;
test flasks: test tubes containing 10 mL medium;
inoculum density: 10000 exponential-growing cells/mL;
test substance stock solution: 1 g/L sterile bidest. water;
test concentrations: 5, 10, 20, 40, 80, 160 and 320 mg/L;
replicates: per test concentration: 4, control: 8;
illumination: permanent artificial light;
light intensity: 10000 LUX white light or 120 µE*S-1m-2;
test tubes were shaken twice a day to hold cells in suspension;
measurements: fluorescence (interval: 24, 48 and 72 h;
value of 0,12 ± 0,01 corresponds to 10000 cells/mL) and pH (interval: 0 and 72 h).
pH-values:
Control: 8.1 (0 h), 9.6 (72 h)
320 mg/L: 8.5 (0 h), 7.0 (72 h)

Test substance: CAS 100-37-8 (2-diethylaminoethanol)

Reliability: (1) valid without restriction
test procedure following national standards

Flag: Critical study for SIDS endpoint

19-JUL-2002 (47) (48)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: other bacteria: Activated sludge from laboratory waste water plant treating municipal sewage.

Exposure period: 30 minute(s)
Unit: mg/l **Analytical monitoring:** no
EC20 : > 1000

Method: Directive 87/302/EEC, part C, p. 118 "Biodegradation: Activated sludge respiration inhibition test"
Year: 1994
GLP: yes

Method: Test mixture (total volume 250 mL) was incubated at 20 +/- 2 deg C for 30 min, after which the respiration rate was measured. Test mixture contained test substance (1000 mg/L), sewage feed (as prescribed by OECD 209) and activated sludge from laboratory wastewater treatment plants treating municipal wastewater.
The following controls were included:
- Inoculum blank: control without test substance but with inoculum (3 flasks)
- Positive control: 3,5-dichlorophenol with inoculum (5 flasks, 1, 4, 10, 50 and 100 mg/L).

Remark: No significant inhibition or stimulation of the respiration rate was observed even at the highest test concentration (1000 mg/L).

Disturbances in the biodegradation process of activated sludge are not to be expected if the test substance is correctly introduced into adapted waste water treatment plants
reason for flagging this study: test was performed with sludge from municipal wwtp

Result:

	Respiration rate (mg O2/L.h)	% inhibition
Test substance	28	7
Inoculum blank	30	-
Reference subst.		
1 mg/L	32	-7 (stimulation)
4 mg/L	28	7
10 mg/L	22	27
50 mg/L	8	73
100 mg/L		

Limit test without replication (3 control replicates) at 1000 mg/L. At 1000 mg/L respiration was inhibited by 7 % compared to the control mean value.

Test substance: CAS 100-37-8 (2-diethylaminoethanol), purity 99.9 %
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
24-JUN-2002 (49)

Species: Pseudomonas putida (Bacteria)
Unit: mg/l **Analytical monitoring:** no

LOEC : = 375

Method: other: cell growth inhibition test
GLP: no data

Reliability: (4) not assignable
Original reference not available
09-OCT-2001 (50)

Species: other bacteria: industrial activated sludge from wwtp of BASF
Exposure period: 30 minute(s)
Unit: mg/l **Analytical monitoring:**
EC10: > 1995

Method: other: Activated Sludge Respiration Inhibition Test

Remark: no inhibition of the respiration was observed up to 1995 mg/L, but a stimulation
Reliability: (2) valid with restrictions
comparable to guideline study with acceptable restrictions.

09-OCT-2001 (39)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

4.5.2 Chronic Toxicity to Aquatic Invertebrates

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

4.6.2 Toxicity to Terrestrial Plants

Species: other terrestrial plant: Chrysanthemum morifolium CV "Indianapolis white"
Endpoint: other: chlorosis
Expos. period: 22 day(s)
Unit: mg/l
EC50: = .12

Method: other
GLP: no data
Test substance: other TS: 2-diethylaminoethanol (DEAE); purity: >99 %

Remark: plants were grown individually in potting-soil consisting of 1 part peat moss : 2 parts vermiculite, amended with lime. A fertilizer was applied at each watering at the rate of 15:1 (water:fertilizer). All plants, with the exception of tomatoes, were grown in 725 ml volume plastic pots (tomatoes: 400 ml volume). Glasshouse experiments were performed at 28 °C +-2°C with a minimum light intensity (10.700 lux; incident light and cool white fluorescent) and 16-h photoperiod.
DEAE was introduced into plants by three methods: (1) ten-fold aqueous dilutions of DEAE were prepared so that 100 ml of solution contained 1E0-1E-5 ml DEAE and each pot received a single application of 100 ml of solution (2) soil in which plants were grown was autoclaved with DEAE-containing steam (3) plants were grown in controlled-environment chambers in either non-sterile or DEAE-steam-sterilized soil and in which atmospheric humidity was enhanced by DEAE-containing steam.
reason for flagging this publication: reliable data on this endpoint

Result: DEAE was found to cause chlorosis in young leaves of chrysanthemum, tomato, corn and bean.
Sensitivity of corn and chrysanthemum to DEAE was cultivar-dependent: chrysanthemum cultivar "Indianapolis White" was sensitive to low concentrations of DEAE, while "Bonnie Jean", "Velvet Ridge" and "Mistletoe" were less so, and corn "3XD50" was sensitive to DEAE while "Ohio 28" was not.
The presence of latent chrysanthemum chlorotic mottle viroid (ChCMV-L) increased the sensitivity of "Bonnie Jean" and "Velvet Ridge" to DEAE.
Infection of tomatoes with mild or severe strains of potato spindle tuber viroid (PSTV) resulted in increased sensitivity to DEAE under conditions of environmental stress.
Leaves of chrysanthemum exhibition DEAE-induced chlorosis contained higher, but non-toxic, levels of iron and other minerals than those from non DEAE-treated plants.

Chrysanthemum cultivars varied in their sensitivity to DEAE. Symptoms were generally restricted to leaves which developed after initiation of DEAE exposure, and included chlorosis, epinasty, stunting and necrosis.

All "Indianapolis White" (4/4) exhibited chlorosis 7 days after exposure to 1E-2 ml DEAE added to non-sterile soil (725 ml pot).
At 1E-4 ml/pot, only 50 % (2/4) of the plants were chlorotic after 22 days.

Reliability: (2) valid with restrictions
acceptable, well-documented publication which meets basic scientific principles

Flag: Critical study for SIDS endpoint

02-JUL-2002 (51)

Species: other terrestrial plant: Chrysanthemum morifolium

Method: other

GLP: no data

Result: Certain varieties of Chrysanthemum morifolium are particularly sensitive to DEAE; 1E-4 ml DEAE per 12.4 cm pot of soil caused chlorosis of the variety Indianapolis White in 22 days.
Other plants found to be sensitive to DEAE are Licopersicum esculentum var. Rutgers, and Morus rubra. Ulmus americana, Zea mays, and Oryza sativa grown in controlled environment chambers displayed symptoms similar to those caused by DEAE in other plants.
Symptoms usually restricted to new leaves produced after contact with DEAE, include interveinal chlorosis, mottling, complete chlorosis, albinism, deformation, and size reduction depending upon species, variety, dosage, and length of exposure.
High concentrations of DEAE caused marginal necrosis of fully mature leaves and death of the growing point.
Chrysanthemum plants infected with the symptomless strain of chrysanthemum chlorotic mottle were at least 10 times more sensitive to DEAE than are uninfected plants.

Reliability: (4) not assignable
only abstract

01-JUL-2002 (52)

Species: other terrestrial plant: Phaseolus vulgaris (pinto bean)

Remark: during the winter of 1972, greenhouse and chamber grown pinto beans (Phaseolus vulgaris) began to display symptoms consisting of dark, bifacial necrotic spots, developing initially along the margins and later in the central portion of the leaves. Marginal spots often coalasced as severity increased. The uniform response suggested toxicant or nutrient involvement.
Live steam used for humidity control in both greenhouse and growth chambers was suspect, and follow-up studies indicate that either of the two compounds (cyclohexylamine or 2 hydroxytriethylamine) used to control the pH of the steam condensate were associated with the observed injury.

Reliability: (4) not assignable
abstract only

08-JUL-2002 (53)

4.6.3 Toxicity to Soil Dwelling Organisms

4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks

Memo:	toxicity on frog tadpoles (Rana bravipoda porosa)
Remark:	the toxicity of solvents used in prepn. of agrochem was tested by detn. of the LC50 (median lethal concn.) of tested solvents on frog (Rana bravipoda porosa) tadpoles in freshwater at 25 °C.
Result:	LC50 (3 h): 360 ppm LC50 (6 h): 230 ppm LC50 (12 h): 300 ppm LC50 (24 h): 230 ppm LC50 (48 h): 85 ppm
Test substance:	Diethylethanolamine
Reliability:	(4) not assignable only abstract in English available (test method and endpoint remains unclear)

12-JUL-2002 (54)

5.0 Toxicokinetics, Metabolism and Distribution

Type: Toxicokinetics

Remark: See chapter 5.11
26-JUL-2002

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Sex: male/female
Vehicle: water
Doses: 177, 708, 1106 and 1416 mg/kg
Value: ca. 1320 mg/kg bw

Method: other: BASF-Test
Year: 1969
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: The test article was administered by gavage. Ten male and 10 female rats were used per dose. The substance was dissolved in water and administered at concentrations of 2 to 20% test substance in water. The doses used were 177, 708, 1106 and 1416 mg/kg bw. Animals were observed over a period of 7 days after administration of the test article.
Remark: Other studies were available reporting essentially similar values. Experiments conducted with the neutralized compound showed toxicity in the range of 5000 to 8000 mg/kg bw.
Result: No animals died within the lowest dose group, but 1/20, 0/20 and 14/20 died in the 708, 1106 and 1416 mg/kg dose groups, respectively. No animals died in the first hour after administration of the test substance, but most deaths occurred within the first 24 hours. The clinical signs were described as apathy and dyspnea. No clinical signs were noted in the lowest dose group; after the first day the 708 mg/kg dose group was symptom free; after 3-4 days no symptoms were observed in the 1106 and 1416 mg/kg dose groups.
Necropsy: Hemorrhaging of the stomach and intestines was observed in the animals that died. The animals that survived to the end had no unusual findings except for chronic bronchitis in 2 animals of the 708 mg/kg dose group.
The original LD50 value was reported to be: LD50 ca. 1500 ul/kg.
Test substance: 2-diethylaminoethanol, purity: ca. 99%.

Reliability: (2) valid with restrictions
Chosen as key study for ICCA Robust Summaries since essential details were available.
Flag: Critical study for SIDS endpoint
10-JAN-2003 (55)

Type: LD50
Species: rat
Sex: male
Value: = 1300 mg/kg bw

Method: other
GLP: no
Test substance: other TS

Remark: the TS was not neutralized
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (2) valid with restrictions
essential details given
05-OCT-2001 (56)

Type: LD50
Species: rat
Value: ca. 2460

Method: other: no data
GLP: no
Test substance: other TS

Method: test substance given as a 10% solution
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
secondary literature, essential details lacking
05-OCT-2001 (57)

Type: LD50
Species: rat
Sex: no data
Vehicle: water
Value: ca. 1300 mg/kg bw

Method: other: no data
GLP: no
Test substance: other TS

Remark: Original value: LD50 was in the neighbourhood of 1.3 g/kg. Late deaths were observed. Deaths occurred between 24 h (for high doses) and 5 days (for lower doses) after dosing. Slight apathy was the only clinical sign. Considerable irritation of the intestinal tract, red bile, congested liver, and pale kidney with congested spleen were noted. The page of the TSCAT with this data was dated Feb. 11, 1942 and signed by Henry F. Smyth, Jr.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
Essential details not given, but the data fits with other existing data.
05-OCT-2001 (58)

Type: LD50
Species: rat
Sex: male
Value: ca. 8000 mg/kg bw

Method: other
GLP: no
Test substance: other TS

Remark: Observation period was 3 days. In one study 3/10 animals died, and in the other 6/10 died. Thus, 9/20 animals died in total.
Test substance: 2-diethylaminoethanol neutralized with HCl prior to administration.
Reliability: (4) not assignable
The study is limited since the observation time was only 3 days.
17-JUL-2002 (59)

Type: LD50
Species: rat
Sex: male
Value: ca. 5600 mg/kg bw

Method: other
GLP: no
Test substance: other TS

Method: According to the report, the approx. LD50 was determined by "feeding" logarithmically graded doses to groups of 5 male rats. In the results section it clarifies that intubation was used. The observation period was 14 d. Calculations were made using the method of Weil (Biometrics, 8, 249-263, 1952).
Result: The 95% confidence interval was reported to be 3.5-9.1 g/kg.
Test substance: 2-diethylaminoethanol neutralized with HCl prior to administration.
Reliability: (2) valid with restrictions
essential details given
02-OCT-2001 (60) (61)

5.1.2 Acute Inhalation Toxicity

Type: other: Inhalation Hazard Test
Species: rat
Sex: male/female
Exposure time: 8 hour(s)

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: The animals were exposed to a 20°C highly saturated vapor-air-mixture for 1, 3 or 8 hours. A total of 6 animals per sex were used for the one hour experiment, and a total of 3 animals per sex were used for the 3 and 8 hour experiments.
Result: No animals (0/12) died within a 7 day period following the 1 hour exposure. In the 3 hour test 1 animal died after 3 days, and 5/6 had died by 9 days after exposure. The last rat remained alive until the end of the observation period (14 days). In the 8 hour test, 2 animals died during exposure, and by day 7 only one animal remained alive. This animal was sacrificed on day 18.

Clinical signs: Severe signs of irritation were noted, namely, attempts to escape, mucous membrane irritation, dyspnoea, gasping.

Necropsy: Corrosion of the snout, eyes, ears and front paws were noted in the animals that were exposed to the vapors for 3 hours.

Since the vapor pressure of the substance at 20°C is 1.9 mbar, the saturated vapor concentration is about 9.2 mg/l. Worst case graphical extrapolation from a probability sheet using the lethality rates after 1 and 3 hours of exposure results in an estimated LT50 of about 2.4 hours. From this a 4 hour LC50 of ca. 4.6 mg/l (4600 mg/m3) can be calculated using Haber's rule.

Test substance: CAS Nr. 100-37-8 (2-diethylaminoethanol), purity: ca. 99%

Reliability: (2) valid with restrictions
Essential details are given for an Inhalation Risk Test; chosen as the key study since a better study to determine the LC50 was not available. The only other acute inhalation toxicity available that reported an LC value in rats was an LCLo reported as 4.5 mg/l (4500 mg/m3) in 4 h and in mice an LC50 of 5 mg/l (5000 mg/m3) with no information on exposure time. Both values were reported in RTECS Update No. 9107 (through August 1991) and the original report (Gigiena Truda i Professional 'nye Zabolevaniya, 14 (11), 52, 70) was not available for an evaluation.

Flag: Critical study for SIDS endpoint

10-JAN-2003 (55)

Type: LCLo
Species: rat
Exposure time: 4 hour(s)
Value: 4.5 mg/l

Method: other: no data
GLP: no
Test substance: other TS

Test substance: 2-diethylaminoethanol, purity not indicated

Reliability: (4) not assignable
secondary literature, essential details lacking

02-OCT-2001 (62)

Type: other: IHT
Species: rat
Sex: male
Exposure time: 4 hour(s)

Method: other: no data
GLP: no
Test substance: other TS

Method: Groups of 6 albino rats were exposed to an atmosphere that had been saturated with the volatile component of the TS generated at room temperature. After exposure animals were held for 2 weeks.

Result: No mortality occurred after a 4 hour exposure.

Test substance: 2-diethylaminoethanol, purity not indicated

Reliability: (2) valid with restrictions
essential details are given for a so-called Inhalation Hazard Test
27-JUN-2002 (56)

Type: other: IHT
Species: rat
Exposure time: 8 hour(s)

Method: other: no data
GLP: no
Test substance: other TS

Remark: One fifth of the exposed rats (no data on number) died by 8 hours inhalation of an atmosphere that had been saturated at 25 degrees Centigrade with the volatile part of the compound. No mortality occurred at 4 hours. Death was delayed, probably due to liver and kidney injury. Eye and nose irritation was seen, but no narcosis. The page of the TSCAT with this data was dated Feb. 11, 1942 and signed by Henry F. Smyth, Jr.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (2) valid with restrictions
essential details are given for a so-called Inhalation Hazard Test
05-OCT-2001 (58)

Type: LC50
Species: mouse
Exposure time: unspecified
Value: 5 mg/l

Method: other: no data
GLP: no
Test substance: other TS

Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
secondary literature, essential details lacking
05-OCT-2001 (62)

Type: LC50
Species: mouse
Exposure time: 2 hour(s)
Value: ca. 5 mg/l

Method: other: no data
GLP: no data
Test substance: other TS

Remark: Original value: LC50 (2 h) = 5000 mg/m3 (1050 ppm).
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
secondary literature, essential details lacking
02-OCT-2001 (63)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: guinea pig
Value: ca. 885 mg/kg bw

Method: other
GLP: no
Test substance: other TS

Method: Penetration of Guinea Pig Skin Method: Doses differed by a multiple of 10. Six animals were used per dose. The sex was not specified. The sample was retained on the abdomen with absorbent cotton over the clipped area for 4 days. The animals were observed for a maximum of 14 days. The dose was retained by covering the cotton with a film of rubber, vinyl or "the like".
Remark: Original value LD50 = 1.0 ml/kg.
No details concerning clinical signs were given.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (2) valid with restrictions
Essential details given; not performed according to today's guidelines, but useful for acute dermal toxicity risk.
Chosen as the key study since more details were available.
Flag: Critical study for SIDS endpoint
13-JAN-2003 (56)

Type: LD50
Species: rabbit
Value: ca. 1100 mg/kg bw

Method: other
GLP: no
Test substance: other TS

Remark: The TLV documentation reads, "Smyth comments that further study indicates...a rabbit skin penetration LD50 of 1.26 (0.85-1.87) ml/kg undiluted. This value is very close to the value reported in a test with guinea pigs performed by Smyth & Carpenter (J. Ind. Hyg. Toxicol., 26, 269-273, 1944), namely a LD50 = 1.0 ml/kg (ca. 885 mg/kg bw). This rabbit data is also cited in a TSCAT from Union Carbide (Date Produced: 3-02-84), which makes reference to Rpt.16-102, 1953.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
Secondary literature, essential details are missing. This value should be considered only in the light of the guinea pig data generated by Smyth and Carpenter (1944); this data is mentioned since the rabbit (or rat) is usually the species of choice.
Flag: Critical study for SIDS endpoint
26-OCT-2001 (57) (58)

Type: LD50
Species: guinea pig
Sex: no data
Vehicle: other: none

Value: ca. 885 mg/kg bw

Method: other
GLP: no
Test substance: other TS

Remark: Original value: LD50 = 1 g/kg. Application of the undiluted test substance for 4 days, local necrosis was observed. The page of the TSCAT with this data was dated Feb. 11, 1942 and signed by Henry F. Smyth, Jr.
Test substance: 2-diethylaminoethanol
Reliability: (2) valid with restrictions
Some essential details are missing, and this report would not be reliable standing alone. Necessary details are available when Smyth & Carpenter (J. Ind. Hyg. Toxicol. 26, 269-273, 1944) is considered.
05-OCT-2001 (58)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Route of admin.: i.p.
Value: = 1220 mg/kg bw

Method: other: no data
GLP: no
Test substance: other TS

Remark: Application in neutralized form.
Test substance: 2-diethylaminoethanol, purity not indicated
27-JUN-2002 (61)

Type: LD50
Species: mouse
Route of admin.: i.p.
Value: ca. 160 mg/kg bw

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: The original data was given as: LD50 ca. 180 ul/kg
Test substance: CAS Nr. 100-37-8 (2-diethylaminoethanol), purity: ca. 99%
27-JUN-2002 (55)

Type: LD50
Species: mouse
Route of admin.: i.p.
Value: 192 mg/kg bw

Method: other: no data
GLP: no
Test substance: other TS

Test substance: 2-diethylaminoethanol, purity not indicated
05-OCT-2001 (64)

Type: LD50

Species: mouse
Route of admin.: i.p.
Value: 308 mg/kg bw

Method: other: no data
GLP: no data
Test substance: other TS

Test substance: 2-diethylaminoethanol, purity not indicated
05-OCT-2001 (65)

Type: LD50
Species: mouse
Sex: no data
Vehicle: no data
Route of admin.: s.c.
Value: = 650 mg/kg bw

Method: other: no data
GLP: no
Test substance: other TS

Test substance: 2-diethylaminoethanol
16-AUG-2000 (66)

Type: LD50
Species: mouse
Sex: no data
Vehicle: no data
Route of admin.: s.c.
Value: = 1561 mg/kg bw

Method: other: no data
GLP: no
Test substance: other TS

Test substance: 2-diethylaminoethanol
18-SEP-2000 (67) (65)

Type: LD50
Species: mouse
Route of admin.: i.m.
Value: 416 mg/kg bw

Method: other: no data
GLP: no
Test substance: other TS

Test substance: 2-diethylaminoethanol, purity not indicated
05-OCT-2001 (68)

Type: LD50
Species: mouse
Route of admin.: i.v.
Value: 188 mg/kg bw

Method: other: no data
GLP: no

Test substance: other TS

Test substance: 2-diethylaminoethanol, purity not indicated
05-OCT-2001 (68)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Exposure Time: 4 hour(s)
Result: corrosive

Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1981
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: One day prior to the substance administration, the animals (New Zealand rabbits) were shaved to prepare sites for substance application. Dorsal and lateral sections of the trunk were used as the application sites (3x3 cm per application site). 0.5 ml/patch were used. Two males and four females were used for the 3 min application time. Three males and three females were used for 1hr and 4 hr application times. Each animal had 4 sites of application (except for the 3 min application: 2 application sites: occlusive and semi-occlusive), namely, a site for:

1 hr application, occlusive
4 hr application, occlusive
1 hr application, semi-occlusive
4 hr application, semi-occlusive

After treatment the patches were removed, and the treated area was rinsed with a polyethylene glycol 400 solution or a polyethylene glycol 400/water (1:1) solution and dried. Observations were made 1 hr after the removal of the patch, and at 24, 48 and 72 hr, as well as 7 days after start of application.

Note: In accordance to OECD Guideline 404 of 1981, "Acute Dermal Irritation/Corrosion", a 4 hour application time was used, but additional application times (3 min and 1 h) were also used.

Result: After a 3 min occlusive exposure, as well as semi-occlusive exposure only slight erythema was observed. It was reversible by the end of the experiment. Some scaling was observed on day 7.

After 1 hr and 4 hr occlusive and semi-occlusive exposure severe erythema, eschar formation and necrosis were observed. Very slight to slight edema was also observed. By day 7 after application the findings were not reversed.

The score for erythema after the 4 hr occlusive exposure was always a 4 at all times, with the exception of one reading of 3 at 1h. The scores for edema after the 4 hr occlusive exposure was 2 in all animals 1 hr after patch removal; 24 hr after the start scores of 2 were seen in 5 animals and a score of 3 was seen in 1 animal; 48 hr after the start scores of 1 were seen in 2 animals, and scores of 2 were seen in 4 animals; the same scores were seen at 72 hr after the start; and at 7 days 3 animals had a score of 1, and 3 had a score of 2.

The scores for erythema after the 4 hr semi-occlusive exposure were reported to be:
2-3 at 1 hr after patch removal; 3-4 at 24 hr after the start; and thereafter it was observed to have a score of 4. The scores for edema after the 4 hr semi-occlusive exposure were reported to be:
1 in 1 animal and 2 in 5 animals one hr after patch removal; 1 in 3 animals and 2 in 3 animals 24 hr after the start; 1 in 2 animals and 2 in 4 animals 48 hr after the start; 1 in 4 animals and 2 in 2 animals 72 hr after the start; and 7 d after the start a score of 1 was reported in all 6 animals.

Necrosis was confirmed histologically. In this regard, in the semi-occlusive 1 hr application group full thickness necrosis was seen in 2/6 animals; in the 4 hr application group full thickness necrosis was seen in 5/6 animals. In the occlusive 1 hr application group full thickness necrosis was seen in 3/6 animals; in the 4 hr application group full thickness necrosis was seen in all animals.

Reliability: (1) valid without restriction
Well documented, guideline study, conducted under GLP-like conditions. Chosen as key study for ICCA Robust Summaries since it was the best study available.

Flag: Critical study for SIDS endpoint

26-JUL-2002 (69) (70)

Species: rabbit
Result: corrosive

Method: Draize Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Reliability: (2) valid with restrictions
Essential details given.

05-OCT-2001 (71) (55)

Species: rabbit

Method: other
GLP: no
Test substance: other TS

Remark: The TS was applied to shaved skin of the belly of an albino rabbit. Observations were made after 24 hours. Its effect was comparable to morpholine.

Test substance: 2-diethylaminoethanol, purity not indicated

Reliability: (4) not assignable
Essential details not given.
05-OCT-2001 (56)

Species: rabbit
Exposure: Occlusive
Exposure Time: 4 hour(s)
Result: corrosive

Method: other
GLP: no data
Test substance: other TS

Method: Applied volume was 0.5 ml. Observations went out to 14 days. Number of animals used:
2 for the 50% solution
2 for the 25% solution
4 for the 10% solution
6 for the 5% solution
Remark: 50% (w/w) and 25% (w/w): severe erythema and necrosis on 2 of 2 from 0.5 ml; ulceration observed from the 50% dilution
10% (w/w): minor to moderate erythema on 6 of 6 rabbits, minor edema on 5, ulceration and necrosis on one from 0.5 ml; 5 rabbits normal at 3 days.
5% (w/w): minor erythema on 4 of 6 rabbits, minor edema on 3 from 0.5 ml; all rabbits normal at 2 days.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (2) valid with restrictions
Essential details given.
05-OCT-2001 (72)

Species: rabbit
Concentration: undiluted
Exposure: Occlusive
Result: corrosive

Method: other
GLP: no data
Test substance: other TS

Method: Six animals (3 males and 3 females) were used for each duration. 0.5 ml was used per treatment. The sample was applied as received (i.e. undiluted).
Result: One hour contact: Moderate to severe erythema and edema on 6 of 6 rabbits, full thickness necrosis on 6, ulceration on 5, ecchymosis on 4 and scabs on 3 from 0.5 ml; animals sacrificed at 2 days for humane reasons.
Three minute contact: minor to moderate erythema on 4 of 6 rabbits, minor edema on 3, superficial necrosis on 3, ulceration on 2, ecchymosis on 3, scabs on 3, desquamation on
4 and alopecia on 3 from 0.5ml; irritation resisted on 4 through 14 days.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (2) valid with restrictions
Essential details given.
05-OCT-2001 (73)

Species: rabbit

Concentration: undiluted
Exposure: Occlusive
Exposure Time: 4 hour(s)
No. of Animals: 1

Result: corrosive

Method: other: according to 29CFR191.11
GLP: no
Test substance: other TS

Remark: Five hundred milligrams of the test substance was applied onto the dry fur-clipped skin of one albino rabbit. After a 24-hour contact period, the application patch was removed and the skin site was washed. The treated site was examined for corrosive effects for at least three days. Necrosis was observed. Result presented only in tabular form. Date of original report: 6/28/72.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
Essential details of the results are not given. However, the data is plausible.
05-OCT-2001 (74)

Species: rabbit
Concentration: undiluted
Result: irritating

Method: other: no data
GLP: no
Test substance: other TS

Remark: On the belly of the rabbit, the undiluted test substance produced erythema. No skin reaction was seen with a 10% solution. No further details were given. The page of the TSCAT with this data was dated Feb. 11, 1942 and signed by Henry F. Smyth, Jr.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
Essential details not given.
05-OCT-2001 (58)

Species: rabbit
Concentration: no data
Exposure: no data
Exposure Time: 4 hour(s)
No. of Animals: 6

Method: other: according to 49 CFR 173.240
GLP: no
Test substance: other TS

Remark: The test substance was applied to six albino rabbits for a 4-hour contact period. Skin sites were observed for 48 hours. At the end of the 4-hour contact period, the treated skin sites were dark grey in color, with a "red surround" and
with sloughed patches of surface epithelium. Subsequently, the sites became thick (hypertrophy) and dry, but remained supple. No signs of dermal destruction were observed.

According to the authors, the test substance was classified as noncorrosive (DOT). No further details given. The pages with the data for this test were dated 8/01/77.

Test substance: 2-diethylaminoethanol, purity not indicated

Reliability: (4) not assignable
Essential details not given.

05-OCT-2001 (75)

Species: guinea pig
Concentration: 5 %
Exposure: Occlusive
Exposure Time: 24 hour(s)
No. of Animals: 10
Result: not irritating

Method: other
GLP: no data
Test substance: other TS

Method: This investigation was a part of a guinea pig sensitization study (preliminary irritation test). Five male and 5 female Dunkin Hartley guinea pigs were treated for 24 hr with a patch containing the test substance at a concentration of 5%.
Result: Slight, well-defined erythema was seen in 1 animal, the remaining 9 animals exhibited no skin response.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (2) valid with restrictions
Reliable for the purpose of the test; i.e. preliminary information for a sensitization test.

05-OCT-2001 (76)

Species: human
Result: irritating

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Reliability: (4) not assignable
essential details are not given

02-OCT-2001 (77)

5.2.2 Eye Irritation

Species: rabbit
EC classificat.: risk of serious damage to eyes

Method: other: BASF-Test
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: 50 µl of the undiluted liquid was applied to the eye. It was not washed out. Two animals were used. As a control, a NaCl solution was applied to the other eye. The observation times were one hour later, 24 hours later, and then 8 days later.

Result: Between one and 24 hours after application corrosion of the conjunctiva and eyelids was seen. It was not reversible after 8 days. Irreversible damage to corneal tissue was observed (staphyloma).

Test substance: CAS Nr. 100-37-8 (2-diethylaminoethanol), purity: ca. 99%
Reliability: (2) valid with restrictions
Essential details are given. Chosen as key study for ICCA Robust Summaries since more details were available.
Flag: Critical study for SIDS endpoint
10-JAN-2003 (55)

Species: rabbit
Result: irritating

Method: other: no data
GLP: no
Test substance: other TS

Remark: 5 mg; strong irritant
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
Secondary literature; essential details not available.
05-OCT-2001 (78)

Species: rabbit

Method: other
GLP: no
Test substance: other TS

Remark: Applied to the cornea undiluted. The effect was compared to ammonium hydroxide.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
Essential details of results not given.
05-OCT-2001 (56)

Species: rabbit

Method: other: no data
GLP: no
Test substance: other TS

Remark: The TLV documentation states, "he regards the major industrial hazard to be eye injury from the fluid (very severe in the rabbit from 0.005 ml undiluted, severe from 15% or more in glycol and not severe from 5% in glycol."
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
Secondary literature, essential details lacking.
05-OCT-2001 (57)

Species: rabbit
EC classificat.: risk of serious damage to eyes

Method: other
GLP: no data
Test substance: other TS

Result:	100% (undiluted), 50% (w/w) and 25% (w/w); 0.1ml: severe corneal injury (with vascularization and irregular shape), iritis and severe conjunctival irritation (with necrosis); injury persisted through 21 days. 100% (undiluted), 50% (w/w) and 25% (w/w); 0.005ml: pinpoint pupils from undiluted sample; moderate to severe corneal injury (with instances of vascularization and irregular shape), iritis and severe conjunctival irritation (with necrosis); injury from undiluted sample persisted through 21 days; 9 of 10 eyes receiving 50% or 25% healed by 21 days. 10% (w/w) and 5% (w/w); 0.005 ml: minor to moderate corneal injury, iritis and moderate to severe conjunctival irritation (with instances of necrosis from 10%); all eyes healed after 7 days.
Test substance:	2-diethylaminoethanol, purity not indicated
Reliability:	(2) valid with restrictions Essential details given, but a description of method was not available and purity is not indicated.
25-JUL-2002	(72)

Species:	rabbit
Method:	other: no data
GLP:	no
Test substance:	other TS
Remark:	In the rabbit eye, 0.001 ml of the test substance caused necrosis. The date on the page where this data was given is Feb. 11, 1942, and it is signed by Henry F. Smyth, Jr.
Test substance:	2-diethylaminoethanol, purity not indicated
Reliability:	(4) not assignable Essential details not given.
05-OCT-2001	(58)

Species:	rabbit
Concentration:	undiluted
Dose:	.1 ml
No. of Animals:	6
Method:	other: no data
GLP:	no
Test substance:	other TS
Method:	One tenth ml of sample was instilled into the conjunctival sac of one eye of each of six albino rabbits. The treated eyes of three rabbits were washed at 20 to 30 seconds after instillation for ca. 1 minute; the treated eyes of the remaining three rabbits remained unwashed. Irritation reactions were scored for 7 days.
Remark:	Date of original report: 8/01/77, performed by Pharmacology Research, Inc.
Result:	In unwashed eyes the cornea opacified promptly and completely obscured the pupil and iris. The conjunctivae became completely necrotic (black) with minimal swelling. Patches of necrosis were seen on the eyelids. No signs of recovery were seen after 7 days. In washed eyes, corneal opacification developed more slowly. During the 1st 2 hours the pupil was constricted and the iris was severely

congested. At 3-4 hours the iris reacted slowly to light; subsequently, it failed to react at all. Initially, the conjunctivae were severely inflamed with minimal swelling and with patches of necrosis. They were completely necrotic after 24 hours. No signs of recovery were seen after 7 days. According to the authors, the TS was considered corrosive by both washed and unwashed applications.

Test substance: 2-diethylaminoethanol, purity not indicated

Reliability: (2) valid with restrictions
Some essential details given.

27-JUN-2002 (75)

5.3 Sensitization

Type: Guinea pig maximization test
Species: guinea pig
Concentration 1st: Induction 5 % intracutaneous
2nd: Induction 25 % occlusive epicutaneous
3rd: Challenge 5 % occlusive epicutaneous
No. of Animals: 20
Vehicle: other: saline or ethanol
Result: not sensitizing

Method: other: according to Magnusson, B. and Kligman, A.M.: J. Invest. Derm. 52, 268
Year: 1969
GLP: no data
Test substance: other TS

Method: The method met the main requirements of OECD Guideline 406. Ten male and 10 female Dunkin-Hartley guinea pigs were used. For induction, the animals were given intradermal injections into 2 sites each of clipped shoulder skin followed by a 48-hour application 7 days later. After removal of the 48-hour patches, the application sites were washed. Epicutaneous challenge was performed by a 24-hour patch at 14 days after epicutaneaous induction (i.e. 21 days after beginning of the study); the challenge patch was applied to a previously untreated site. Observation times after challenge: 24 and 48 h after removal of occlusive dressings. For the positive control, 10 guinea pigs were treated with 1-chloro-2,4-dinitro-benzene (DNCB) using a concentration of 0.1% for induction (intradermal and topical) and challenge (topical).

Result: None of the animals treated with the test substance (0/20) exhibited skin responses. All 10 positive control animals challenged with 0.1% DCNB showed a clear skin response. Except for one animal which had a score of 1 (meaning weak), all irritation control animals were free of skin responses.

Test substance: 2-diethylaminoethanol, purity not indicated

Reliability: (2) valid with restrictions
Well documented study. Essential details were given, but purity is not indicated. This study was chosen as the key study for the ICCA Robust Summaries since it was the most recent. Other studies were also available which showed the substance to be non-sensitizing.

Flag: Critical study for SIDS endpoint

25-JUL-2002 (76)

Type: Draize Test
Species: guinea pig
Concentration 1st: Induction .1 % intracutaneous
2nd: Challenge .1 % intracutaneous

No. of Animals: 10
Vehicle: water
Result: not sensitizing

Method: other: according to Draize et al.: J. Pharmacol. Exp. Ther. 82, 377-390
Year: 1944
GLP: no
Test substance: other TS

Method: Ten guinea pigs were used.
Induction: intradermal injections of 0.1% aqueous solutions every other day for a total of 10 doses.
Challenge: single intradermal injection of a 0.1% aqueous solution at 14 days after the last induction application.
Evaluation: 24 hours after challenge injection.
Remark: Original date of report: March 13, 1958 from Pharmacology Research, Inc.
Result: According to the authors, the test substance was not a sensitizer in this study. Zero out of 10 animals responded to DEAE.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (2) valid with restrictions
Not according to the guidelines of today, but suitable for its time.

27-JUN-2002 (75)

Type: Guinea pig maximization test
Species: guinea pig
Result: not sensitizing

Method: other: Magnusson, B. and Kligman, A.M.: J. Invest. Derm. 52, 268
Year: 1969
GLP: no data
Test substance: other TS

Method: Females of the Hartley strain were used. Induction was made via intradermal injection of 10,000 ppm in olive oil and topical treatment with a 50,000 ppm solution in olive oil. Twenty one days after the initial intradermal injection, 0.1 ml aliquots of various non-irritating concentrations of DEAE were applied in saline for the challenge (0, 1,250, 2,500, 5,000 and 10,000 ppm). The observation time after the challenge application was at 48 hours.
Result: Sensitization was not observed in any of the DEAE-challenged animals (0/10 of the controls responded, 0/10 of the animals challenged with 1,250 ppm responded, 0/10 of the animals challenged with 2,500 ppm responded, 0/10 of the animals challenged with 5,000 ppm responded and 0/10 of the animals challenged with 10,000 ppm responded).
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (2) valid with restrictions
Essential details given.

01-JUL-2002 (79)

5.4 Repeated Dose Toxicity

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of administration: inhalation
Exposure period: 14 weeks
Frequency of treatment: 6 hr/day, 5 days/week
Post exposure period: 4 weeks
Doses: 0.053, 0.120 and 0.365 mg/l (53, 120 and 365 mg/m3; original values: 11, 25 and 76 ppm)
Control Group: yes, concurrent no treatment
NOAEL: = .053 mg/l
LOAEL: = .12 mg/l

Method: other: guideline-like; mentions conforming to U.S. EPA guidelines for particular parameters, but, the exact guideline was not specified
GLP: yes
Test substance: other TS

Method: Animals were approx. 10 weeks old at the start of treatment. Twenty rats/dose/sex were exposed to 0, 11, 25 or 76 ppm (approx. 0, 53, 120 or 365 mg/m3) of DEAE for 6h/day, 5 days/week for 14 weeks using a whole body exposure method. These doses were chosen based on results from a 2 week study (Hinz et al., 1992; Exxon, 1990). Half of the animals were terminated at the end of week 14. In-chamber group observations were performed daily. Individual in-life observations and body weights were determined weekly. Food and water consumption was determined monthly. Ophthalmological examinations were performed prior to exposure initiation and monthly during the study. Urine for urinalysis (qualitative and quantitative) was collected during the 13th week and during the last week in the recovery experiment. Terminal assays, performed at both week 14 and after recovery included hematology, serum chemistry, cholinesterase, gross necropsy examination, organ weight, and histopathology evaluations. Neurologic exams were preformed monthly using a modified "Irwin Screen" during the exposure period. The remaining animals were given a four week post-exposure recovery period prior to sacrifice. Full histological exams [nasal cavity/turbinates, adrenal glands, bone and bone marrow (sternum), brain, epididymes, eyes, heart, kidneys, larynx, liver, lung, cervical lymph node, gastrocnemius muscle, gonads, parathyroid, pituitary, spinal cord, spleen, thymus, thyroid, trachea, urinary bladder and uterus] were conducted in the high dose group and control, but in the low and middle dose groups only the nasal cavity/turbinates were evaluated. The examination of the nasal cavity/turbinates (4 sections) was conducted according to the method of Young (Fund. Appl. Toxicol., 1, 309-312, 1981).

Nominal and actual exposure concentrations were determined daily. Actual exposure conc. are used in this report, which were measured by GC analysis. Samples were obtained hourly. Samples were drawn from 5 points in a horizontal plane within each exposure chamber.

STATISTICAL METHODS: Bartlett's test, ANOVA, Dunnett's, Kruskall-Wallis test and several other tests if applicable.

Temperature and relative humidity were monitored regularly and according to the report were within the ranges specified in U.S. EPA guidelines.

Remark: The average analytical concentrations were 10.5, 25.5 and 76 ppm. These concentrations are comparable to ca. 13, 29 and 88 mg/kg bw per day doses assuming 100% lung deposition and absorption.

Result: No animals died as a result of exposure to DEAE. During exposure, dose-dependent transient signs of mild to moderate respiratory irritation (sneeze-like sounds or rales) were noted. They usually cleared within one hour after exposure. In the high dose group, some animals continued to exhibit these signs overnight. Nasal discharge was observed at the beginning of the study, but this subsided as the study progressed. Corneal opacities were observed in control and DEAE-treated animals. DEAE exposure appeared accelerate the appearance of this lesion in the middle and high concentration groups. According to the authors, aging F344 rats are genetically predisposed toward developing these corneal lesions. Prolonged exposure to an alkaline compound such as DEAE might have accelerated an underlying predisposition toward corneal dystrophy. Since the opacity was thought to be due to a calcium precipitate, this problem may have also been exacerbated by the high vitamin D diet which would increase calcium absorption.

No outstanding effects on blood chemistry, urinalysis or neurobehavioural parameters were observed.

Through the first 7 weeks of exposure the high dose group had a slight, but statistically significant decrease in body weight gain as compared to controls. Subsequently the rate of growth paralleled the other groups, but the initial decrement was never regained. Mean body weights of the high dose groups never decreased more than about 7% from the controls. At week 14 there was a slight, but statistically significant increase in the absolute male liver and kidney weights in the high dose group (8.0 and 7.1%, respectively), as well as in their relative weights (increased by 5.9 and 7.1%, respectively), but histologic changes were not associated with these findings. Histomorphologic changes in nervous tissues were not observed. In females, only the high dose relative kidney weight was slightly increased (7.9%, $p < 0.05$).

The low dose group was free of exposure-related histologic changes in the nasal cavities and turbinates, but changes were noted in the middle and high dose groups sacrificed in the 14th week of exposure. These consisted of an increased incidence [45% (50% M, 40%F) at the middle concentration & 95% (90% M, 100% F) at the high concentration] and severity of focal hyperplasias alone or in association with squamous metaplasia of the respiratory epithelium, and multi-focal mixed infiltrations of inflammatory cells in the nasal mucosa. Changes were most evident in the anterior sections of the nasoturbinates and on the lateral wall of the nasal cavity. In the high dose group

hypertrophic goblet cells were seen in the nasal septum, along with a low incidence of focal necrosis and exudate in the lumen of the nasal cavity. The findings in the middle and high dose groups after the 4 week recovery period were similar to those seen in the 14 week rats, however, the incidence of focal hyperplasia with squamous metaplasia was decreased. The incidence of focal hyperplasia alone, infiltrations of inflammatory cells and goblet cell hypertrophy were comparable to what was noted at 14 weeks. There were no exposure-related findings in the other areas of the respiratory system to indicate any irritating effect on the lower respiratory tract.

This study indicated that DEAE lacked systemic toxic properties, and the point of contact (eyes and upper respiratory tract) was the site of action. Since no systemic toxicological effects were observed, the NO[A]EC for systemic toxicity was the highest dose tested, i.e. 0.365 mg/l (76 ppm, or 365 mg/m3). The NO[A]EC for local toxicity, based on the lack of observed effects in the nasal cavity/turbinates, was 0.053 mg/l (11 ppm, rounded off to 10 ppm, or 53 mg/m3). The noises or rales at this concentration were considered an adaptive effect, but not an adverse effect, since no histological changes were observed at this concentration. However, since an effect (rales) was seen at the lowest concentration, a NOEC was not reached.

NO[A]EC, rat (inhalation) 14 weeks, systemic toxicity: 0.365 mg/l (76 ppm or 365 mg/m3)

NO[A]EC, rat (inhalation) 14 weeks, local toxicity: 0.053 mg/l (10 ppm or 53 mg/m3)

LO[A]EC, rat (inhalation) 14 weeks, local toxicity: 0.12 mg/l (25 ppm or 120 mg/m3)

Test substance: 2-diethylaminoethanol, purity: 99% pure, Pennwalt Corp.

Reliability: (1) valid without restriction
Well documented, GLP certified, guideline-like study; mentions conforming to U.S. EPA guidelines for particular parameters, but, the exact guideline was not specified. Chosen as the key study for the ICCA Robust Summaries since more details were available.

Flag: Critical study for SIDS endpoint

07-JAN-2003 (80) (81) (82) (83)

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of administration: inhalation
Exposure period: 2 weeks
Frequency of treatment: 6 hr/day, 5 days of exposition followed by a 2 day pause, then 4 more days of exposure
Post exposure period: no
Doses: 0.048, 0.272 and 1.463 mg/l (48, 272 and 1463 mg/m3, respectively; original data: 10, 56 and 301 ppm, respectively)
Control Group: yes, concurrent no treatment
NOAEL: = .048 mg/l
LOAEL: = .269 mg/l

Method: other
GLP: no data
Test substance: other TS

Method: Ten animals/dose/sex were used and were exposed a total of 9 times over a 2 week period. Histopathological examinations that included the gonads were performed in the control and 56 ppm group. In the 10 ppm group only the nasal turbinates were examined. Due to the high mortality, histological examinations were not performed in the 301 ppm group.

Remark: This experiment was conducted to determine the doses to be used for a subchronic study.

Result: Ten and 56 ppm exposures did not cause any major treatment-related changes. Generally, male rats in the 56 ppm group did not gain as much weight as the controls, however, this difference was not statistically significant. There was no mortality in either group. Urinalysis, hematology and serum chemistry failed to show any significant DEAE-induced differences. At necropsy, no treatment-related macroscopic changes were noted, and absolute and relative organ weight values were unremarkable. The principle histologic lesions found occurred only in the anterior sections of the nasal turbinate mucosa. Inflammation of the nasal turbinate and lateral wall mucosa were noted in half of the animals of the 56 ppm group. The epithelium in the infiltrated areas appeared to be flattened, with early squamous cell metaplasia evident in one male of the 56 ppm group. The histopathologic changes were dose-related and most evident in the 56 ppm group. The 10 ppm was basically free of abnormalities. There were no signs of systemic toxicity.

301 ppm exposure caused overt signs of ocular, nasal and respiratory distress during and immediately after exposure. Ocular discharge, opacities and ulcerations, minor skin sores, nasal discharge, rales, labored breathing and gasping, decreased activity and responsiveness, impaired coordination and reflexes, hypothermia, and increasing emaciation were noted as the study progressed. Group mean values for food and water consumption were significantly ($p < 0.01$) lower than controls. Animals lost weight throughout the study. Deaths occurred in 9/10 males and 5/10 females, with deaths occurring sooner in males than in females. These deaths made statistical analyses difficult. None-the-less, the urinalysis, hematology and serum chemistry of survivors was not comparable to controls (data not shown), and there were no consistent trends. Surviving animals exhibited a number of gross changes: under sized spleens, thymuses and gonads, nasal discharges, enlarged adrenals and intestinal gas. Although organ weights were lower than controls, due to the depressed body wt. their relative organ weights appeared to be comparable to controls. Autolytic changes precluded meaningful necropsy evaluations in animals that died as a result of exposure to DEAE.

SUMMARY
The NOAEC was the 10 ppm dose (48 mg/m3 or 0.048 mg/l) based on the lack of local toxicity to the upper respiratiory tract, and the LOAEC was the 56 ppm dose (269 mg/m3 or 0.269 mg/l) based on local toxicity. No systemic toxicity was observed at these two doses.

Test substance: 2-diethylaminoethanol, purity: 99% pure, Pennwalt Corp.

Reliability: (2) valid with restrictions
Essential details given for a dose setting experiment.

03-JUL-2002 (81)

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 1, 3 and 6 months
Frequency of treatment: 6 hr/d, 5 d/wk
Post exposure period: no data
Doses: 0.97 mg/l (970 mg/m3, i.e. 200 ppm)
Control Group: yes, concurrent no treatment

Method: other: no data
GLP: no
Test substance: other TS

Method: 50 males were exposed to DEAE vapors using a whole body method. 32 rats were exposed to the "air flow" in a similar chamber to serve as a control. Animals were exposed to the TS by metering DEAE into a vaporizing unit maintained slightly above room temperature. Vapors were picked up by the air stream passing through the vaporizer and carried into the top of the vapor chamber. Chamber concentrations of DEAE were measured daily by 30-minute sampling into glacial acetic acid and titration with perchloric acid.

Animals were sacrificed and hemoglobin, hematocrit, RBCs, WBCs, differential cell counts, serum protein, serum glutamic oxaloacetic transaminase, ratios of liver and kidney wt to body wt and histopathologic observations were made.

The sacrifice schedule was as follows:
at 1 month 8 animals/group,
at 3 months 12 animals/group,
at 6 months 11 control animals and 23 DEAE-exposed animals.

Result: During the 1st month 7/50 animals lost weight (reduced by 15% compared to controls) and died from bronchial pneumonia (based on histologic examination). Other parameters were not markedly different from controls. In the 2nd month one control rat died. By the end of 3 months the weight of both groups were nearly comparable. After 6 months there was no significant difference between exposed animals and the controls in regard to body weight and hematology, clinical chemistry and histopathology.

Test substance: 2-diethylaminoethanol, purity not indicated

Reliability: (4) not assignable
Essential details not given (clinical symptoms, information on post exposure observation period, details of airway histological examinations, gonads were not examined).

02-JUL-2002 (60)

Species: rat **Sex:** male/female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 5 days
Frequency of treatment: 6 hr/day
Post exposure period: not data
Doses: 0.97 mg/l (970 mg/m3 or 200 ppm)
Control Group: yes, concurrent no treatment

Method: other: no data
GLP: no
Test substance: other TS

Method: 8 males and 8 females (ca. 200-250 g) were exposed to DEAE vapors using a whole body method. Animals were exposed to the TS by metering DEAE into a vaporizing unit maintained slightly above room temperature. Vapors were picked up by the air stream passing through the vaporizer and carried into the top of the vapor chamber. Chamber concentrations of DEAE were measured daily by 30-minute sampling into glacial acetic acid and titration with perchloric acid. Animals were sacrificed and hemoglobin, hematocrit, RBCs, WBCs, differential cell counts, serum protein, serum glutamic oxaloacetic transaminase, ratios of liver and kidney wt to body wt and histopathologic observations were made.
Result: Mild irritation to the eyes was observed during the first day; slight nasal irritation occurred at the end of 3rd exposure. Both symptoms did not progress. Body weight development was similar to controls. The histopathology of the lung, brain, heart, spleen, adrenal gland, kidney and liver were comparable to controls.
Test substance: 2-diethylaminoethanol, purity not indicated
Reliability: (4) not assignable
Essential details not given (number of control animals, information on post exposure observation period, details of airway histological examinations).
02-JUL-2002 (60)

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: 5 days
Frequency of treatment: 6 hr/day
Post exposure period: yes, no details
Doses: 2.43 mg/l (2430 mg/m3 or 500 ppm)
Control Group: yes, concurrent no treatment

Method: other: no data
GLP: no
Test substance: other TS

Method: 20 males (ca. 200 g) were exposed to DEAE vapors using a whole body method. Animals were exposed to the TS by metering DEAE into a vaporizing unit maintained slightly above room temperature. Vapors were picked up by the air stream passing through the vaporizer and carried into the top of the vapor chamber. Chamber concentrations of DEAE were measured daily by 30-minute sampling into glacial

acetic acid and titration with perchloric acid. Animals were sacrificed and hemoglobin, hematocrit, RBCs, WBCs, differential cell counts, serum protein, serum glutamic oxaloacetic transaminase, ratios of liver and kidney wt to body wt and histopathologic observations were made.

Result: During the 1st exposure day, irritation of the eyes and nose were seen; all animals exhibited tremors of the head and forlegs. These symptoms continued throughout the five-day exposure period. After the 3rd exposition corneal opacity was observed. Four animals died (one on exposure day 4 and 3 died 3 days after exposure had ceased). All animals had lost 40 to 80 g of body weight when compared to controls. Histopathological findings: acute purulent bronchiolitis and bronchopneumonia; other tissues were similar to controls.

Test substance: 2-diethylaminoethanol, purity not indicated

Reliability: (4) not assignable
Essential details not given (number of control animals, length of post exposure observation period, details of airway histological examinations).

02-JUL-2002 (60)

Species: rat **Sex:** no data
Strain: no data
Route of administration: inhalation
Exposure period: 5 months
Frequency of treatment: 4 hr/day
Post exposure period: no data
Doses: 128 ppm (ca. 622 mg/m3 or 0.622 mg/l)
Control Group: no data specified

Method: other: no data
GLP: no
Test substance: other TS

Result: Treated rats exhibited symptoms of excitation of the CNS, clonicotonic convulsions, irritation of the respiratory tract, and depressed body weights.

Test substance: 2-diethylaminoethanol

Reliability: (4) not assignable
Secondary literature. Essential details are lacking.

02-JUL-2002 (84)

Species: rat **Sex:** male/female
Strain: other: albino rats from Charles River Breeding Lab.
Route of administration: oral feed
Exposure period: 6 months, 12 months and 2 years
Frequency of treatment: continuously in the food
Post exposure period: not indicated
Doses: 200, 500 and 1000-10,000 ppm (the high dose group was gradually increased to 10,000 ppm); corresponding to ca. 11, 25, 50-400 mg/kg bw/day, respectively. These were the doses of the free base, but the TS was given as the HCl salt.
Control Group: yes, concurrent no treatment

Method: other
GLP: no data
Test substance: other TS

Method: For the DEAE-treated groups, 35 rats/sex were used, and in the control there were 60 rats/sex. Observations were made 6 days/week for signs of toxicity. Body weights and food consumption were recorded weekly for the 1st 26 wks, and biweekly for the next 26 wks. In the 2nd year, body weights and food consumption were measured every 4 weeks. Hematocrits, hemoglobin determinations and total and differential leucocyte counts were made from 5 rats of each sex and group on day 30, 45, 90, 180, 360, 540 and 720. Complete blood counts were performed on 5 additional females from the control and high dose group on day 180, and total white cell counts were performed on 5 additional rats of each sex from all groups on day 360. Urine analyses (albumin, acetone, bilirubin, color, occult blood, sugar, pH, appearance and microscopic sediment examination) were made on day 30, 45, 60, 90, 180, 360, 540 and 720 from pooled sample groups of the same rats used for the blood tests. At 6 and 12 months, 5animals/sex/group were sacrificed and complete necropsies were performed. Representative tissues from each animal were fixed in formalin. These tissues were: 3 sections of the brain, two sections each of the stomach and small intestine, one section each of the pituitary, thyroid, heart, lung, liver, spleen, kidney, adrenal, pancreas, large intestine, urinary bladder, gonads, bone marrow and any unusual lesion. Animals which died or which were moribund were taken and when post-mortem autolysis was not advanced, target tissues as well as tumors were examined histologically. All of these tissues from the control group and the high dose group were examined microscopically from the 6 and 12 month sample groups. At the end of 2 years, all surviving animals were necropsied. Ten animals/sex from controls and the high dose group were examined histologically. The gonads of all groups of the 2 year sampling were eventually examined histologically. Organ weights and organ/terminal body weights were recorded from all scheduled sacrificed animals.

Remark: The doses were based on the free base, but the substance was given as a HCl salt. The dietary levels of the free base were: 0, 200, 500 and 1000 ppm. After week 47 the 1000 ppm group was gradually raised to 10,000 ppm as follows:
Week 48 - 56, 1500 ppm;
Week 57 - 64, 2500 ppm;
Week 65 - 72, 3500 ppm;
Week 73 - 80, 5000 ppm;
Week 81 - 84, 7500 ppm;
Week 85 - 104, 10000 ppm.

Result: None of the treated animals displayed gross signs of substance-induced toxicity. Adverse signs occurred mainly in the last 6 months in all groups and were associated with aging (this included general poorer health and an increase in mortality). According to the report, since the incidence of mortality of the DEAE-treated groups compared favorably with the controls, DEAE did not produce any earlier or greater numbers of deaths at any dose level.

Instances of anorexia were also reported in this study, but the data on individual animals was not given.

According to the report, the animals were said to have generally had a vigorous appetite and the the average weekly body weight and feed consumption values for males and females were generally comparable to controls at the corresponding interval. However, in the last 12 weeks of the study the high dose male body weight was on average 8.6% (maximum 11%) lower than the controls.

No significant hematological changes were seen. In both sexes of the high dose group, the hematocrit and hemoglobin values were slightly decreased at the 720 day time point. At 6 months no testicular atrophy was observed. At 12 months one case of slight testicular atrophy was grossly observed in a 200 ppm dosed male. In the 24 month samples testicular atrophy was observed in:
0/34 control animals,
3/18 (17%) animals of the 200 ppm dose group,
2/17 (12%) animals of the 500 ppm dose group and
4/15 (27%) animals of the 1000-10000 ppm dose group.
In the high dose group, 3 cases were grossly described as slight atrophy in one testis, and this was confirmed histologically; the fourth case was not grossly observed, but the histologic description indicated that 2/3 of the testis had a "moderately severe" generalized degree of atrophy present with only Sertoli cells which remained within most of the seminiferous tubules.

According to the sponsor, the lack of testicular atrophy in the controls was surprising given the historical control range of this lesion (data not available). It should be noted that this is not an unusual lesion in ageing rats (Glaister, 1986). One high dose female had gonadal atrophy, but the report considered this fortuitous. It should be emphasized that in the six month samples, the more appropriate time point for examining reproductive toxicity, no testicular effects were observed. The atrophy often occurred bilaterally.

Careful histologic examination of the cerebellums of the high dose animals revealed no anomalies. No other signs of toxicity were observed. Roundworms were found in the colon of 2 control and 3 high dose animals.

Given the lack of a DEAE-related effect seen in the 6 month and 12 month samples, the NOAEL was the highest dose tested for these time points, i.e. 1000-1500 ppm/day, or ca. 50-70 mg/kg/day. The gonadal degeneration seen in 2 year old DEAE-treated animals was confounding since it was not dose-dependent, however, due to the presence of this lesion, a NOAEL could not be assigned for the 2 year time point. See section 5.7 for a description of the results in regard to carcinogenicity.

Test substance: According to the report, 1.000 ml contains 0.577-0.585 g of Diethylaminoethanol or 0.758-0.766 g Diethylaminoethanol hydrochloride; Pennsalt Chemicals Corp.

Reliability: (2) valid with restrictions
Some essential details are given. A limitation is the lack of a detail on the anorexia observed (i.e. was it associated with DEAE treatment?). A maximum tolerated dose was not achieved, thus, there is no clear basis for the doses

chosen. For today's requirements, the number of animals used is a limitation (for the 2 year carcinogenicity endpoint); however, in the 1960s there were no international guidelines. No basis is given for the dose selection.

26-JUL-2002 (85) (86) (87)

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of administration: drinking water
Exposure period: 4 weeks
Frequency of treatment: continuous
Post exposure period: no data
Doses: ca. 500 mg/kg/d
Control Group: no data specified

Method: other: no data
GLP: no
Test substance: other TS

Remark: The dose level was described as 80-120 mg/rat/day, according to the report. Male rats were maintained on normal diets and received DEAE neutralized with HCl in the drinking water at a level of 4 mg/ml. The weight of the rats was given as 150-175 g at the start. Taking averages, the dose was estimated to be ca. 80 mg/0.162 kg/day, i.e. ca. 500 mg/kg.

The only effect noted after 4 wk of DEAE treatment was a slight elevation of the kidney wt to body wt ratio ($p < 0.05$). Liver lipids, serum lipids, cholesterol levels and liver wt to body wt ratios were not effected by DEAE. No significant histological changes were noted in the lung, liver, kidney or spleen. No further information was available.

Test substance: 2-diethylaminoethanol neutralized with HCl, purity not indicated
Reliability: (4) not assignable
Essential details not given.

19-OCT-2001 (59)

Species: rat **Sex:** male
Strain: Sprague-Dawley
Route of administration: drinking water
Exposure period: 1, 2 and 6 months
Frequency of treatment: continuous
Post exposure period: no data
Doses: ca. 150 and 300 mg/kg bw/day (2000 and 4000 mg/l of neutralized DEAE)
Control Group: yes, concurrent no treatment

Method: other: no data
GLP: no
Test substance: other TS

Method: Weight at study initiation: 200-250 g
Exposure period: up to 6 months
Doses: 0, 50 and 100 mg/rat/day (the article states that the rats consumed 25-30 ml of a water solution containing 0, 200 or 400 mg per 100 ml). That corresponds to approx. 0, 150 and 300 mg/kg bw/d. 15 males/dose were used. 5

animals/group were sacrificed after 1, 2 and 6 months. Parameters investigated: Body weight, liver and kidney weights, hemoglobin, clotting time, liver lipids, serum total lipids, cholesterol(esters), phospholipids and histopathology (liver, kidney, heart, spleen). Statistical methods were not indicated.

Remark: According to the 1996 TLV Documentation supplement, rats were "fed" diethylaminoethanol at 50 and 100 mg/kg, however, this is a misreading of the original report.

Result: Body weights of treated animals were comparable to control values up to day 30. Thereafter, decreased body weights were observed in treated animals. In this regard at 60 days, the low dose group had lost about 30 g and the high dose had lost about 50 g when compared to the control group (reduced ca. 8 and 14% from the control value). After 6 months rats receiving the low dose recovered from their decreased body weight, but high dose rats remained below control body weights (by ca. 11%). No effects were seen in hematology and clinical chemistry parameters at the 1, 2 or 6 month time points. Nor was an effect on the liver to body weight ratio seen. The only difference noted between DEAE-treated animals and controls seen at autopsy was that the ratio of kidney weight to body weight was slightly elevated in both treated groups at the 1, 2 and 6 months time points. No changes in the kidney were noted histologically in treated animals at any of the scheduled sacrifices. Nor were histologic changes noted in the other organs investigated (liver, heart, spleen).

Test substance: 2-diethylaminoethanol neutralized with HCl, purity not indicated

Reliability: (4) not assignable
The study is limited by the low number of animals/group and only a few organs were examined histologically.

19-OCT-2001 (60) (88)

Species: dog **Sex:** male/female
Strain: Beagle
Route of administration: oral feed
Exposure period: 1 year
Frequency of treatment: continuous (with some exceptions)
Post exposure period: no
Doses: ca. 20, 40, 200 (80), and 400 mg/kg/d, [i.e. 500, 1000, 5000 (2000) and 10000 ppm]. These were the doses of the free base, but the TS was given as the HCl salt.
Control Group: yes, concurrent no treatment

Method: other
GLP: no
Test substance: other TS

Method: The concentration was calculated on the basis of the free base to be ca. 20, 40, 200 (80) and 400 mg/kg/day. Original data: 500, 1000, 5000 (2000), 10000 ppm. The 5000 ppm dose group was given from day 0 to 39, then after a pause dosing started again on day 134 with 2000 ppm for 6 days/wk in gelatin capsules. Three animals/dose/sex were used.

Result: None of the animals in the 500 ppm group displayed signs of toxicity; however, tremors and/or shaking of the head from side to side were described in the 1000 ppm group. This

occurred intermittently at first and eventually occurred continuously in a few animals. All dogs of the next two dose groups exhibited severe cases of weakness, tremors, convulsions and ataxia, with two animals in the 5000 ppm group dying (one on d 35 and one on d 41). All animals in the 10,000 ppm group died between days 18 and 39 of the study. After stopping treatment in the 5000 ppm group, the animals showed signs of improvement; however, the ataxia and tremors were still occurring when dosing (now with 2000 ppm) was resumed on day 134. This group displayed an increase in ill effects after dosing resumed, but some improvement occurred with time.

Body wt and food consumption appeared normal in the 2 lowest dose groups. No pronounced treatment-related findings were observed in the blood or urine in any group.

With the exception of the findings in moribund animals of the 2 highest dosed groups, clinical examinations showed no abnormalities with respect to pulse rate, reflexes or condition of the mucous membranes. ECG tracings showed no DEAE-related damage to the heart.

Gross necropsy of the animals that died in the 1st 180 days showed congestion and hemorrhages of the lungs, congestion of the kidneys, reddish mottled coloration of the spleen, hardness of the liver, and numerous enlarged and congested lymph nodes. Gross necropsy of the animals that survived to the termination revealed no gross pathological changes attributable to treatment. Terminal body and organ weights for control and DEAE treated animals showed no pronounced differences.

Microscopic examination of the tissues of the 5000 (2000) ppm group showed atrophy of the thyroid gland (one male and 3 females) and gonads (three males), which according to the report was interpreted as a non-specific secondary response to the metabolic or toxic insult of the TS. One female in this group had to a decrease in oogenesis. Cerebellar changes were also observed in this group and occurred in all males and one female. These changes consisted of irregular patchy degeneration and loss of small to moderate numbers of Purkinje cells, with occasional mild decreases in the cellularity of the granular layer. Foci of
tissue calcification were present in the one female.

Test substance: 2-diethylaminoethanol neutralized with HCl; according to the report, 1.000 ml contains 0.577 g of Diethylaminoethanol or 0.758 g Diethylaminoethanol hydrochloride; Pennsalt Chemicals Corp.

Reliability: (4) not assignable
The study was limited to summary information only. Tables and individual animal data were not available for an assessment.

26-JUL-2002 (75) (87)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Standard plate test and preincubation test with Salmonella typhimurium TA1535, TA100, TA1537, TA98
Concentration: 0, 20,100, 500, 2500 and 5000 µg/plate
Metabolic activation: with and without
Result: negative

Method: OECD Guide-line 471
Year: 1983
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Method: The S-9 mix was prepared from Aroclor 1254 pretreated rats. Three plates per dose and per control were tested. The study was performed under GLP-like conditions.

The following positive controls were used (dissolved in DMSO):
with S-9 mix, 10 ug 2-aminoanthracene,
without S-9 mix, 5 ug MNNG for strains TA 100 and TA 1535,
10 ug 4-nitro-o-phenylendiamine for TA 98, and 100 ug
9-aminoacridine chloride monohydrate for TA 1537.

A parallel "negative" solvent control with and without S-9 mix was carried out for each tester strain to determine the spontaneous mutation rate.

Evaluation Criteria-a positive result had to fulfill the following:
- a doubling of the spontaneous mutation rate (control)
- a dose-response relationship
- reproducibility of the results

N.B.: This study followed the OECD Guideline 471 of 1983 and not the current OECD guideline 471 of1997. That is why E. coli and TA 102 were not included.

Remark: Similar negative results were reported by Zeiger et al. (Environ. Mutagen. 9, Suppl.9, 1-110, 1987) and in another guideline-GLP study sponsored by the Synthetic Organic Chemicals Manufacturing Association (Life Science Research, Report No. 91/SHG001/0251, Diethylaminoethanol: Assessment of mutagenic potential in histidine auxotrophs of Salmonella typhimurium, 2 July 1991).

Result: No increase in the number of his+ revertants was seen in any of the bacterial strains tested with the test substance. The test substance was completely soluble in water in the dose range tested. A weak bacteriotoxic effect was occasionally observed using TA 1537 with S-9 mix (standard plate test) and with TA 1535, TA 1537 and TA 98 without S-9 mix (preincubation test) at 5000 ug/plate. All positive controls produced the expected effects.

Test substance: CAS No. 100-37-8 (2-diethylaminoethanol), purity: > 99%

Reliability: (1) valid without restriction
Well conducted guideline study conducted under GLP-like conditions. Chosen as the key study for the ICCA Robust Summaries.

Flag: Critical study for SIDS endpoint
28-JUN-2002 (89)

Type: Ames test
System of testing: Standard plate test with Salmonella typhimurium TA1535, TA1537, TA1538, TA98 and TA100
Concentration: 50 to 5000 µg/plate
Metabolic activation: with and without
Result: negative

Method: OECD Guide-line 471
Year: 1983
GLP: yes
Test substance: other TS

Method: N.B.: This study followed the OECD Guideline 471 of 1983 and not the current OECD guideline 471 of1997. That is why E. coli and TA 102 were not included.
Test substance: CAS No. 100-37-8 (2-diethylaminoethanol), purity: 99.8%, Atochem North America
Reliability: (1) valid without restriction

Well conducted guideline study conducted under GLP conditions.
28-JUN-2002 (90)

Type: Ames test
System of testing: Preincubation modification of the Salmonella/microsome test in the absence and presence of exogenous metabolic activation (S. typhimurium TA 98, TA 100, TA 1535, TA 1537)
Concentration: 33, 100, 333, 1000, 2500 und 3333 µg/Platte
Metabolic activation: with and without
Result: negative

Method: other: according to Haworth, S. et al.: Environ. Mutagen. 5, Suppl. 1, 3-142
Year: 1983
GLP: no data
Test substance: other TS

Method: Preincubation modification of the Salmonella/microsome test in the absence of exogenous metabolic activation and in the presence of liver S-9 from Aroclor-induced male Sprague-Dawley rats and Syrian hamsters. S. typhimurium strains TA 98, TA 100, TA 1535 and TA 1537 were used.
Test substance: CAS No. 100-37-8 (2-diethylaminoethanol), purity: "99+", Fluka
Reliability: (2) valid with restrictions
Essential details are given.
28-JUN-2002 (91)

Type: HGPRT assay
System of testing: Chinese hamster V79 cell mutation system
Concentration: 1st experiment: 4.8 to 3000 µg/ml;
2nd experiment: 5.6 to 3500 µg/ml
Metabolic activation: with and without
Result: negative

Method: OECD Guide-line 476
Year: 1984
GLP: yes
Test substance: other TS

Method: The test conformed to the OECD Guideline 476 of 1984. The study was also carried out in accordance to EPA (TSCA) guidelines (1985, revised 1987).

Cell type: V79 clone 6
Metabolic activation system: rat-liver derived S9-mix (Arochlor 1254-treated rats).

Dosing: 1st expt.: 4.8, 24, 120, 600, 3000 ug/ml; 2nd expt.: 5.6, 28, 140, 700, 3500 ug/ml
Number of replicates: 3 plates/dose group

Negative control: distilled water (vehicle)
Positive controls:
-S9, ethylmethanesulphonate
+S9, dimethylbenzanthracene

Selection agent: 6-thioguanine (6-TG)
Treatment procedure: 7.5 x 10E5 cells/dose group were seeded in 25 cm2 flasks for 24 hours and then were treated for 3 hours. After treatment the cell sheet was washed and non-selective medium was added. A sample of cells was taken to measure survival after treatment. Cells were then passaged to maintain subconfluence for an expression time of 7 days. Then, cells were plated for the mutant selection (10E5 cells/plate/3-fold) and for the plating efficiency (200 cells/plate/3-fold); after 6 days the resultant colonies were scored.
FOLLOW UP REPEAT STUDY: independent repeats were performed.
CRITERIA FOR EVALUATING RESULTS: a dose dependent increase in the number of 6-TG resistant colonies compared to the solvent control.

Result: GENOTOXIC EFFECTS:
With and without metabolic activation: negative
Cultures exposed to diethyaminoethanol showed no increases in 6-TG resistant colony numbers and no significantly increased mutant frequencies compared to solvent controls.

CYTOTOXIC CONCENTRATION:
With and without metabolic activation: In both experiments in the highest dose level of 3000 - 3500 ug/ml, no effect on the surviving cells were observed in the plating efficiency. However, in both experiments at the end of the exposure time, changes in the cell morphology were observed.

No precipitation was observed. DEAE caused a concentration-related increase in pH of the treatment medium.
Test substance: CAS No. 100-37-8 (2-diethylaminoethanol), purity: 99.8%
Reliability: (1) valid without restriction
Well conducted guideline study conducted under GLP conditions. Chosen as the key study for the ICCA Robust Summaries.
Flag: Critical study for SIDS endpoint
26-JUL-2002 (92)

Type: other: DNA Damage in E. Coli
System of testing: WP2, WP67 and CM871
Concentration: 35 to 3500 µg/ml
Metabolic activation: with and without
Result: negative

Method: other: EPA OTS Sect. 798.5500
Year: 1985
GLP: yes
Test substance: other TS

Test substance: CAS No. 100-37-8 (2-diethylaminoethanol), purity: 99.8%, Atochem North America
Reliability: (1) valid without restriction
Well conducted guideline study conducted under GLP conditions.
19-OCT-2001 (93)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay
Species: mouse **Sex:** male/female
Strain: ICR
Route of admin.: oral unspecified
Doses: 20, 100 and 500 mg/kg bw
Result: negative

Method: OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year: 1983
GLP: yes
Test substance: other TS

Method: N.B.: The test conformed to the OECD Guideline 474 of 1983 and US EPA Guidelines of 1985.

TEST ORGANISMS
4-5 week old mice, 18-28 g at study initiation, 5/sex/dose/sampling time

ADMINISTRATION
Vehicle: 0.9% saline
Frequency of treatment: single oral dose
Dosing volume: 10 ml/kg
Sampling times: 24 hr (all groups), 48 hr (control + high dose) and 72 hr (control + high dose).
Controls:
negative, 0.9% saline
positive, 30 mg/kg chlorambucil
N.B.: The doses were chosen based on a preliminary toxicity test using 2 animals/sex/group treated with 312.5, 625, 1250 and 2500 mg/kg bw.

Three bone marrow smears per animal were made.
Clinical observations were made daily. Body weight was measured on day 0 and at the termination.

The frequency of micronucleated cells per at least 1000 polychromatic erythrocytes, as well as the frequency of micronucleated cells per at least 1000 mature erythrocytes was determined. The ratio of polychromatic to mature cells was also determined.

Statistical method: Mann-Whitney U-test.

Result: TOXIC RESPONSE/EFFECTS BY DOSE LEVEL
Mortality and time to death: One male at 500 mg/kg was killed in extremis 42 hours after dosing.
Clinical signs: no signs observed at 20 mg/kg; at 100 mg/kg hunched posture and piloerection (1 male); at 500 mg/kg 1 male was killed in extremis and showed rales, piloerection, hunched posture and a swollen abdomen, and 16 of the remaining animals showed rales, piloerection, hunched posture as well and/or irregular respiration.
Body weight changes: body weight loss was noted in 12/30 mice at 500 mg/kg during the period before termination; other incidences of wt loss were noted throughout the study, but these were small and not dose-related.

The PCE/NCE ratio in the preliminary study was 0.9, 0.8 and 0.5 in the 312.5, 625 and 1250 mg/kg dose groups, respectively. This indicated that the TS reached the bone marrow.

EFFECT ON PCE/NCE RATIO
PCE/NCE ratio (males and females combined):
at 24 hours: 0.9 (all doses); 0.8 (saline control)
at 48 hours: 0.9 (500 mg/kg); 0.9 (saline control)
at 72 hours: 0.7 (500 mg/kg); 0.7 (saline control)

GENOTOXIC EFFECTS
Mean number of micronucleated PCE/1000 PCE (males and females combined)
- 0.9% saline control: 1.2, 0.6 and 0.6 at 24, 48 and 72 hours, respectively;
- 20 mg/kg: 0.8 at 24 hours;
- 100 mg/kg: 0.7 at 24 hours;
- 500 mg/kg: 0.6, 0.8 and 0.3 at 24, 48 and 72 hours, respectively.

STATISTICAL RESULTS
Frequencies of micronucleated polychromatic erythrocytes were not significantly different from controls at any dose or sampling time. Positive controls gave the expected response.

CONCLUSIONS
Under the conditions of this test, diethylaminoethanol did not exhibit a chromosome-damaging (clastogenic) effect, nor was there an indication of an impairment of mitotic chromosome distribution.

Test substance: CAS No. 100-37-8, diethylaminoethanol, purity: > 99%

Reliability: (1) valid without restriction
Well conducted guideline study conducted under GLP conditions. Chosen as the key study for the ICCA Robust Summaries.

Flag: Critical study for SIDS endpoint
26-JUL-2002 (94)

5.7 Carcinogenicity

Species: rat **Sex:** male/female
Strain: other: albino rats from Charles River Breeding Laboratories
Route of administration: oral feed
Exposure period: 2 years
Frequency of treatment: continuously
Post exposure period: no
Doses: 200, 500 and 1000 ppm (the high dose group was gradually increased to 10,000 ppm); corresponding to ca. 11, 25, 50-400 mg/kg bw/day, respectively
Result: negative
Control Group: yes

Method: other
GLP: no
Test substance: other TS

Method: For the DEAE-treated groups, 35 rats/sex were used, and in the control there were 60 rats/sex. Observations were made 6 days/week for signs of toxicity. Body weights and food consumption were recorded weekly for the 1st 26 wks, and biweekly for the next 26 wks. In the 2nd year, body weights and food consumption were measured every 4 weeks. Hematocrits, hemoglobin determinations and total and differential leucocyte counts were made from 5 rats of each sex and group on day 30, 45, 90, 180, 360, 540 and 720. Complete blood counts were performed on 5 additional females from the control and high dose group on day 180, and total white cell counts were performed on 5 additional rats of each sex from all groups on day 360. Urine analyses (albumin, acetone, bilirubin, color, occult blood, sugar, pH, appearance and microscopic sediment examination) were made on day 30, 45, 60, 90, 180, 360, 540 and 720 from pooled sample groups of the same rats used for the blood tests. At 6 and 12 months, 5 animals/sex/group were sacrificed and complete necropsies were performed. Representative tissues from each animal were fixed in formalin. These tissues were: 3 sections of the brain, two sections each of the stomach and small intestine, one section each of the pituitary, thyroid, heart, lung, liver, spleen, kidney, adrenal, pancreas, large intestine, urinary bladder, gonads, bone marrow and any unusual lesion. Animals which died or which were moribund were taken and when post-mortem autolysis was not advanced, target tissues as well as tumors were examined histologically. All of these tissues from the control group and the high dose group were examined microscopically from the 6 and 12 month sample groups. At the end of 2 years, all surviving animals were necropsied. Ten animals/sex from controls and the high dose group were examined histologically. The gonads of all groups of the 2 year sampling were eventually examined histologically. Organ weights and organ/terminal body weights were recorded from all scheduled sacrificed animals.

Remark: According to personal communication with Charles River (Patricia A. Mirley, 24 June 2002), the rats used were likely to be Sprague-Dawleys.
The concentrations were based on the free base, but the substance was given as a HCl salt.
The dietary levels of the free base were:
0, 200, 500 and 1000 ppm
After week 47, the 1000 ppm group was periodically raised as to 10,000 ppm as follows:
Week 48 - 56, 1500 ppm;
Week 57 - 64, 2500 ppm;
Week 65 - 72, 3500 ppm;
Week 73 - 80, 5000 ppm;
Week 81 - 84, 7500 ppm;
Week 85 - 104, 10000 ppm.

Result: There was no increase in the number of tumors in the treated animals as compared to the controls. For information on the interim sacrifices, see section 5.4 (Repeated Dose Toxicity).

CONTROLS AND HIGH DOSE GROUP LESIONS (10 ANIMALS/SEX/GROUP):
Almost all rats of each sex of the control and high dose group which were examined completely showed a mild degree of chronic bronchitis and/or pneumonitis, occasionally of the aspiration variety, plus a mild chronic interstitial nephritis. Minimal squamous metaplasia of thyroid follicular epithelium was found in one male animal of the control and high dose group. Perivascular iron deposition in macrophages in the pancreas was found to a mild degree in four control males and one high dose group male. Roundworms were encountered within the colon of two control and high dose group rats. Patchy adrenal cortical degeneration was present in five control and eight high dose group animals. Cystitis was seen in one control and two high dose group rats. Testicular atrophy was conspicuous in four high dose group males but was absent from the control group, and ovarian atrophy was similarly found in one experimental female only. Miscellaneous findings included one animal each with fatty metamorphosis of the liver, a chronic gastric ulcer, chronic sialadenitis, and spicarditis, all within the high dose group. Careful examination of the sections of the cerebellum in the high dose group animals showed no degenerative changes, cell loss, or other abnormality.

Tumor were numerous in the forty animals which were examined completely. These included pituitary ademonas in 9 animals each in the control and high dose group groups; mammary gland fibromas, adenomes or fibroadenomes in 8 control and 4 high dose group females; and miscellaneous tumors which included one ganglioneuroma, one pheochromocytoma and two renal embryomas in the control group; adrenal cortical adenomas in one control and three high dose group females; and one pancreatic duct adenoma, one hepatoma and three granulosa cell tumors in the high dose group.

Test substance: According to the report, 1.000 ml contains 0.577-0.585 g of Diethylaminoethanol or 0.758-0.766 g Diethylaminoethanol hydrochloride; Pennsalt Chemicals Corp.

Reliability: (2) valid with restrictions
Some essential details are given. A limitation is the lack of a detail on the anorexia observed (i.e. was it associated with DEAE treatment?). A maximum tolerated dose was not achieved, thus, there is no clear basis for the doses chosen. For today's requirements, the number of animals used is a limitation (for the 2 year carcinogenicity endpoint); however, in the 1960s there were no international guidelines. No basis is given for the dose selection.
03-JUL-2002 (95) (87)

5.8.1 Toxicity to Fertility

5.8.2 Developme ntal Toxicity/Teratogenicity

Species: rat **Sex:** female
Strain: Sprague-Dawley
Route of administration: inhalation
Exposure period: days 6 to 15 of gestation
Frequency of treatment: 6 h/d
Duration of test: until day 21 of gestation
Doses: 0.160, 0.320 and 0.486 mg/l (160, 320, and 486 mg/m3; original values: 33, 66, 100 ppm)
Control Group: yes, concurrent no treatment
NOAEL Maternal Toxity: = .16 mg/l
NOAEL Teratogenicity: = .486 mg/l

Method: other
GLP: yes
Test substance: other TS

Method: The concentrations used were selected based on results from a range finding study using 8 pregnant females/group exposed to 10, 50, 100, 150, 200 ppm of the TS on GD 6-15. In the main study, the developmental toxicity of the test substance was evaluated in groups of 25 pregnant rats. The rats were exposed to vapours of the test substance at concentrations of 0 (control), 33, 66, and 100 ppm (ca. 0, 0.158, 0.316, and 0.486 mg/l, respectively). All dams were sacrificed on day 21 of gestation.

Age at start: 83-91 days
Weight at day 0 of gestation: 290-297 g
Route of administration: inhalation (whole body)
Air changes: 12/hour

MATING PROCEDURES: 1 female/1male; day 0 of gestation was confirmed by the presence of a vaginal plug or sperm.

PARAMETERS ASSESSED DURING STUDY:
Mortality/clinical observations: daily
Body weight/food consumption: day 0,6,9,12,15, 18 and 21 of gestation
Examination of uterine content: uterine weight, number of implantation sites, number of corpora lutea, early and late resorptions

Examination of fetuses: weight, number of live and dead fetuses, sex and eternal viscera (1/2 of fetuses) and skeletal abnormalities (1/2 of fetuses)

ORGANS EXAMINED AT NECROPSY: histopathology of abnormal tissues was performed.

Analytical Methods: analytical concentration were determined by an online GC. Nominal concentration were calculated daily from the amount of test substance used and the airflow through the exposure chamber. Analytical concentrations were measured hourly. Samples were drawn from 4 points around the horizontal center plane of each of the exposure chambers to determine homogeneity of the TS distribution.

STATISTICAL METHODS: Bartlett's test, Dunnnett's test, linear regression, Kruskal-Wallis test, Fisher's test, chi-square test, Armitage test

Remark: The average analytical concentrations were 33, 66, 100 ppm These concentrations are comparable to ca. 38, 76 and 116 mg/kg bw per day doses assuming 100% lung deposition and absorption.

Result: Actual dose levels: 0, 33, 66, 100 ppm (analytical); 0, 37, 72, 112 ppm (nominal). The TS remained at least 99.88% pure during the study.

No deaths occurred as a result of exposure to DEAE. Maternal toxicity was observed in the high dose group and included reduced body weights (up to 6% on GD 15), and reduced body weight gain (up to 52%) during the entire exposure period (GD 6-15). Dry rales were observed in up to one third of the animals at the high concentration over GD 11 to 21. Decreased body weight gain was also observed in the 66 ppm group during GD 12 to 15. Statistically significant decreases in mean maternal food consumption were observed during the exposure period in the mid and high dose group and during the post-exposure period in the high dose group.

No treatment-related effects were seen on gestational parameters, including pre- and post-implantation loss or sex ratio. Mean fetal body weights in the treated groups were similar to controls. A statistically significant decrease in mean resorptions was observed in the high dose group. There was no increase in the incidence of malformations (external, visceral, or skeletal) individually or by category. The incidence of a single developmental variation (hypoplastic bones of the forepaw) was significantly (statistically) decreased in the high dose group relative to controls. This was only significant when analyzed on a per fetus basis, and was not significant when analyzed on a per litter basis. [N.B.: A decreased incidence of a developmental variation was not considered an adverse effect.] A statistically significant ($p < 0.05$) increasing dose-trend in the incidence of advanced ossification of the hind paw was reported, but it was not significant when analyzed on a per fetus or per litter basis. In this regard, the number of fetuses effected were 18/185, 18/183, 23/183 & 33/195, and the litters effected were 9/24, 9/25, 14/24 & 13/25 in the 0, 33, 66 and 100 ppm concentration groups, respectively. This increased incidence of advanced

ossification was higher than expected in all groups, including the control, compared to the historical control range (0 - 2.3%) from this laboratory. Thus, this finding was not considered treatment related or biologically relevant.

The no observed adverse effect concentration (NO[A]EC) for maternal toxicity was 0.160 mg/l (160 mg/m3, i.e. 33 ppm) and the NO[A]EC for developmental toxicity was the highest dose tested, i.e. 0.486 mg/l (486 mg/mg3 or 100 ppm).

Test substance: 2-diethylaminoethanol, purity 99.88%, Elf Atochem North America

Reliability: (1) valid without restriction
Well documented, guideline-like study (the major points of OECD Guideline 414 are covered), conducted under GLP conditions. Chosen as the key study for the ICCA Robust Summaries since it was the best study available.

Flag: Critical study for SIDS endpoint

10-JAN-2003 (96) (97)

Species:	rat	**Sex:**	female
Strain:	Sprague-Dawley		
Route of administration:	inhalation		
Exposure period:	days 6 to 15 of gestation		
Frequency of treatment:	6 h/d		
Duration of test:	until day 21 of gestation		
Doses:	ca. 0.05, 0.24, 0.48, 0.73, 0.97 mg/l (i.e. ca. 50, 240, 480, 730 and 970 mg/m3 respectively, or 10, 50, 100, 150, 200 ppm, respectively)		
Control Group:	yes, concurrent no treatment		

Method: other: range-finding study
GLP: yes
Test substance: other TS

Result: The aim of this study was to determine the dose-range for a developmental toxicity study. Groups of 8 pregnant rats were exposed to vapors of DEAE at concentrations of 0 (control), 10, 50, 100, 150, and 200 ppm on gestational days (GD) 6 to 15 and were sacrificed on GD 21. No deaths occurred. Clinical signs were limited to rales and nasal or ocular discharge (150 and 200 ppm). Dams exposed to 150 and 200 ppm lost body weight. Body weight gains were markedly reduced at 100 ppm (GD 6-15) and slightly reduced at 50 ppm (GD 12-15). Decreased food consumption was noted at 100 ppm and above. Pregnancy rates, mean uterine implantation data and fetal body weights were similar in all groups. Percentages of post-implantation loss varied slightly; according to the authors, this was not of biological significance. A relatively high incidence of resorptions was seen in several groups, including the control. According to the authors, this may have been indicative of effects due to general stress associated with inhalation exposure, including the absence of food and water during the daily exposure period. Fetuses were free of any observable abnormalities upon external examination. External fetal malformations were limited to abnormal flexure of the hind-limb in one fetus each of the 50 and 100 ppm groups. Based on these results, concentrations of 0, 33, 66, and 100 ppm were selected for the main study.

Test substance: CAS No. 100-37-8 (2-diethylaminoethanol), purity: 99.8%, Atochem North America
Reliability: (2) valid with restrictions
Meets the necessary criteria of a range finding study.
10-JAN-2003 (97)

Species: rat **Sex:** female
Strain: Sprague-Dawley
Route of administration: gavage
Exposure period: days 0 to 11 of gestation
Frequency of treatment: daily
Duration of test: until day 12 of gestation
Doses: 10, 30, 100 and 250 mg/kg bw
Control Group: yes

Method: other
GLP: yes
Test substance: other TS

Method: The TS was administered to 5 bred female Crl:CD(SD)Br rats/ group. To achieve the desired doses of 10, 30, 100 and 250 mg/kg bw, the dosage volume used was 1, 3, 3.3 and 8.3 ml/kg of 10, 10, 30 and 30 mg/ml solutions. The control group received 8.3 ml/kg of the vehicle. Clinical observations were made twice daily. Body weight and food consumption were measured on GD 0, 1, 3, 7, 9, 11 and 12. The doses were chosen based on a preliminary toxicity study (7 days of treatment in non-mated females). On day 12 the thoracic, abdominal and pelvic cavities were opened and examined. The uterus and ovaries were exposed and examined, and any abnormalities were recorded. The no. of corpora lutea in each ovary were recorded. The uterus was opened and the number of embryos, early and late resorptions and the total number of implantation sites were recorded. The liver and kidneys were weighed at necropsy from all groups, and in the control and high dose group these tissues were prepared for microscopic examination. Paired organs were weighed collectively. The liver, kidneys and gross lesions from all maternal animals were preserved in formalin. Uteri with no macroscopic evidence of nidation were opened and put in 10% ammonium sulfide for the detection of early implantations.

Remark: According to the report, the NOEL was 100 mg/kg bw for maternal toxicity and embryotoxicity. The basis for this was the observation of rales in 2/5 dams of the 250 mg/kg dose and the lack of this finding in the 100 mg/kg dose. Thus, the LOEL for the dams was 250 mg/kg bw. Histologic examinations were limited to the kidneys and liver. Due to the low number of animals in the study, the assignment of clear substance-related embryotoxic effect at 250 mg/kg bw is also difficult since the increase in postimplantaion loss and the decrease in live litter size was due to one animal with 9 resorptions.

Result: All animals survived to sacrifice. The only treatment-related clinical finding in was rales seen in 2/5 dams in the 250 mg/kg bw dose. No internal findings were seen macroscopically. Body weights, body weight gain, food consumption and organ weights of the dams were not effected by treatment. No treatment-related microscopic findings were seen in the liver and kidneys of the 250 mg/kg dosed

dams. In the 250 mg/kg bw dose group post implantation loss was increased by 16.6% (S.D. 20.90), and the number of viable embryos was decreased by 15% (83.4% in the 250 mg/kg group versus 98.6%) in controls). The increase in postimplantation loss and the decrease in live litter size in this group was predominantly due to one female with nine early resorptions (52.9%). Intrauterine parameters were unaffected by treatment in the 10, 30 and 100 mg/kg dose groups.

Test substance: 2-diethylaminoethanol, "100% pure", Elf Atochem North America

Reliability: (2) valid with restrictions
Performed under GLP conditions, the protocol was not widely used. Only early embryo-toxicity can be addressed due to the study design. The study is limited by the number of females used (n = 5).

25-JUL-2002 (98)

5.8.3 Toxicity to Reproduction, Other Studies

5.9 Specific Investigations

5.10 Exposure Experience

Remark: An odor threshold of 0.011 ppm has been reported.

Reliability: (2) valid with restrictions
2.2; basic data given, restrictions

Flag: Critical study for SIDS endpoint

12-AUG-2002 (99)

Remark: An attempt by a laboratory worker to remove animals from an inhalation chamber containing approx. 100 ppm 2-diethylaminoethanol resulted in nausea and vomiting within 5 minutes after a fleeting exposure; no irritation of the eyes or throat was noted during this brief exposure. Other persons in the same room also complained of a nauseating odor but showed no ill effects.

Reliability: (2) valid with restrictions
2.2; basic data given, restrictions

Flag: Critical study for SIDS endpoint

12-AUG-2002 (60)

Remark: Two boilers were prepared for operation by adding corrosion inhibiting chemicals, 2-diethylaminoethanol and cyclohexylamine. Steam produced by the boilers was used for humidity in the work area. Symptoms consistent with acute toxic effects of 2-diethylaminoethanol and cyclohexylamine were noted in 65 of the employees. These included nausea, dizziness, vomiting, and eye, nose, and throat irritation. Exposure concentration is not known.

Reliability: (2) valid with restrictions
2.2; basic data given, restrictions

Flag: Critical study for SIDS endpoint

12-AUG-2002 (100)

Remark: 2-diethylaminoethanol was used to humidify the air in a building. Of 14 samples taken, only two had detectable amounts of 2-diethylamioethanol (0.05 and 0.04 mg/m3). Two bulk samples contained about 30 mg per square meter of the exposed area. A total of 16 of the 35 employees, who participated in medical interviews, complained of eye irritation, 13 of skin irritation, and 6 of headache, nose and throat irritation, or dizziness. Six females reported gynecological problems. Since 2-diethylaminoethanol has a low vapour pressure and was detected on surfaces, skin contact with surfaces was a possible route of absorption.

Reliability: (2) valid with restrictions
2.2; basic data given, restrictions

Flag: Critical study for SIDS endpoint

12-AUG-2002 (101)

Remark: Through a leak in the steam heating system, the anticorrosive agent 2-diethylaminoethanol was released into the air of a large office building. Irritative symptoms of the respiratory tract, and ear, nose and throat were experienced by most of the 2500 employees, and 14 workers developed asthma within 3 months of exposure. Seven of the 14 cases were defined as "confirmed" and 7 of 14 as "suspect", using the NIOSH case definition of occupational asthma. Spirometry obtained in 12 cases was positive in 4 and peak flow testing in 10 of 11 tested persons. Three cases were diagnosed on the basis of work-related symptoms and physical examination alone.

Reliability: (2) valid with restrictions
2.2; basic data given, restrictions

Flag: Critical study for SIDS endpoint

12-AUG-2002 (102)

Remark: Approximately 15 employees in the office support area of a production building had been experiencing rashes. A medical evaluation, consisting of interviews, skin examinations, and a review of medical records was conducted. 2-diethylaminoethanol was identified as the only volatile component. However, environmental samples did not reveal any 2-diethylamioethanol in air samples. Skin examinations revealed an irritant-type rash on the exposed areas of the faces, neck, and hands. The distribution of the rash was consistent with and suggestive of a phototoxic skin reaction. Both the environmental and medical evaluations indicated the source of the dermtitis to be the air-handling system. However, no specific etiologic agent has been identified.

26-JUN-2002 (103)

Remark: Two subjects received 5.6 grams of diethylaminoethanol hydrochloride (CAS 14426-20-1) intravenously in 11.2 % solution. The same two subjects received 5.6 grams of diethylaminoethanol hydrochloride orally in aqueous solution. About 25 % of the drug was excreted in the urine; the remainder was metabolized by an unknown route. A single dose is almost completely metabolized or excreted in 8 hours. The effect of diethylaminoethanol hydrochloride was tested in 14 subjects with ventricular premature contractions in a dose ranging from 05. to 5 grams injected

at a rate of 1 gram per minute. The ectopic ventricular beats disappeared in 13 of 14 cases. In 10 cases it was transient, lasting from 3 to 20 minutes. In 3 cases the ectopic rhythm had not reappeared within a week. Shortly after the injection, most subjects noted a peculiar taste variously described as bitter, metallic, or peppermint-like,
followed by a sensation of warmth, dizziness and fluttering in front of the eyes. Nauseas and vomiting were observed in about 10 to 15 min. in about 15 % of the cases but did not occur until the change in rhythm had been effected. These side effects were usually transient and disappeared 10 to 15
min. following injection. In some instances a transitory fall in both the diastolic and systolic blood pressure was noted which disappeared within 20 minutes.
Diethylaminoethanol is a product of hydrolysis, in vivo, of procaine.

26-JUN-2002 (104) (105)

Remark: Report of therapeutic i.v. administration (1 g in 5 ml, given once a day for up to 10 consecutive days) of diethyaminoethanol in small groups of patients with perioheral circulatory disturbances, hypertension, and bronchial asthma. Feeling of warmth, sweet taste, double vision, dizziness, and nausea were the reported side effects. No further information was given on the galenic of the drug (Dehydasal).

26-JUN-2002 (106)

Remark: Inhibition of lactation was observed in women receiving diethylamioethanol for eclampsia (1 g i.v. once a day for up to 11 days or given as suppository for up to 5 days, dosage of the suppository and the galenic of the drug `Dehydasal` not given). Feeling of warmth, dry mouth, flickering in front of the eyes, and dizziness were the reported side effects.

26-JUN-2002 (107) (108)

5.11 Additional Remarks

Type: Biochemical or cellular interactions

Remark: To determine whether concentrations of DEAE and procaine below those that reduce the amplitude of action potentials might alter the excitability of brain cells, a single microelectrode intracellular recording technique was used to measure firing threshold and action potential amplitude of pyramidal cells in rat hippocampal slices. At low concentrations of both DEAE (less than or equal to 5 mM) and procaine (less than or equal to 0.5 mM), firing threshold was significantly increased ($P < 0.01$), whereas action potential spike amplitude was minimally altered. At higher concentrations, both drugs significantly decreased action potential spike amplitude ($P < 0.025$) as well as increased firing threshold ($P < 0.001$). DEAE tended to increase threshold relatively more than procaine, when drug concentrations that similarly reduced action potential amplitude were compared. All actions of DEAE and procaine

were reversible. Inhibition of action potentials by DEAE and procaine was clearly concentration-dependent (P <= 0.015). DEAE effects on threshold were marginally concentration-dependent (P = 0.08); procaine did not demonstrate clear concentration-dependent effects (P = 0.33) over the concentrations tested in this study. These similar actions of procaine and DEAE on brain cells suggest a mechanism by which intravenous local anesthetics may contribute to the general anesthetic state. Moreover, it appears possible that procaine metabolism and DEAE accumulation may underlie the prolonged effects sometimes seen after intravenous procaine administration.

Test substance: 2-diethylaminoethanol

29-APR-2002 (109)

Type: Biochemical or cellular interactions

Remark: To test whether the products of procaine hydrolysis have local anesthetic actions resembling those of procaine, the authors compared the ability of procaine and its metabolites DEAE and para-aminobenzoic acid (PABA) to block compound action potentials in excised, desheathed frog and rat sciatic nerves. Studies were performed in solutions of impermeant buffers at pH 7.4 (corresponding to mammalian physiologic pH) and at pH 9.2 (close to the pKa of procaine and DEAE) to test for extracellular pH-dependent increases in drug permeation and potency. Both procaine and DEAE inhibited compound action potentials at pH 7.4 and 9.2 in a reversible and dose-dependent manner, and both were approximately ten-fold more potent at pH 9.2 than at pH 7.4, procaine inhibiting the action potential height by 50% at 0.15 mM (pH 9.2) and 1.1 mM (pH 7.4), DEAE at 4 mM (pH 9.2) and 70 mM (pH 7.4). In contrast, PABA at concentrations up to 25 mM and at either pH failed to inhibit compound action potentials, and did not modify the effects of DEAE when both drugs were given together. Procaine produced greater use-dependent block at the higher pH and at higher stimulation rates (100 Hz vs. 40 Hz); DEAE produced almost no use-dependent block. These observations suggest: 1) that DEAE might account for some of the neuropharmacologic activity of procaine in techniques that favor the accumulation of metabolites (such as those requiring large doses or prolonged infusions); and 2) that alkalinization of procaine and DEAE solutions appears to increase their potency for both resting and use-dependent block of action potentials.

Test substance: 2-diethylaminoethanol

01-OCT-2001 (110)

Type: Biochemical or cellular interactions

Remark: 3.1 mmol/l of DEAE inhibited in vitro cholinesterase activity by 50 %. Cholinesterase was isolated from bovine erythrocytes.

Test substance: 2-diethylaminoethanol solution neutralized to pH 6.8 to 7.2 prior to use

01-OCT-2001 (61)

Type: Biochemical or cellular interactions

Remark: In male rats the daily oral application of DEAE at 100 mg/kg bw for 2 weeks led to a statistically significant increase in the liver protein synthesis rate (159% of the control value). Six animals were used per group.

Test substance: 2-diethylaminoethanol

01-OCT-2001 (111)

Type: Biochemical or cellular interactions

Remark: Rats given DEAE for 2 weeks at a level of 200 mg/kg of feed had a slight increase in the level of acetyl coenzyme A (increased from ca. 12 to ca 16 ug/g of tissue) and a decrease in the level of coenzyme A (reduced from ca. 38 ug/g to 30 ug/g tissue). According to the report, the changes were statistically significant. This effect was not seen in tissues from the cerebral cortex, heart, muscle or duodenum.

Test substance: 2-diethylaminoethanol

10-NOV-1993 (112)

Type: Biochemical or cellular interactions

Remark: The effect of the test substance on the release of free oxygen radicals (FOR) by polymorphonuclear (PMN) leukocytes obtained from rabbits and humans was studied.
New Zealand rabbits were given daily i.m. injections of the test substance (15 mg/kg/d) for 35 days; another group of rabbits served as control. Further, human leukocytes (isolated from the peripheral blood of 10 healthy volunteers) were treated with the test substance. The FOR released by the PMN leukocytes were evaluated by in vitro chemoluminescence. Addition of the test substance had no effect on the FOR by PMN leukocytes of control rabbits. In rabbits treated with the test substance, the release of FOR by PMN leukocytes was much more reduced. In treated rabbits, the intensity of the emitted light was 3.46 mV (control: 6.74 mV). An inhibitory effect of the test substance on the FOR release was observed in the human PMN cells stimulated with opsonized zymosan (50 mV in treated cells vs. 67.7 mV in control cultures). According to the authors, the fact that the inflammation was associated with accumulation of free radicals suggested the opportunity to evaluate the test substance as an antioxidant agent.

Test substance: 2-diethylaminoethanol

01-OCT-2001 (113)

Type: Chemobiokinetics general studies

Remark: In a gavage study with rats, 14C-labeled-2-diethylaminoethanol-HCl was reported to be rapidly absorbed into the blood stream. With a dose of 68 mg/kg the maximum concentration in the blood was reached in 30 minutes. With 679 mg/kg the maximum concentration in the blood was reached within 1 hour. Elimination occurred primarily via

the kidney. Elimination via exhalation and the feces played only minor role. The kinetics of urinary elimination were affected by the dose. In this regard, by 6 hours after the application of a 679 mg/kg bw dose 40% was eliminated in the urine, and by 24 hours after application 58.5% was eliminated. When a 68 mg/kg dose was given, then after 6 and 24 hours 17.5% and 37.4% were excreted via the urine, respectively. In the experiment with 679 mg/kg 2-diethylaminoethanol, 90% of the test substance had been eliminated via the urine 10 days after treatment. Some radioactivity was still detectable in the urine 40 days after treatment. 2-Diethylaminoethanol was predominantly (> 60%) excreted unchanged over the first 96 hours. In the same period, the following metabolites were seen based on the recovery of radioactive compounds: 2-ethylaminoethanol (ca. 1%), phosphoric acid-mono-(2-diethylaminoethylester) (2-8%), diethylaminoacetic acid (ca. 10%) and the N-oxide of DEAE (ca. 15-19%). Incorporation into phospholipids was observed. In this study, autoradiography indicated that 2-diethylaminoethanol was widely distributed throughout the body after gavaging. 2-Diethylaminoethanol was concentrated in the liver, reaching a maximum at 7 hours, but thereafter, it decreased. Initially, the central nervous system showed very low levels of activity, but by day 7 it had increased. For the oral dose of 679 mg/kg the biological half-life was 19 hours and for the 67.9 mg/kg dose it was 36 hours.

Test substance: 2-diethylaminoethanol

Flag: Critical study for SIDS endpoint

10-JAN-2003 (114)

Type: Chemobiokinetics general studies

Remark: N.B.: The test substance was never clearly identified, but it was presumably 2-diethylaminoethanol.

Experimental radiopharmacokinetic studies were carried out on female Wistar rats, 23 months and 5 months old, injected with 99mTc-DEAE 2.5 mg/kg b.w., via i.m. administration, and 7.5 mg/kg via p.o. The absorption and the biodistribution of the labeled product were followed in seven organs, including the brain (in thirteen areas of the brain), during the first 240 minutes after administration. The results allowed the conclusion that DEAE is rapidly absorbed and distributed in the different organs, irrespective of administration. The affinity of the different organs or brain areas to DEAE depends on age. Investigations regarding the fate of 99mTc-DEAE in the rat body point out that it undergoes a metabolic splitting leading to ethanolamine, glycine and urea. Elimination studies infer that DEAE is eliminated unchanged or as the mentioned metabolites, especially by the kidney, following first order elimination kinetics. The elimination time is about 72 hours and the half time about 28.

Test substance: 99m-Tc-DEAE, radiochemical purity > 95%, and radionuclidic purity 99.9%; no further data.

07-AUG-2002 (115)

Type: Distribution

Remark: In a study with 2 humans the plasma concentration peaked 3 hours after an oral administration of 5.6 g of 2-diethylaminoethanol-HCl, but was almost undetectable after 8 hours. About 25% of the 2-diethylaminoethanol was excreted unchanged in the urine within 48 hours. Similar excretion results were observed after intravenous administration.

In the same article it was reported that 2-diethylaminoethanol-HCl given to dogs by intravenous infusion (71 mg/kg bw) , distributed rapidly. Three hours after infusion the level of 2-diethylaminoethanol was higher in the tissues examined (muscle, heart, brain, lung, liver and spleen) than in the plasma.

Test substance: 2-diethylaminoethanol-hydrochloride

26-JUL-2002 (116)

Type: Excretion

Remark: Male Sprague-Dawley rats received 15 mmol/kg via gavage. 24 hr later urine was collected, and measurements were made for several amines: approx. 1% of the dose applied was found in the form of trimethylaminoxide, 0.1 % as diethylamine and 0.05% monomethylamine.

Test substance: 2-diethylaminoethanol

29-APR-2002 (117)

Type: Excretion

Remark: 14C-Labeled-2-diethylaminoethanol-HCl was given to rats by intravenous injection at doses of 2.9 µmol/rat (ca. 1.94 mg/kg bw). Cumulative excretion of 19.9 and 42.2% of the radioactivity in the urine was observed after 24 and 48 hours, respectively. Additionally, 8.5 and 29.5% of the radioactivity was excreted via the feces during the same time interval. Excretion via the bile was only measured over the first 6 hours, and was reported to be 5%.

Test substance: 2-diethylaminoethanol

26-JUL-2002 (118)

Type: Metabolism

Remark: The article cites IARC (vol. 17, 1978) to say that on the basis of the chemical structure there is the potential for DEAE to be nitrosated to form N-nitrosodiethylamine and N-nitrosoethylethanolamine, both carcinogens in animals. It also mentions that nitrosation of tertiary amines is normally slower as compared to secondary amines, however, conditions exist where tertiary amines can be readily nitrosated. No data on the kinetics of such reactions was available.

Test substance: 2-diethylaminoethanol

02-OCT-2001 (119)

Type: Metabolism

Remark: Abstract only: Unmetabolized diethylaminoethanol and diethylmethylethanolamine was found in the liver of rats fed the test substance.
Test substance: 2-diethylaminoethanol, no further data

27-JUN-2002 (120)

Type: Metabolism

Remark: The nitrosation potential of the test substance is discussed. Based on the chemical structure, the test substance is presumed to have the potential to be nitrosated to N-nitrosodiethylamine and N-nitrosoethylethanolamine. According to the author, both of these compounds are regarded as potent carcinogens in animals. Considering the nitrosation potential of the test substance, contamination with secondary amines, such as diethanolamine, ethylethanolamine, and diethylamine (which can be nitrosated to N-nitrosodiethanolamine, N-nitrosodiethylamine, and ethylhydroxy-ethylnitrosmine) should be taken into account.
Test substance: 2-diethylaminoethanol

29-APR-2002 (121)

Type: other: Absorption

Remark: The dermal penetration rate (flux) of a saturated aqueous solution of the test substance was calculated to be 3.44 mg/cm3 per hour based on its physical properties. Based on these calculations, the test substance is expected to have a high dermal penetration rate and has a potential for dermal toxicity. According to the authors, this suggests that dermal absorption of the test substance would raise the biological levels above those occurring during inhalation of concentrations equal to the threshold limit value (0.05 mg/L).
Test substance: 2-diethylaminoethanol

08-JAN-2003 (122)

Type: other: Dermal toxicity

Remark: Based on modeling data, DEAE has been predicted to be readily absorbed by via the skin (Fiserova-Bergerova et al., 1990); however, this article reports that the model of Fiserova-Bergerova et al. was too conservative, and is likely to overestimate percutaneous penetration.
Test substance: 2-diethylaminoethanol

29-APR-2002 (123)

Type: other: MAK Value

Remark: The MAK value (1997) was given as 5 ml/m3 (ppm) which corresponds to 24 mg/m3.

07-JAN-2003 (124)

Type: other: NEG and NIOSH Basis for an Occupational Health Standard

Test substance: 2-diethylaminoethanol

27-JUN-2002 (125) (121)

Type: other: OSHA PEL

Remark: The current OSHA standard for DEAE is 10 ppm (50 mg/m3) averaged over an 8 hr work shift. This is also known as the permisible exposure limit (PEL).

Test substance: 2-diethylaminoethanol

29-APR-2002 (126)

Type: other: TLV Citations

Test substance: 2-diethylaminoethanol

29-APR-2002 (127) (128) (129) (130)

Type: other: Waltzing syndrome

Remark: The test substance did not produce the waltzing syndrome (hyperactivity and impaired coordination) in rats.

Test substance: 2-diethylaminoethanol

29-APR-2002 (131)

6.1 Analytical Methods

6.2 Detection and Identification

7.1 Function

7.2 Effects on Organisms to be Controlled

7.3 Organisms to be Protected

7.4 User

7.5 Resistance

8.1 Methods Handling and Storing

8.2 Fire Guidance

8.3 Emergency Measures

8.4 Possib. of Rendering Subst. Harmless

8.5 Waste Management

8.6 Side -effects Detection

8.7 Substance Registered as Dangerous for Ground Water

8.8 Reactivity Towards Container Material

(1) BASF AG, Safety Data Sheet N,N-DIETHYLETHANOLAMINE, 05.07.2000

(2) Commission Directive 2000/33/EC, 25 April 2000 (27th adaption to the technical progress of 67/548/EEC)

(3) TRGS 900 (Technical guidance for hazardous substances - Technische Regeln für Gefahrstoffe) (Germany) of 09/2001

(4) VwVwS (Administrative Regulation on the Classification of Substances Hazardous to Waters into Water Hazard Classes - Verwaltungsvorschrift wassergefährdende Stoffe - VwVwS) (Germany) of 17.05.1999

(5) National Chemical Inventories, 2001 Issue 2

(6) BASF AG, Analytik und Messtechnik, unpublished data, 126157, 05.11.1985

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10.1 End Point Summary

10.2 Hazard Summary

10.3 Risk Assessment