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NEG and NIOSH Basis for an Occupational Health Standard

2-Diethylaminoethanol

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PREFACE

A memorandum has been signed between the Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health (NIOSH), USA, and the Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals (NEG), Sweden. The purpose of the memorandum is to exchange information and expertise in the area of occupational safety and health. One product of this agreement is the development of documents to provide scientific basis for establishing recommended occupational exposure limits. The exposure limits will be developed separately by each country according to the different national policies.

This document on the health effects of occupational exposure to 2-diethylaminoethanol is a product of that agreement. The document was written by Kjell Torén, MD (Department of Occupational Medicine, Sahlgrenska Hospital, St. Sigfridsgatan 85, S–412 66 Gothenburg, Sweden), and was reviewed by NEG and the Education and Information Division (EID), NIOSH.

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1 PHYSICAL AND CHEMICAL PROPERTIES

Chemical name:	2-Diethylaminoethanol
CAS number:	100–37–8
Synonyms:	N,N-Diethylethanolamine; DEAE; DEEA; 2-diethylaminoethyl alcohol; diethyl-(2-hydroxiethyl)amine
Summary formula:	$C_6H_{15}NO$
Structure formula:	$CH_3\text{-}CH_2\text{-}N(\text{-}CH_2\text{-}CH_2\text{-}OH)\text{-}CH_2\text{-}CH_3$
Molecular weight:	117.2
Boiling point (101 kPa):	163°C
Melting point:	–70°C
Density (25°C):	0.88
Vapor pressure (20°C):	0.19 kPa
Flash point (closed cup):	52.2°C
Autoignition temperature:	250°C
Conversion factors:	1 ppm = 4.8 mg/m^3 1 mg/m^3 = 0.21 ppm

Alkanolamine 2-diethylaminoethanol (DEAE) is a colorless, hygroscopic, liquid base with a nauseating odor. Its explosive limit in air is between 1.9% and 28%. DEAE is soluble in water, alcohol, benzene, and ether. Its water solubility has been stated as unlimited (2). The odor threshold is reported to be 0.05 mg/m^3 (0.011 ppm) (2).

2 OCCURRENCE AND USE

2.1 Occurrence

The alkanolamines have been widely used in industry, especially in the chemical and pharmaceutical industries (3). The tertiary amine DEAE is mainly used as an anticorrosive agent in humidifiers and in water-based steam heating systems. Owing to its alkalinity, it reacts with gases such as carbon

dioxide to neutralize the acidity and thus prevent the corrosion of different metals such as iron. DEAE has also been used as a reagent in different chemical analyses. In anion exchange chromatography, DEAE is coupled to cellulose as the anion exchanger (22). It has also been used as a reagent in a colorimetric method for the determination of trinitrotoluene in air (14).

2.2 Air Concentrations in the Environment

A laboratory worker removing animals from an exposure chamber was described as having been exposed to an estimated concentration of 480 mg/m^3 (100 ppm) or less (8).

The concentrations of DEAE in steam condensates were analyzed by Malaiyandi et al. (23). In the first hospital, 225 g of DEAE was added daily to the boiler. The levels in the steam were highest in samples taken 30 min after the addition of DEAE (2,090 mg/l), and decreased during the following 24 hr to about 15 mg/l. In the second hospital, a mixture of DEAE and octadecylamine (ODA) were continuously metered into the boiler feed water (2,400 g each 24-hr period). The levels of DEAE and ODA were fairly constant over time: 3.6–5.2 mg/l for DEAE and 0.11–0.14 mg/l for ODA.

In a museum, air concentrations of 0.05 and 0.04 mg/m^3 were found in 2 of 14 samples. The DEAE had been added to the humidification system (10).

In a laboratory investigation, release of steam from a boiler system resulted in air concentrations between 0.04 mg/m^3 (8.6 ppb) and 0.14 mg/m^3 (29.8 ppb) (20, cited from ref. 17).

The air concentrations of DEAE were assessed in a combined office and electrical laboratory in the basement of a building that was steam heated and steam humidified (9). A mixture of DEAE and cyklohexylamine was added to the water. The humidity in the investigated room varied between 42% and 61%. Cyklohexylamine and DEAE were collected in four 5-min sample periods hourly for a total of 30 hr.

When the humidity was 42%, the mean concentration was 0.0029 mg/m^3 (0.6 ppb); when the humidity was increased to 61%, the mean concentration of DEAE was 0.012 mg/m^3 (2.4 ppb). At the end of the study, the humidifier was put at maximum, after which the concentration of DEAE increased to 0.039 mg/m^3 (8.2 ppb).

In the above-cited situations, the concentrations of cyclohexylamine were 0.7 ppb, 0.8 ppb, and 3.8 ppb, respectively.

2.3 Methods for Analysis of Air Concentrations

The general procedure of analyzing DEAE is to sample it on silica gel and then desorb with methanol. The solution is alkalinized and then analyzed by gas chromatography (30).

Earlier DEAE aerosols in air were absorbed in distilled water and then extracted with purified ethylene chloride (26). Methyl orange was then added, and the complex of methyl orange and DEAE was determined colorimetrically.

3 KINETICS

3.1 Absorption

DEAE is absorbed in the airways, in the gastrointestinal tract, and through the skin. The dermal penetration rates for 132 substances (including DEAE) have been calculated based on their physical properties (11). DEAE was found to have a high dermal penetration rate, meaning that dermal absorption of DEAE will raise the biological levels 30% above those occurring during inhalation of concentrations equal to the TLV. Other substances with comparable properties were ethanolamine and diphenylamine. Besides this study, no quantitative estimations of the absorption of DEAE have been found in the literature.

3.2 Distribution

A dog was given 11 g DEAE intravenously; 3 hr later, the distribution in various tissues was examined (33). The highest concentration (1,227 mg/kg) was found in the spleen. The concentrations in the liver, lungs, brain, and heart were 995, 447, 223, and 134 mg/kg, respectively. The concentration in the plasma was 70 mg/kg.

After oral administration of 5.6 g DEAE to two humans, the peak plasma levels were reached after 3 hr (33).

^{14}C-labeled DEAE was administered intravenously to rats. High concentrations of DEAE were found in the lungs, hypophysis, and adrenals (25).

3.3 Elimination

Two subjects received 5.6 g of DEAE intravenously, which they excreted in the urine (20% and 21%, respectively) as unchanged DEAE (33). The same subjects also received 5.6 g DEAE orally, which they excreted (27% and 23%, respectively) as unchanged DEAE. The time period for the excretion is not mentioned in the paper.

In rats given radioactively labeled DEAE intravenously, 20% was excreted in the urine during the first 24 hr and 43% after 48 hr (25). In feces, 9% was excreted after 24 hr and 30% was excreted after 48 hr. No radioactivity was found in the expired air from rats. The biliary excretion was monitored through a canula in the common bile duct; after 6 hr, 5% of the DEAE was excreted in the bile.

3.4 Metabolism

In rats, about 70% of DEAE is excreted unmetabolized in feces or urine (25). DEAE was administered to five rats by orogastric intubation (37). After 24 hr, small amounts of triethylamine oxide, diethylamine, and monomethylamine were found in the urine. Unmetabolized DEAE and choline were found in the livers of rats fed DEAE (4). The authors claimed that they also found diethylmethylethanolamine in the livers (4).

Procaine, a local anesthetic drug, is rapidly metabolized in serum to DEAE and paraaminobenzoic acid (PABA) (5). This hydrolysis is catalyzed by plasma cholinesterase, also known as procaine esterase (19).

3.5 Biological Indicators of Exposure

No systematic studies of such indicators have been found in the literature. However, DEAE is excreted in the urine (25), and this may be used as a method of assessing exposure.

4 GENERAL TOXICOLOGY

4.1 Noninhalation Toxicology

LD_{50} (rat orally)	
• Neutralized DEAE	5.6 g/kg (8)
• Nonneutralized DEAE	1.3 g/kg (35)
• Given as water solution (10%)	2.5 g/kg (1)
LD_{50} (guinea pig, dermal, undiluted)	1.0 ml/kg (35)
LD_{50} (rabbit, dermal, undiluted)	1.3 ml/kg (1)
LD_{50} (rat, intraperitoneal)	1.2 g/kg (34)
LD_{50} (mouse, intraperitoneal)	0.3 g/kg (34)
LD_{50} (mouse, intramuscular)	0.4 g/kg (34)
LD_{50} (mouse, intravenous)	0.2 g/kg (34)
LD_{50} (mouse, subcutaneous)	1.6 g/kg (34)

4.2 Inhalation Toxicology

Only two published papers have evaluated the inhalation toxicology of DEAE in animals (8, 17). In this chapter, study designs and observations regarding general toxicology are presented. The organ-specific observations are presented separately for each organ system.

Twenty rats were exposed to DEAE (2,400 mg/m^3 [500 ppm]) for 6 hr daily over 5 days. All animals lost 20–40% of their weight; four rats died (8). In the second part of the study, 16 rats were exposed to 960 mg/m^3 (200 ppm) DEAE for 6 hr daily over 5 days. In this group, the animals gained about 10% in weight; no animals died. It is not stated clearly in the paper whether there were controls in this part of the study. In the third part of the study, 50 rats were exposed to 960 mg/m^3 (200 ppm) for 6 hr daily, 5 days a week, for up to 6 months. As controls, 32 rats were exposed to air. The rats were periodically sacrificed and examined. During the first month, seven of the exposed rats showed progressive weight loss and died. The remaining animals also showed depression of growth during the first month as compared with the controls. However, at the end of the observation period, the exposed and unexposed animals were comparable with respect to body and organ weights.

Sixty rats (20 for each exposure group, 10 for each gender) were exposed to DEAE for 5 plus 4 days, with 2 intermediate exposure-free days, to 48 mg/m^3 (10 ppm), 270 mg/m^3 (56 ppm), or 1,440 mg/m^3 (301 ppm) (17). There were also 19 unexposed rats. In the 1,440-mg/m^3 (301-ppm)

group, 90% of the male rats and half of the female rats died. In the other exposure groups, no rats died during the exposure.

The study also included long-term exposure; 40 rats were exposed 6 hr a day, 5 days a week, for 14 weeks. The exposure levels were 53 mg/m^3 (11 ppm), 120 mg/m^3 (25 ppm), and 365 mg/m^3 (76 ppm). Twenty rats served as unexposed controls. Rats exposed to 365 mg/m^3 (76 ppm) exhibited a slower growth rate during the first 2 weeks, and this initial decrement was never recovered. In the long-term study, mortality did not increase.

5 ORGAN EFFECTS

5.1 Systemic Symptoms

Fourteen patients with ventricular premature arrhythmias were given 0.5 g–5 g DEAE intravenously as an 11.2% water solution (33). Shortly after the injection, most subjects felt sensations of warmth, dizziness, and fluttering in front of their eyes. Fifteen percent experienced nausea and vomiting. These symptoms disappeared after 15 min.

A laboratory worker who was removing animals from an exposure chamber was exposed for 30 sec to 480 mg/m^3 (100 ppm) or less DEAE. Within 5 min, he became nauseated and vomited (8).

In 1981, employees in the office area of a production building complained of headaches. DEAE had been added to the air-handling system (24, cited from ref. 28).

In 1988, most of the workers in an assembly industry developed nausea, vomiting, and dizziness (16, 28). Cyclohexylamine and DEAE had been added to the humidification system, but sampling 4 days after the incident failed to identify any remaining DEAE.

The case reports (10, 16, 24) are described in greater detail in chapter 10.

5.2 Upper Airways and Skin

Twenty rats were exposed to DEAE (2,400 mg/m^3 [500 ppm]) for 6 hr daily for 5 days. On the first exposure day, the animals showed signs of marked eye and nasal irritation, which continued throughout the whole exposure period. Among the rats, corneal opacities were observed. Sixteen rats exposed in a similar way to 960 mg/m^3 (200 ppm) DEAE showed mild eye irritation on the first day and slight nasal irritation on the third day. However, in a subsequent 6-month inhalation study of 50 rats exposed to 960 mg/m^3 (200 ppm), there were no signs of nasal and eye irritation as compared with 32 air-exposed control rats. In this study, it is not stated whether histopathological examinations of the upper airways were performed (8). Rats exposed to 1,440 mg/m^3 (301 ppm) of DEAE for 2 weeks showed marked signs of nasal distress, ocular discharges, and opacities (17). This was not noted among the control rats or in rats exposed to 48 mg/m^3 (10 ppm) or 270 mg/m^3 (56 ppm). However, 10 of 20 rats exposed to 270 mg/m^3 (56 ppm) showed mononuclear inflammatory cell infiltrations in the mucosa of the nasal turbinate. This was found in 1 of 19 rats in the 48-mg/m^3 (10-ppm) group and also in 1 rat in the control group.

In the same study, 20 rats were exposed for 14 weeks to 53 mg/m^3 (11 ppm), 120 mg/m^3 (25 ppm), or 365 mg/m^3 (76 ppm) DEAE (17). There were also 20 unexposed control rats. The main findings in this long-term study were histopathological changes in the upper respiratory tract (such as infiltration of inflammatory cells, hypertrophy of the goblet cells, and hyperplasias), indicating an inflammatory reaction in the upper airways (Table 1).

There was also a high incidence of corneal opacities among the rats (17). This was first noticed in the high-exposure group, but by the end of the study it was observed in all animals, including unexposed controls.

Table 1. Prevalence of histopathological changes* in the nasal mucosa after 14 weeks of exposure to DEAE†

Concentration (mg/m^3)	Histopathological examination			
	Immediate post-exposure week 14		One month post-exposure week 18	
	Percent	Fraction	Percent	Fraction
365 (76 ppm)	95	19/20	70	14/20
120 (25 ppm)	55	9/20	65	13/20
53 (11 ppm)	25	5/19	50	10/20
Unexposed	15	3/20	40	8/20

*Defined as infiltration of inflammatory cells and hypertrophy or hyperplasia of the goblet cells.
†Data from ref. 17.

ACGIH cited unpublished information which stated that 0.005 ml undiluted DEAE or a 15% solution of DEAE in glycol (unspecified) instilled in the eyes of a rabbit caused severe eye injury. However, if a 5% solution of DEAE in glycol is instilled, the eye injury will not be classified as severe (1).

In 1981, 24 employees in an office developed skin rashes. Many of them also complained of dry throats. DEAE had been added to the air-handling system of the office. Investigators from the National Institute for Occupational Safety and Health (NIOSH) concluded that the skin rashes resulted from exposure to a condensation or reaction product of DEAE (24, cited from ref. 28).

In a museum, 1,982 workers complained of eye irritation (10). DEAE had been added to the humidification system, and DEAE concentrations of 0.05 and 0.06 mg/m^3 were found in the air in 2 of 14 samples.

In 1988, 70 of 84 workers in an assembly industry complained of nausea and irritation of the nose, eyes, and throat (16). It was found that DEAE and cyclohexylamine had been added to the humidification system, but measurements 4 days after the accident did not reveal any remaining DEAE.

5.3 Effects on the Lower Airways

Sixteen of 20 rats were autopsied after 5 days exposure to 2,400 mg/m^3 (500 ppm) DEAE (8). Four of the rats died during the exposure. All of them showed acute purulent bronchiolitis with infiltration of inflammatory cells in the walls of the bronchioles. Rats exposed to 960 mg/m^3 (200 ppm) for 5 days showed no histopathological changes in the lower airways. Seven of the 50 rats exposed to 960 mg/m^3 (200 ppm) DEAE during 6 months (and 1 of 32 unexposed controls) died during the first 2 months. The probable cause of death for all of them was bronchopneumonia. Histopathological examinations of the surviving animals after exposure ceased showed no increased prevalence of abnormalities in the airways.

Rats exposed to 1,440 mg/m^3 (301 ppm) DEAE for 9 days showed overt signs of respiratory distress such as rales, labored breathing, and gasping (17). Such effects were not observed in groups exposed to 48 mg/m^3 (10 ppm) or 270 mg/m^3 (56 ppm).

In a 14-week study, the rats were either exposed to 48 mg/m^3 (10 ppm), 120 mg/m^3 (25 ppm), or 365 mg/m^3 (76 ppm) DEAE, or they were unexposed. In the 365-mg/m^3 (76-ppm) group, rales and other respiratory noises were observed in the second week. Among the less exposed animals, the same observations were made in subsequent weeks. Every day, the respiratory noises disappeared within 1 hr after exposure, except in the 365-mg/m^3 (76-ppm) group, where some rats continued to exhibit these signs overnight. In the necropsied animals, no exposure-related findings were present in the lower respiratory tracts.

5.4 Effects on the Liver

Fifteen rats were given 50 or 100 mg DEAE daily in their drinking water for 6 months; they showed no exposure-related changes in function or histopathology of the liver (8). Neither were such signs observed among rats exposed to 2,400 mg/m^3 (500 ppm) for 5 days or 960 mg/m^3 (200 ppm) for 6 months (8).

No effects on the liver were reported in rats exposed to 48 mg/m^3 (10 ppm), 270 mg/m^3 (56 ppm), or 1,440 mg/m^3 (301 ppm) DEAE for 2 weeks, or in rats exposed to 53 mg/m^3 (11 ppm) or 120 mg/m^3 (25 ppm) for 14 weeks (17).

However, rats exposed to 365 mg/m^3 (76 ppm) DEAE for 14 weeks showed slightly but significantly increased liver weight (17).

5.5 Renal Effects

Among rats fed 50 or 100 mg DEAE daily for 6 months, increased weight of the kidneys was observed, but no microscopic abnormalities were found (8).

Among rats exposed to 48 mg/m^3 (10 ppm), 270 mg/m^3 (56 ppm), or 1,440 mg/m^3 (301 ppm) DEAE for 2 weeks, no macroscopic or functional abnormalities of the kidneys were reported (17). Rats exposed to 53 mg/m^3 (11 ppm) or 120 mg/m^3 (25 ppm) DEAE for 14 weeks showed no

exposure-related abnormalities with regard to kidney or kidney function. Among the rats exposed to 365 mg/m^3 (76 ppm) DEAE for 14 weeks, increased weight of the kidneys was observed.

5.6 Gastrointestinal Effects

Rats exposed to 2,400 mg/m^3 (500 ppm) or 960 mg/m^3 (200 ppm) DEAE for 5 days and rats exposed to 960 mg/m^3 (200 ppm) DEAE for 6 months had no exposure-related abnormalities in the gastrointestinal tract (8).

At necropsy, rats exposed to 1,440 mg/m^3 (301 ppm) DEAE for 2 weeks showed pathological amounts of intestinal gas. No exposure-related abnormalities in the gastrointestinal tract occurred among animals exposed to 48 mg/m^3 (10 ppm) or 270 mg/m^3 (56 ppm) DEAE (17).

5.7 Effects on the Cardiovascular System

Four grams of DEAE administered intravenously to a man resulted in a prompt rise in the skin temperature, which was maintained for a *considerable period of time* (32). In dogs, DEAE was somewhat more effective than procain in reversing cardiac arrhythmias to sinus rhythm. In a middle-aged hypertensive woman, cardiac arrhythmia was rapidly suppressed by 0.5 g DEAE administered intravenously (32).

Dogs given intravenous injections of DEAE (up to 0.4 g per kg) had no side effects (33). Fourteen patients with ventricular premature beats were given 0.5 g–5 g DEAE intravenously. In 10 of the patients, a transient, therapeutic effect was observed. In three cases, the premature beats had not reappeared in a week. Patients with ventricular tachycardia, auricular fibrillation, and supra-ventricular tachycardia have also been treated with DEAE intravenously with no effect on the arrhythmias (33).

In a review paper, DEAE is mentioned, without further comments, as exhibiting a hypotensive effect of short duration (31).

5.8 Effects on Blood and Bloodforming Organs

Rats fed 50 mg or 100 mg DEAE daily for 6 months showed no alterations of the hemoglobin concentrations in the blood or in the histopathology of the spleen (8). This was also the case when rats were exposed to 2,400 mg/m^3 (500 ppm) or 960 mg/m^3 (200 ppm) DEAE for 5 days or 960 mg/m^3 (200 ppm) DEAE for 6 months.

Rats exposed to 1,440 mg/m^3 (301 ppm) DEAE for 9 days showed reduced weight of the spleen at necropsy. Hematological parameters (counts of erythrocytes, leucocytes, reticulocytes, platelets, and hemoglobin concentration) were not available for the 1,440-mg/m^3 (301-ppm) group, but they were normal among the rats exposed to 48 mg/m^3 (10 ppm) or 270 mg/m^3 (56 ppm) DEAE for 9 days. The hematological parameters and the spleen were not affected among rats exposed to 53 mg/m^3 (11 ppm), 120 mg/m^3 (25 ppm), or 365 mg/m^3 (76 ppm) DEAE for 14 weeks (17).

5.9 Effects on the Central Nervous System

In the 1940s, DEAE has been used with good effect for post-operative analgesia (32). Certain amines have been shown to cause a *waltzing syndrome* (i.e., hyperactivity and impaired coordination) in rats. In a study where several amines were screened with regard to this, DEAE was not found to produce the *waltzing syndrome* (13).

Rats were decapitated and their brains were removed and placed in artificial cerebrospinal fluid (7). DEAE was added to the fluid in different concentrations. DEAE increased the firing threshold in certain brain cells. At higher concentrations, DEAE also decreased the action potential spike amplitude.

5.10 Effects on Peripheral Nerves

As a main metabolite of procaine, DEAE has a local anesthetic effect (32). It has been shown that DEAE inhibits action potentials (15), especially when the DEAE solution is alkaline (6).

5.11 Other Effects

Rats exposed to 1,440 mg/m^3 (301 ppm) DEAE for 9 days showed increased weight for the adrenals at necropsy (17). This was not observed in rats exposed to 48 mg/m^3 (10 ppm) or 270 mg/m^3 (56 ppm) for 9 days, or in rats exposed to 53 mg/m^3 (11 ppm), 120 mg/m^3 (25 ppm), or 365 mg/m^3 (76 ppm) for 14 weeks.

6 IMMUNOTOXICITY

Rats exposed to 1,440 mg/m^3 (301 ppm) of DEAE for 9 days showed decreased weight of the thymus (17). This was not observed at lower exposure concentrations.

7 MUTAGENICITY AND GENOTOXICITY

DEAE was not mutagenic in Salmonella strains TA98, TA100, TA1535, and TA1537, with or without metabolic activation (36).

8 CARCINOGENICITY

Squamous metaplasia was found in the nose of one rat exposed to 270 mg/m^3 (56 ppm) for 2 weeks (17). When exposed for 14 weeks, squamous metaplasias were found immediately post-exposure in the noses of five rats exposed to 120 mg/m^3 (25 ppm) and in nine rats exposed to 365 mg/m^3 (76 ppm). One month post-exposure, squamous metaplasias were found in three rats exposed to 120 mg/m^3 (25 ppm) and in six rats exposed to 365 mg/m^3 (76 ppm) (17). Procain, which is rapidly metabolized to DEAE and PABA, is not regarded as a carcinogen (21).

The nitrosation potential of DEAE has been discussed earlier (29). Nitrosation is normally slower for tertiary amines (such as DEAE) than for secondary amines (27). However, the nitrosation potential is hard to predict, as it is affected by many factors such as alkalinity, substrate concentration, and presence of microorganisms (18). On the basis of its chemical structure, DEAE has the potential to be nitrosated to N-nitrosodiethylamine (NDEA) and N-nitrosoethyl-ethanolamine. Both of these compounds are regarded as potent carcinogens in animals (18). However, no data on such reactions in the work environment have been found.

When considering the nitrosation potential of DEAE, one should be aware that the commercial product may be contaminated with different secondary amines such as diethanolamine, ethylethanolamine, and diethylamine (29), which could be nitrosated to N-nitrosodiethanolamine (NDELA), NDEA, and ethylhydroxy-ethylnitrosamine.

9 EFFECTS ON REPRODUCTION

Rats exposed to 1,440 mg/m^3 (301 ppm) DEAE for 9 days showed decreased gonad weight at necropsy (17). This was not observed in rats exposed to 48 mg/m^3 (10 ppm) or 270 mg/m^3 (56 ppm) for 9 days, or in rats exposed to 53 mg/m^3 (11 ppm), 120 mg/m^3 (25 ppm), or 365 mg/m^3 (76 ppm) for 14 weeks.

Any differences between the sexes were not mentioned in the paper. Procaine, which is rapidly metabolized to DEAE and PABA, has not been associated with an increased risk of congenital malformations (12).

10 CASE REPORTS

There are three reports of clusters of cases associated with exposure to DEAE.

In 1981, 24 employees in the office of a factory developed skin rashes. Many of them also complained of dry throat, headache, and chest tightness (24). DEAE had been added to the air-handling system, and NIOSH investigators concluded without further specification that the dermatitis resulted from exposure to a condensation or reaction product of DEAE.

In 1982, employees in a museum where DEAE had been added to the humidfication system reported eye irritation and dermatitis (10). DEAE had been added to the water in 1977 in a concentration of approximately 15 ppm. Ten air samples obtained with a low sampling rate showed no DEAE; the detection limit was 0.4 mg/m^3. In two of four air samples obtained with a high flow rate, concentrations of 0.05 mg/m^3 and 0.04 mg/m^3 were found. With high flow rates, the detection limit was 0.04 mg/m^3. The employees had also noticed an oily film on the surfaces of the display cases. The film contained 30 mg DEAE/m^2 of exposed area. Sixteen of 35 employees reported eye irritation, and 13 reported some sort of skin irritation since beginning work at the museum. The investigators concluded that sporadic contact with surfaces containing DEAE may have been associated with some of the reported irritative effects.

In 1988, 70 of 84 assemblers in an electrical manufacturing firm developed nausea, vomiting, dizziness, and eye, nose, and throat irritation (16, 28). The symptoms occurred shortly after the employees detected an ammonia or radiator-like smell. The odor coincided with the introduction of steam (derived from the plant boiler) into the building for humidification. The steam was turned off, but when it was reintroduced 3 days later, the same odor appeared. NIOSH investigators discovered that DEAE and cyclohexylamine had been added to the boiler at four times the normal strength. Four days later, the steam was once again reintroduced for collecting samples from air and boiler water. However, no remaining DEAE or cyclohexylamine was detected. The investigators thought this might be caused by dilution in the system over the preceding 4 days.

11 EXPOSURE-EFFECT RELATIONSHIP

The effects of DEAE on humans and experimental animals are summarized in Tables 2 through 4.

Table 2. Effects of DEAE on man

Dose	Effects	Reference
0.5 g–5 g (oral)	Feeling of warmth, dizziness, and fluttering in front of the eyes	33
4 g (intravenous)	Increased skin temperature	32
5 g (intravenous)	Transient effect on premature ventricular beats	33
480 mg/m^3 (maximum value inhalation)	Nausea and vomiting	8

Table 3. Effects of DEAE on experimental animals for noninhalation exposure routes

Route	Dose	Animal	Effects	Reference
Oral	5,600 mg/kg*	Rat	LD_{50}, neutralized	8
Oral	2,500 mg/kg	Rat	LD_{50}, water solution 10%	1
Subcutaneous	1,600 mg/kg	Mouse	LD_{50}	34
Oral	1,300 mg/kg	Rat	LD_{50}, alkaline	35
Intraperitoneal	1,200 mg/kg	Guinea Pig	LD_{50}	34
Oral	500 mg/kg daily for 6 months	Rat	Slightly decreased growth; increased kidney weights	8
Intramuscular	400 mg/kg	Mouse	LD_{50}	34
Intraperitoneal	300 mg/kg	Mouse	LD_{50}	34
Oral	250 mg/kg daily for 6 months	Rat	Increased kidney weights	8
Intravenous	200 mg	Mouse	LD_{50}	34

*mg/kg of body weight.

Only a few studies permit the assessment of dose-dependent effects. In man, exposure around 400–500 mg/m^3 for 30 sec has produced nausea and vomiting within 5 min.

In rats, exposure to concentrations exceeding 1,400 mg/m^3 for a few days seems to produce a wide range of toxicological effects. The most pronounced effects seem to be severe irritation of both the upper and lower airways. Mortality is also high. Exposure to 100–1,400 mg/m^3 results in less severe irritation in both the upper and lower airways. The lowest concentration at which increased mortality was observed was 960 mg/m^3. The rats died of bronchopneumonia. The lowest concentration at which valid histopathological signs of inflammation in the upper airways could be found was exposure to 120 mg/m^3 for 14 weeks.

However, rats exposed to 53 mg/m^3 developed rales after some weeks of exposure. No histopathological changes were found in the lower airways of those rats. Exposure to concentrations less than 53 mg/m^3 for 14 weeks seems not to cause any morphological changes in the upper airways, and no sign of irritation has been reported.

Table 4. Effects of DEAE in rats during inhalation studies

Concentration (mg/m^3)	Period	Effects	Reference
2,400	6 hr/day for 5 days	Decreased weight, severe ocular, nasal, and respiratory irritation; 4/20 rats died	8
1,440	6 hr/day for 9 days	14/20 rats died; severe nasal and respiratory distress	17
960	6 hr/day for 5 days	Mild irritation in eyes and nose; no pathological changes in lower airways	8
960	6 hr/day, 5 days/week for 6 months	Initial growth depression eye and nasal irritation; 7/50 rats died of broncho-pneumonias	8
365	6 hr/day, 5 days/week for 14 weeks	Decreased growth, nasal irritation, rales	17
270	6 hr/day for 9 days	Nasal irritation	17
120	6 hr/day, 5 days/week for 14 weeks	Nasal irritation	17
53	6 hr/day, 5 days/week for 14 weeks	No signs of nasal irritation; rales after 2 weeks	17
48	6 hr/day for 9 days	No signs of irritation in upper or lower respiratory tract	17

12 RESEARCH NEEDS

DEAE probably has many uses in different industrial processes and as a corrosion inhibitor in water-based systems. There is a remarkable lack of exposure data. Hence, studies investigating exposure in different occupational groups should be performed. Exposure assessments regarding nitrosamines are also needed.

DEAE is excreted in urine, and studies should be performed to investigate whether this could be used for biomonitoring.

On the basis of theoretical calculations, DEAE seems to be absorbed through the skin. This property should be evaluated in experimental studies.

There is a great need for basic toxicological testing regarding sensitization and reproductive and developmental effects. Testing for mutagenicity and genotoxicity is also needed. Cancer studies should be conducted.

There is also a great need for inhalation studies in the lower-dose interval (<100 mg/m^3), both in man and in animals. These studies should investigate inflammatory changes in the upper and lower airways.

13 DISCUSSION AND CONCLUSIONS

In animals, the critical effects of DEAE seems to be irritation of the mucous membranes in both lower and upper airways. The very limited information for humans indicates that the critical effect of DEAE is irritation of the mucous membranes and skin. DEAE also affects the nervous system and the heart, but this is not important in occupational settings.

Like other alkanolamines, DEAE is a potent irritant of the mucous membranes in the airways (probably owing to its alkalinity). In rats, there is some support for a dose-response relationship regarding irritation in the upper airways. In rats, effects on the upper airways seem to develop at exposure concentrations of 120 mg/m^3.

The exposure time is important. Rats exposed to 48 mg/m^3 for 9 days showed no signs of respiratory impairment. Rats exposed to 53 mg/m^3 developed rales after 2 weeks of exposure. These exposure concentrations (53 mg/m^3 and 48 mg/m^3) are the lowest to which animals have been exposed. Hence, it is not possible on the basis of the literature to determine a no-effect concentration for DEAE.

14 SUMMARY

Torén K. 2-Diethylaminoethanol. NEG and NIOSH Basis for an Occupational Health Standard. Arbete och Hälsa 1994;25:1–17.

The literature on 2-diethylaminoethanol has been reviewed and health effects of DEAE have been evaluated. There is very limited information on health effects in humans. Based on these limited data, the critical effect seems to be irritation of the mucous membranes and skin. In animals, the critical effect seems to be irritation of the mucous membranes of both lower and upper airways.

Key words: 2-diethylaminoethanol, occupational exposure, occupational exposure limits

15 SUMMARY IN SWEDISH

Torén K. 2-Dietylaminoetanol. NEG och NIOSH underlag för hygienskt gränsvärde. Arbete och Hälsa 1994;25:1–17.

Genomgång av litteraturen om 2-dietylaminoetanol samt utvärdering av hälsoeffekter. Informationen om hälsoeffekter hos människa är mycket begränsad. På grundval av dessa data tycks den kritiska effekten vara irritation av slemhinnor och hud. Hos djur tycks den kritiska effekten vara irritation av slemhinnor i övre och nedre luftvägar.

Nycdkelord: 2-diethylaminoetanol, hygieniskt gränsvärde, yrkesmässig exponering

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APPENDIX I.

Permitted or recommended maximum levels of 2-diethylaminoethanol in air

Country	ppm	mg/m^3	Comments	Year	Reference
Denmark	10	50	H	1988	1
Finland	10	15	15 min, H	1993	2
Iceland	—	—	—	1989	3
Netherlands	10	50	H	1994	4
Norway	10	50	H	1989	5
Sweden	—	—	—	1993	6
USA (ACGIH)	10	48	Skin	1991–92	7
(NIOSH)	10	50	Skin	1990–91	8

H = dermal absorption

Skin = the cutaneous route, including mucous membranes and eyes (vapour or contact) contributes significantly to the overall exposure.

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