FOREWORD INTRODUCTION

3-AMINOPROPYLDIMETHYLAMINE

CAS N°: 109-55-7

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	109-55-7
Chemical Name	3-Aminopropyldimethylamine
Structural formula	H_2N-CH_2-CH_2-CH_2-N(CH_3)$_2$

CONCLUSIONS AND RECOMMENDATIONS

The chemical is currently of low priority for further work

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

In Germany 3-Aminopropyldimethylamine is produced by two companies. In 1994 the total production volume was about 15 000 t. 3-Aminopropyldimethylamine is used as an intermediate in the production of binding agents, ion-exchange materials, flocculating agents (water treatment), cosmetic agents, washing and cleaning agents (betaines), additive for petrol and other fuels, polyurethane fibres and lubricants, dyes, agrochemicals, agents used in the photographic and textile industries, etc. 3-Aminopropyldimethylamine is also used directly as a hardener in epoxy resins in the plastics industry, as a cross-linking agent for cellulose fibres in the paper industry and as an anti-shriking agent for leather.

Environment

3-Aminopropyldimethylamine has a log Kow of –0.35, a vapour pressure of 8 hPa and is miscible in water.. The substance is strongly basic. The pK_1 value is 9.9 and the pK_2 value 7.7. Therefore, it can be assumed that under environmental conditions the compound is completely protonated. The log Kow of -0.35 measured for the neutral 3-Aminopropyldimethylamine is not useful for modelling the environmental distribution properties of the ionized form.

Experimental data about adsorption of 3-Aminopropyldimethylamine onto soils or sediments are not available. However, due to the physical chemical properties soil sorption via ion-exchange and chemisorption are possible. As 3-Aminopropyldimethylamine in aqueous solutions is always protonated, no volatilisation from treatment plants or surface waters is expected. Based on the physico-chemical properties, the preferred environmental compartment of 3-Aminopropyldimethylamine is the hydrosphere (Mackay I: ca. 97 %).

3-Aminopropyldimethylamine can be classified as readily biodegradable without fulfilling the 10-day window criterion.

No bioaccumulation studies with DMAPA are available.

In short-term tests with fish, daphnids and algae the following results were found: *Leuciscus idus*: 96 h-LC_{50} = 122 mg/l; *Daphnia magna*: 48h-EC50 = 60 mg/l; *Scenedesmus subspicatus*: 72h-EC50 = 56 mg/l. With these data the substance can be classified as moderately toxic. With an assessment factor of 1000 a PNECaqua of 56 µg/l can be calculated from the EC50 for green algae.

Human Health

3-Aminopropyldimethylamine has been found to be harmful follwing oral administration to rats. Based on the results of the sensitisation test on the skin 3-Aminopropyldimethylamine has been classified as having a sensitising effect. 3-Aminopropyldimethylamine showed strong irritating or

corrosive effects. In a oral 28-day subchronic toxicity study with rats, the no-observed-adverse effect-level (NOAEL) was 50 mg /kg bw/day. In the oral reproduction/developmental toxicity sreening test the no-observed-adverse effect-level (NOAEL) was 200 mg/kg bw/day. 3-Aminopropyldimethylamine was not mutagenic in the Ames Test and in a mouse micronucleus assay. The corrosive property of the compound prompts workers to limit the potential exposure to this chemical.

IF FURTHER WORK IS RECOMMENDED, SUMMARISE ITS NATURE

No need for further work

3-Aminopropyldimethylamine

CAS-NO.: 109-55-7			PROTOCOL	RESULTS
PHYSICAL CHEMICAL				
2.1	Melting Point		DIN 51597	< 60 °C
2.2	Boiling Point		DIN 51751	135 °C (at101.3 kPa)
2.3	Density		DIN 51 757	818 kg/m^3
2.4	Vapour Pressure		NA	8 hPa at 20°C
2.5	Partition Coefficient (Log Pow)		OECD 107	-0.352
2.6 A	Water solubility			miscible at 20°C
ENVIRONMENTAL FATE / BIODEGRADATION				
3.1.1	Photodegradation		calc. (Atkinson)	In air $T_{1/2}$ = 4.8 hour
3.3	Transport and Distribution		calculated (fugacity level 1 type)	In air % In water 97 % In sediment % In soil % In biota %
3.5	Biodegradation		OECD 301 D	readily biodegradable, without fulfilling 10-day window criterion

CAS-NO.:109-55-7		SPECIES	PROTOCOL	RESULTS
ECOTOXICOLOGY				
4.1	acute/prolonged toxicity to fish	Leuciscus idus	DIN 38 412 / 15	LC_{50} (96hr) =122 mg/l
4.2	acute/prolonged toxicity to aquatic invertebrates (daphnia	Daphnia magna	79 /831 / EEC, C.2	EC_{50} (48hr) = 60 mg/l
4.3	toxicity to aquatic plants e. g. algae	Scenedesmus subspicatus	UBA	EC_{50} (72hr) = 56 mg/l $EC2_0$ (72hr) = 45.5mg/ll
TOXICOLOGY				
5.1.1	acute oral toxicity	rat	NA	LD_{50} = 922mg/kg
5.1.2	acute inhalation toxicity	rat	NA	$LC_{50\ (4h)}$ > 4.31 mg/l
5.4	repeated dose toxicity	rat	NA	NOAEL = 50 mg/kg
5.5	genetic toxicity in vitro			
A.	bacterial test (gen mutation)	S. typhimurium	Ames	- (with metabolic activation) - (without metabolic activation)
5.6	mammalian cytogenetic in vivo test	mouse	OECD 474	negative
5.8	toxicity to reproduction	rat	OECD 421	NOAEL = 200 mg/Kg (rep. tox. parental, rats)
5.9	developmental toxicity / teratogenicity	rat	OECD 421	NOEL = 200 mg/Kg (pregnancy/litter) NOEL = 200 mg/Kg (foetal data)
5.11	experience with human exposure			

SIDS INITIAL ASSESSMENT REPORT

1. IDENTITY

Name:	3-Aminopropyldimethylamine
Synonyms:	N,N-Dimethyl-1,3-diaminopropane Dimethyl amino-propylamine 1-Amino-3-(dimethylamino) propane DMAPA
Cas-No:	109-55-7
Empirical Formula:	$C_5H_{14}N_2$
Molecular Weight:	102.18 g/mol
Structural Formula:	$H_2N\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}N(CH_3)_2$
Water solubility:	miscible (20 °C)
log Pow:	-0.35
Vapour pressure:	8 hPa (20 °C)

2. GENERAL INFORMATION ON EXPOSURE

In Germany 3-Aminopropyldimethylamine (DMAPA) is produced by two companies. In 1994 the total production volume was about 15 000 t [1].

Two other companies are cited in the IUCLID data sheet. One is located in Germany and imports DMAPA in an amount of 1000 - 5000 t/a. The other European company has a production capacity for DMAPA of 1000 - 5000 t/a.

There is no information on other production sites. No further information is available on imports, exports or total consumption in Germany.

DMAPA is produced from acrylonitrile and dimethyl amine in a 2-stage process. In the first stage the reaction of the starting materials, acrylonitrile and dimethyl amine lead to raw reaction products containing approximately 99 % 3-dimethyl aminoproprionitrile. This addition product is hydrogenated to DMAPA in the second stage of the manufacturing process. As a result of competing and follow-on reactions occuring during the course of synthesis, a number of by-products are produced. These are removed from the DMAPA through multiple-stage distillation [1]. The pure product has a DMAPA content of > 99.5 %.

DMAPA is used as an intermediate in the production of binding agents, ion-exchange materials, flocculating agents (water treatment), cosmetic agents, washing and cleaning agents (betaines), additive for petrol and other fuels, polyurethane fibres and lubricants, dyes, agrochemicals, agents used in the photographic and textile industries, etc.

DMAPA is also used directly as a hardener in epoxy resins in the plastics industry, as a cross-linking agent for cellulose fibres in the paper industry and as an anti-shriking agent for leather [1].

3. ENVIRONMENT

3.1 Environmental Exposure

3.1.1 General Discussion

a) Releases into the environment

Releases into the environment may occur during production, processing, direct use as hardener and during the use of subsequent products due to possible residues of DMAPA.

From the information on the quantitative use pattern the two German manufacturers gave it can be estimated that about 10 000 t/a are used as intermediate for the production of flocculating agents and washing and cleaning agents, further 5000 t/a are used as intermediate for other products and only about 150 t/a are used directly as hardener in expoxy resins.

The total production amount from one German manufacturer is sold and processed at other sites, whereas at the second manufacturing site both production and processing takes place [1].

There are no environmental monitoring data of DMAPA available.

b) Degradation

The calculated half-life due to photochemical-oxidative degradation in the atmosphere by OH-radicals is 3.2 h.

The biodegradability of DMAPA was examined in a closed bottle test comparable to OECD guideline 301 D. After 20 days a biodegradation of 69 % was achieved with adapted inoculum and of 65 % with non-adapted sludge. However, the 10-day window criterion was not fulfilled. In a Zahn-Wellens test according to OECD guideline 302 B using industrial activated sludge an elimination of 100 % after 15 days was found.

From the cited test results it can be concluded that DMAPA is readily biodegradable. As the 10 day window criterion is not fulfilled a biodegradation rate constant for waste water treatment plants of 0.3 h^{-1} is assumed.

According to the model Simpletreat the following distribution and elimination in wwtp can be estimated based on the above cited physico-chemical properties as well as the biodegradation rate constant of 0.3 h^{-1}:

% to air	0
% to water	33
% to sludge	0
% degraded	67
% removal	67

c) Environmental distribution

DMAPA is strongly basic. The pK_1 value is 9.9 and the pK_2 value 7.7. Therefore, it can be assumed that under environmental conditions the compound is completely protonated. The log Kow of -0.35 measured for DMAPA is not useful for modelling the environmental distribution properties.

Experimental data about adsorption of DMAPA onto soils or sediments are not available. The log Pow of -0.35 indicates a low physisorption to soil solids. However, due to the physical chemical properties soil sorption via ion-exchange and chemisorption are possible.

As DMAPA in aqueous solutions is always protonated, no volatilisation from treatment plants or surface waters is expected.

Based on the physico-chemical properties, the preferred environmental compartment of DMAPA is the hydrosphere (Mackay I: ca. 97 %).

d) Bioaccumulation

No bioaccumulation studies with DMAPA are available. The log Kow of -0.35 indicates a low bioaccumulation potential.

3.1.2 Predicted Environmental Concentration

3.1.2.1 Aquatic compartment

Local Exposure

a) Releases during prodcution

For the calculation of a **generic exposure scenario** a production volume of 10 000 t/a is used. It is assumed that production and processing take place at the same site. The following input parameters are used according to the Technical Guidance Document [2]:

- release factor for production: 0.3 %
- release factor for formulation: 0.7 %
- elimination in stp: 67 %
- duration of emission: 300 d
- flow-rate of receiving river: 60 m^3/s

A PEC_{local} of **21.2 µg/l** can be calculated.

For the two German production sites **site-specific PEC_{local}** can be calculated due to more precise data.

Production site 1:

From production and processing of DMAPA it is estimated that in 1994 less than 4 t are released with the waste water into the wwtp. Using an elimination of 67 % and the site-specific flow-rate of the receiving river of 734 m^3/s a PEC_{local} of **0.07 µg/l** can be calculated.

Production site 2:

All produced DMAPA is sold, i.e. no processing takes place. Due to the production method no emissions of DMAPA into the waste water occur. Releases may only occur during cleaning of the reaction vessels.

b) Releases during processing

From one manufacturer the total production amount of DMAPA (5000 t/a) is sold. 150 t/a are used as hardener in epoxy resins. The other 4850 t/a are used as intermediate. As the number of customers is unknown it is assumed that the total amount used as intermediate is processed at one site.

For the calculation of the PEClocal the following paramters according to the TGD are used:

processing volume:	4850 t/a
release factor during processing:	0.7 %
number of processing days:	300 d/a
elimination in wwtp:	67 %
flow rate of receiving river:	60 m3/s

A PEClocal of **7.2 µg/l** can be calculated.

c) Released during use as hardener in epoxy resins

The release during use as hardener in epoxy resins is estimated according to the A/B-tables of the TGD. The following assumptions are made:

volume:	150 t/a
content of hardener in expoy resin:	5 %
release factor during use:	0.005 % (Tab. A 3.11)
fraction of main source:	0.15 (Tab. B 3.9)
number of days:	180 d/a (Tab. B 3.9)
elimination in wwtp:	67 %
flow rate of wwtp:	2000 m^3/d
dilution factor:	10

A PEClocal of **0.1 µg/l** can be calculated.

d) Release during use of subsequent products

No information about subsequent products, their emissions and residual contents of DMAPA are available. Therefore, no PEC can be calculated for this exposure scenario.

e) Sediment

According to chapter 3.1.1 c the distribution of DMAPA between water and sediment is unclear (influence of ionization). Therefore, no exposure model for the sediment compartment can be calculated.

3.1.2.2 Atmosphere

During production at the German sites, no significant emissions into the atmosphere occur [1]. In aqueous solution the substance is ionized, and therefore volatilisation from waste water treatment plants is unlikely.

For the use as hardener in epoxy resins the following exposure scenario can be calculated according to the A/B-tables in appendix I of the TGD:

volume:	150 t/a
release factor during use:	0.15 (Tab. A 3.11)
fraction of main source:	0.15 (Tab. B 3.9)
number of days:	180 d/a (Tab. B 3.9)

A Clocal_air of **5 µg/m^3** is calculated.

3.1.2.3 Terrestrial Compartment

Releases of DMAPA into the terrestrial compartment are expected from aerial deposition. From the local concentration in air of 5 µg/m^3 an annual average deposition flux of 0.0188 mg/m^2/d can be calculated. From this a local soil concentration of **2 µg/kg** soil can be derived. The respective pore water concentration is **8.5 µg/l**. (see Annex 1). However, it has to be kept in mind that the pore water concentration cannot be estimated properly due to the uncertainty in soil behaviour (unclear influence of ionization).

3.2 Effects on the Environment

3.2.1 Aquatic Effects

a) Toxicity to fish

Leuciscus idus: 96 h-LC_0 = 100 mg/l
96 h-LC_{50} = 122 mg/l
96 h-LC_{100} = 140 mg/l
(static, nominal concentration; at 10 - 500 mg/l there was a concentration-related increase in pH value: max. pH: 10.6 at 500 mg/l)

b) Toxicity to invertebrates

Daphnia magna: 24 h-EC_0 = 50 mg/l
24 h-EC_{50} = 68.3 mg/l
24 h-EC_{100} = 100 mg/l

48 h-EC_0 = 25 mg/l
48 h-EC_{50} = 59.5 mg/l
48 h-EC_{100} = 100 mg/l

(static; nominal concentration; effect: immobilisation; pH: 7.92 - 9.87)

c) Toxicity to algae

Scenedesmus subspicatus 72 h-EC_{20} = 45.5 mg/l
72 h-EC_{50} = 56.2 mg/l
72 h-EC_{90} = 105.6 mg/l

96 h-EC_{20} = 37.1 mg/l
96 h-EC_{50} = 57.5 mg/l
96 h-EC_{90} = 110.3 mg/l

(nominal concentration; effect: growth rate)

At low concentrations, DMAPA was found to have an eutrophizing effect.

d) Toxicity to microorganisms

Pseudomonas putida: 17 h-EC_{10} = 70 mg/l
17 h-EC_{50} = 95 mg/l
17 h-EC_{90} = 120 mg/l

(nominal, effect: growth inhibition)

e) Derivation of $PNEC_{aqua}$

Short-term tests with species from three trophic levels are available. *Daphnia* and algae were the most sensitive species having effect values of 59.5 mg/l and 56.2 mg/l.

As the test media in all tests were not neutralized the effects found may partly be due to the basicity of the test substance.

For the derivation of the PNECaqua an assessment factor of 1000 is applied to the 72h-EC_{50} of 56.2 mg/l found with *Scenedesmus subspicatus*.

Therefore: **PNECaqua = 56.2 mg/l / 1000 = 56.2 µg/l**

3.2.2 Terrestrial Effects

There are no tests with terrestrial organisms available. Therefore, the risk assessment for this compartment has to be conducted by using the PNECaqua.

3.3 Initial Assessment

3.3.1 Aquatic compartment

With a PNEC of 56 µg/l, the exposure/effect ratios are:

Life cycle	PEC [µg/l]	PEC / PNEC
production and processing (generic)	21.2	0.38
production and	0.07	0.001

processing (site-specific)		
processing (generic)	7.2	0.13
use as hardener in epoxy resins (generic)	0.1 µg/l	0.002

3.3.2 Terrestrial compartment

There are no tests with terrestrial organisms available. Therefore, the risk assessment for this compartment has to be conducted by using the PNECaqua of 56 µg/l.

With the calculated porewater concentration of 8.5 µg/l a PEC/PNEC ratio of 0.15 is resulting.

4. HUMAN HEALTH

a) <u>Acute Toxicity</u>

Animal data:

are between 922 mg/kg bw for male rats and 5.730 mg/kg bw for mice.

Single oral administration of DMAPA revealed a LD 50 of 1.037 mg/kg body weight in female rats and 922 – 1.870 mg/kg body weight in male rats.

The acute oral toxicity of DMAPA is considered to be moderate. LD 50 values after single oral administration

Following oral administration of DMAPA to mice, LD 50 values of 1.500 and 1.640 mg/kg body weight were determined, for the neutralized BASF product an LD 50 of 5.739 mg/kg body weight is given.

Oral administration of 2.618 or 5.235 mg neutralized DMAPA/kg bw to rabbits resulted to the deaths of all three animals in each dose group, while 1.309 mg/kg bw led to the death of one of 3 animals within 30 minutes after treatment.

Following inhalation exposure of rats an LC 50 (4 h) of > 4.31 mg/L was determined.

In male mice a threshold concentration for the depression of respiration frequency by 50% (RD 50) of 748 mg/m³ (176 ppm) was determined (95 % confidence interval: 642 – 837 mg/m³ or 151 – 197 ppm).

Applicaton of DMAPA has, depending on its concentration, a strongly irritating or corrosive effect on the skin and mucous membranes.

Based on the results of the skin sensitisation test according to OECD 406 (Maximisation Test), DMAPA has been classified as having a sensitising effect.

Human experience:

Job-related contact with DMAPA resulted in the repeated occurrence of a scaly, itchy rash on the person's face and right hand palm (the job included feeding a high-temperature reactor with chemicals). Patch tests conducted with the chemicals in question yielded positive reactions only for the 1% dilution of DMAPA.

Conclusion:	Harmful if swallowed causes severe burns
Recommendation:	no need for follow-up test
Priority setting:	low priority or concern

b) Repeated Dose Toxicity

Animal data:

Groups of 5 male and 5 female Wistar rats received DMAPA by oral gavage at dose levels of 0, 10, 50 or 250 mg/kg body weight per day for 28 days and were necropsied on day 29. Because 3 females of the 250 mg/kg bw group died during the study period, 5 females received DMAPA at the dose level of 250 mg/kg bw per day for 28 days again and were necropsied on day 29.

Toxicological examinations were carried out on mortalities, clinical signs, body weight, food consumption, examination of eyes, haematology, clinical biochemistry, urinalysis, organ weights, macroscopic post mortem findings and histopathology.

Intercurrent mortality occurred in four of ten females of the high dose group.

One male animal of the high dose group showed irregular respiration as well as respiratory sounds at day 11 and 12 of the study. The following clinical signs were observed in female animals of the high dose group sporadically between day 11 and 24 of the study: decreased spontaneous activity, stilted gait, swollen abdomen as well as impaired respiration. The clinical signs were mainly seen in those females which died intercurrently. Behavior and state of health remained unaffected by the administration of the test compound in all other dose groups.

Body weight development, food and water consumption remained unaffected by the administration of the test compound in all groups.

No treatment-related changes were detected by urine analysis.

Clinicochemical and haematological examination also failed to reveal any significant changes compared with the untreated control animals.

Organ weights, as well as their gross and histological examination, in those animals killed following termination of the study, also failed to reveal any substance-related effects.

The four high dose female rats which died intercurrently showed macroscopically visible changes such as discoloration of lungs with multiple red spots on its surfaces and foamy content. One of them also showed a small spleen.

Histopathological examinations revealed lesions in the four females of the high dose group dying intercurrently. These lesions included congestion of organs, pulmonary hemorrhage, and edema,

consistent with cardiorespiratory failure as cause of death. In addition, one of these females exhibited marked loss of lymphatic follicles of the spleen with massive marginal zone and periarteriolar lymphooid sheath atrophy. In the one high dose male rat which had shown clinical signs, focal ballooning degeneration of the squamous epithelium of the forestomach was found.

In particular, no pathological findings were reported for the genitals. Neither were any neurological disturbances observed.

In conclusion DMAPA caused clinical symptoms and mortality in male and female Wistar rats when administered 28 times during 29 days at the dose level of 250 mg/kg body weight. The female rats seem to be more sensitive.

No compound-related adverse effects were observed after repeated administration of DMAPA at the dose levels of 50 or 10 mg/kg body weight per day.

Based on the findings the „No-Observed-Adverse-Effect-Level“ (NOAEL) was 50 mg DMAPA/kg body weight/day, by gavage for 28 days.

Human experience:

In a field study (USA, 1974), workers showed impaired respiration (wheezy breath, constricted chest, irrition of mucosa of the eyes, nose and pharynx) as a result of occupational exposure to DMAPA (2.34 – 5.87 mg/m³ = 0.55 – 1.38 ppm).

A cross-sectional, serial examination was conducted at the same factory in 1977, again with 34 workers. An average DMAPA concentration of 0.55 mg/m³ (0.13 ppm) was measured in the respiratory zone of the assemblers. Of the 28 persons exposed to DMAPA, 5 complained of irritation of the nasal mucosa and 2 of increased mucous formation in the respiratory tract. Only among the 6 workers with non-specified tasks was a significant reduction (3.9%) in vital capasity found at the end of the first working day of the week compared with results obtained prior to starting work. Neither among the assemblers nor among the pressmen was any impairment of respiration during the course of the working day observed. Comparison of the data on pulmonary function in the different subgroups showed no significant differences between the groups. A LOEL (Lowest-Observed-Effect-Level) would thus be in the range of 0.425 – 0.85 mg/m³ (0.1 – 0.2 ppm).

Conclusion:	With regard to the 28-subacute oral toxicity study with male and female Wistar rats a no-observed-adverse-effect-level (NOAEL) of 50 mg/kg body weight was established.
Recommendation:	no need for follow-up test
Priority setting:	Low priority or concern

c. <u>Carcinogenicity</u>

Animal data:

No data available

d. <u>Reproductive Toxicity</u>

Animal data:

A Reproduction/Development Toxicity Screening Test of Dodecyldimethylamine by oral administration to Sprague-Dawley Rats according OECD method 421 was carried out with four groups of 10 male and 10 female rats each. The rats received 0 (control), 10, 50 or 200 mg/kg bw/day; males: 14 days prior to mating and during the 14-day mating period, females: 14 days prior to mating and during the mating period, pregnancy and lactatoin period.

Examinations were carried out on mortality, clinical signs, body weight, food consumption, reproduction, macroscopic post mortem findings/organ weights of parent animals and histopathology.

Under the conditions of this reproduction/developmental toxicity screening test according OECD method 421, the oral administration of DMAPA by gavage to rats had no adverse effects on reproductive performance or fertility of the F0 parenteral animals of all substance-treated groups. Mating behavior, conception, gestation, parturition and lactation as well as the determined sexual organ weights, gross and histopathological findings of these organs were similar between the substance-treated animals and the corresponding controls. With the exception of each one male and female F0 parental rat in the control group and mid dose group all F0 parental rats proved to be fertile. Thus, the observable difference was regarded to be incidental in nature and not of toxicological or biological concern.

Signs of general, systemic toxicity in the F0 parental animals were confined to the male rats of the 200 mg/kg bw/day group. Toxicity was characterized by decreased food consumption. If calculated for the whole treatment period, it was about 6% below the concurrent control value. The high dose F0 parental males showed also impairments in body weight gain during the whole treatment period. If calculated for the entire treatment period (weeks 0 – 4) body weight gain was about 35% lower than the concurrent control value although there was a statistically significant increase in body weight gain during weeks 2 – 3. Indications for a slight impairment in the general state of health were noted in two F0 male animals (piloerection, respiratory sounds).

No compound-related adverse effects were observed in female rats up to the highest dose level of 200 mg/kg bw/day.

There were no signs of developmental toxicity in the progeny of the F0 parents up to and including the high dose group (200 mg/kg bw/day). Observed differences did not show any biological relevance between the substance-treated groups and the control group.

Thus, the NOAEL (no observed adverse effect level) for reproductive performance and fertility was 200 mg/kg bw/day for the F0 parental rats.

The NOAEL for general, systemic toxicity of the test substance was 200 mg/kg bw/day for the F0 parental females, while it was 50 mg/kg bw/day for the F0 parental males.

The NOAEL for developmental toxicity could be fixed at 200 mg/kg bw/day for the F1 progeny.

Human experience: no data available

Conlusion: In the above mentioned study, a clear-cut no-observed-adverse-effect level (NOAEL) of 200 mg DMAPA/kg bw/day, by gavage, was determined for reproductive performance, fertility and developmental toxicity.

Recommendation:	Based on the results of the Reproduction/Developmental Toxicity Screening Test, no further assessment of DMAPA on fertility/teratogenicity is necessary.
Priority setting:	Low priority or concern

e. Genetic Toxicity

Experimental data:

DMAPA was tested for mutagenicity with the strains TA 100, TA 1535, TA 1537, TA 1538, TA 98, TA 1950, his G46 of Salmonella typhimurium (Ames Test).

The mutagenicity studies were conducted in the absence and in the presence of a metabolizing system derived from rat liver homogenate. A dose range up to 10.000 microgram/plate was used.

DMAPA did not show in these bacterial test systems either with or without exogenous metabolic activation at the dose levels investigated a dose dependent increase in the number of revertants in any of the bacterial strains.

Based on this results it can be stated that DMAPA is not mutagenic in these bacterial test systems.

A micronucleus assay in bone marrow cells of the mouse was performed to investigate the potential of 3-Dimethylaminopropylamine to induce micronuclei in polychromatic erythrocytes in the bone marrow of the mouse.

The substance was dissolved in deionised water. Deionised water was used as vehicle control. 40 mg/kg bw cyclophosphamide administered i.p. was used as positive control which showed a substantial increase of induced micronucleus frequency. The volume administered intraperitoneally (i.p.) was 10 ml/kg bw. 24 h and 48 h after a single administration of 25, 50, and 100 mg/kg bw (24 h preparation interval) and 100 mg/kg bw (48 h preparation interval). The highest dose (100 mg/kg) was estimated in pre-experiments to be suitable. Ten animals (5 males, 5 females) per test group were evaluated for the occurrence of micronuclei.

The mean number of normochromatic erythrocytes (NCE) was increased after treatment with DMAPA at the highest dose as compared to the mean value of NCE of the vehicle control indicating that the substance had cytotoxic properties in the bone marrow. There was no statistically significant or biologically relevant enhancement in the frequency of the detected micronuclei at any preparation interval after administration of the test item and with any dose level used.

It can be stated that during the study described and under the experimental conditions reported, 3-Dimethylaminopropylamine in bone marrow cells of the mouse is considered to be non-mutagenic in this micronucleus assay.

Human experience: no data available

Conclusion:	A number of Ames tests, with or without metabolic activation through S9-Mix, and a mouse micronucleus assay failed to provide any evidence for a mutagenic effect of DMAPA
Recommendation:	No need for follow up test
Priority setting:	Low priority or concern

4.3 Initial Assessment for Human Health

DMAPA have been found to be harmful follwing oral administration to rats.

Based on the results of the sensitisation test on the skin DMAPA has been classified as having a sensitising effect.

DMAPA showed strong irritating or corrosive effects.

In a 28-day subchronic toxicity study, the no-observed-adverse effect-level (NOAEL) was 50 mg /kg bw/day.

In the reproduction/developmental toxicity sreening test the no-observed-adverse effect-level (NOAEL) was 200 mg/kg bw/day.

DMAPA was not mutagenic in the Ames Test and in a mouse micronucleus assay.

The corrosive property of the compound prompts workers to limit the potential exposure to this chemical.

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

The substance is considered of low potential risk and low priority for further work.

5.2 Recommendations

No need for further work.

6. REFERENCES

1.: BUA report 197: Dimethyl aminopropylamine (DMAPA); 1996; ISBN: 3-7776-0837-8

2.: Technical Guidance Documents in Support of the Commission Directive 93/67/EEC on the Risk Assessment for New Notified Substances and the Commission Regulation (EC) 1488/94 on Risk Assessment for Existing Substances

3.: Einstufungsbegründung Fa. Hoechst, 12.6.1991