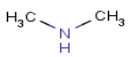
SIDS INITIAL ASSESSMENT PROFILE

<table>
<tr><td>Category Name</td><td colspan="2">Aliphatic Secondary Amines</td></tr>
<tr><td>Category Members:

CAS Registry Numbers, Chemical Names</td><td colspan="2">124-40-3 Dimethylamine (DMA)
109-89-7 Diethylamine (DEA)
142-84-7 Dipropylamine (DPA)
108-18-9 Diisopropylamine (DIPA)
111-92-2 Dibutylamine (DBA)
110-96-3 Diisobutylamine (DIBA)

<u>DPeA - A mixture of the following 3 isomers</u>:
2050-92-2 Dipentylamine
61361-18-0 N-(2-methylbutyl)-1-pentanamine
27094-65-1 2-Methyl-N-(2-methylbutyl)-1-butanamine</td></tr>
<tr><td rowspan="3">Structural Formula(s)</td><td>124-40-3
DMA</td><td>  </td></tr>
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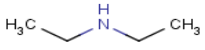
DEA</td><td>  </td></tr>
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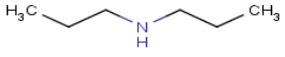
DPA</td><td>  </td></tr>
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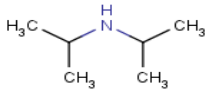
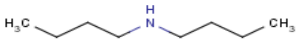
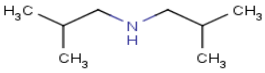
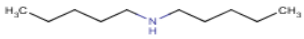
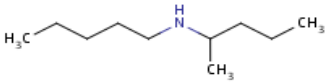
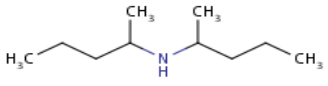
	108-18-9 **DIPA**	
	111-92-2 **DBA**	
	110-96-3 **DIBA**	
	2050-92-2 **One isomer of DPeA**	
	61361-18-0 **One isomer of DPeA**	
	27094-65-1 **One isomer of DPeA**	

SUMMARY CONCLUSIONS OF THE SIAR

Analogue/Category Rationale

The Aliphatic Secondary Amines category is limited to the nine sponsored substances as mentioned above.

Structure and physical chemical properties

The Aliphatic Secondary Amines category is represented by the structure R-NH-R', where R is an alkyl group that may be linear or branched; the alkyl group may include an atom or group that will not react with or substantially affect the properties of the amine function. The tendency to share the nonbonded electron pair on the nitrogen underlies the chemical behavior of amines as a group.

The Aliphatic Secondary Amines category members are structurally similar showing a trend in physical-chemical properties and ecotoxicity and similar toxicological properties. This category is defined as below:

- a structure which contains only aliphatic organic substituents; elemental compositions of carbon, hydrogen and nitrogen;
- a consistent incremental change across the group consisting of an increasing number of carbon atoms or branching. The change is constant in that it is restricted to adding elements that do not greatly change the physico-chemical properties of the amino moiety. This is evidenced by the consistency of pKa values of the protonated forms, which vary across the narrow range of 10.73 to 11.16; and
- molecular weights of < 500 Dalton, classifying the aliphatic secondary amines as low molecular weight aliphatic amines.

Toxicological profile

Observed corrosive properties overwhelm the systemic toxicity of the aliphatic secondary amines in most cases, including acute toxicity; the known acute oral, dermal and respiratory effects are generally related to the alkaline properties and are expected to be a general feature of the category. Structure-activity similarities for mammalian toxicity and structure-activity relationships (SAR) shown for aquatic toxicity endpoints lend support to the category.

Metabolic profile

In general, members of the Aliphatic Secondary Amines category can be considered to be comparable in metabolism. Metabolism of aliphatic secondary amines to aldehydes can be viewed as a bioactivation reaction since aldehydes are biologically reactive. However, DIPA is a known outlier for which some data are available to cover the endpoints. Due to structural differences, DIPA may be metabolized by different pathways (oxidized to acetone and either isopropylamine or N-hydroxy-isopropylamine) than the rest of the category.

Using the category approach, read across has been performed from the tested members to those without available data. Read-across approach has been used for addressing the mammalian toxicity and environmental endpoints where no data were available on individual substances (see below). Taking a precautionary approach, category members without toxicity or environmental fate data are regarded the same as the worst case read across approach. Specifically, where no toxicity data exist or are limited, category members will be considered irritating/corrosive, to be clastogenic in vitro, cause effects on male reproductive organs and parameters (except DPeA), or cause developmental toxicity (except DMA and DPeA).

Substance	Eye irritation	Skin sensitization	Repeated dose	In vitro mutagenicity[(1)]	In vivo mutagenicity	Effects on reproductive organs or fertility	Developmental toxicity

DMA	X	Read across	X	X	X	Read across	X
DEA	X	X	X	X	X	X	Read across
DPA	X	Read across	Read across	Read across (CA)	Read across	Read across	Read across
DIPA	X	X	X	X	Read across	X+Read across	Read across
DBA	X	X	X	X	X	X	X
DIBA	Read across	Read across	Read across	Read across (CA)	Read across	Read across	Read across
DPeA	Read across	X	X	X	Read across	X	X

X = data available; (1) Chromosome aberration = CA

Substance	**Acute aquatic toxicity**		
	Fish	Aquatic invertebrates	Aquatic plants
DMA	X	X	X
DEA	X	X	X
DPA	Read across	X	X
DIPA	X	X	X
DBA	X	X	X
DIBA	X	X	X
DPeA	X	X	X

Note that DPeA is a mixture of three isomers (CAS No 2050-92-2: 15-30%; CAS No 61361-18-0: 50-65%; and CAS No 27094-65-1: 10-25%). The reported physical-chemical properties tests were conducted with CAS No 2050-92-2. Human health and environmental toxicity testing was conducted with the mixed isomers, with the exception of the bacterial reverse mutation assay, for which the test substance could not be determined.

In some cases, the tested substance was the salts of amines to avoid damage to the gastrointestinal tract following gavage administration due to the caustic mode of action. Testing the salt also provides the ability to distinguish between symptoms caused by local effects such as irritation or corrosion and symptoms that are due to systemic toxicity as follows:

Substance	**Toxicokinetics**	***In vitro* chromosome aberration**	**Carcinogenicity**	**Developmental toxicity**
DMA	Tested as the hydrochloride (dimethylamine hydrochloride (CAS No. 506-59-2))	Tested as the hydrochloride (dimethylamine hydrochloride (CAS No. 506-59-2))	-	Tested as the hydrochloride (dimethylamine hydrochloride (CAS No. 506-59-2))
DEA	-	-	Tested as the hydrochloride (diethylamine hydrochloride (CAS No. 660-68-4))	-
DBA	-	-	-	Tested as the hydrochloride (dibutylamine hydrochloride, CAS No. 6287-40-7))
DPeA	-	-	-	Tested as the hydrochloride (diamylamine hydrochloride)*

*Repeated dose and reproductive endpoints also tested

Physical-chemical Properties

The substances are gases (**DMA** only) or liquids, with measured (or not specified) melting points that range from -92.2 °C (**DMA**) to -7.85°C (**DPeA**). The measured (or not specified) boiling points range from 7.0 °C (**DMA**) to 202.5 °C (DPeA). Measured (or not specified) vapor pressures range from 0.203 hPa at 25 °C (**DPeA**) to 1688 hPa at 20 °C (**DMA**). Water solubility correlates well with structure; longer chain functionalities result in lower water solubility values. Water solubility values range from miscible at 25 °C for **DMA** and **DEA** to 0.798 g/L for DPeA at 20 °C. Measured data on the log Kow are available for all members except **DPeA**; modeling was used to fill this endpoint. The log Kow values are <3 for the category members (except for **DPeA** = 3.61 - 3.76 for the three isomers; estimated; uncharged molecule). pH adjustment was not mentioned for the measured log Kow values (pH adjustment was mentioned for DMA). The pKa values are similar for the aliphatic secondary amines (protonated), with measured and estimated values between 10.73 and 11.16, but the neutral, or uncharged, aliphatic secondary amines have pKas ranging from 30 to 40.

Human Health

For those category members for which read-across is applied, the lowest effect value (for example, $LC(D)_{50}$ or N(L)OAEC/N(L)OAEL) is used, as well as overall toxicity for other endpoints. The attached Annex provides a summary of the read across values for mammalian toxicity.

Absorption and distribution of aliphatic secondary amines by the dermal, oral and inhalation routes is expected because they have low molecular weights and are both water and lipid soluble. The primary excretory pathway for the aliphatic secondary amines is expected to be urinary excretion based on data with **DMA**. Metabolism of aliphatic secondary amines to aldehydes can be viewed as a bioactivation reaction since aldehydes are biologically reactive. Due to structural differences, **DIPA** may be metabolized by different pathways (oxidized to acetone and either isopropylamine or N-hydroxy-isopropylamine).

Acute inhalation studies are available for all of the aliphatic secondary amines. Four hour vapor LC_{50} values (rat) ranged from 0.28 mg/L (**DPeA**; EPA OPP 81-3) to 17.3 mg/L (**DEA**; similar to OECD TG 403). Clinical signs and findings at gross necropsy were consistent with generally severe local effects of eye and respiratory irritation, respiratory distress and lung damage. Dermal LD_{50} values (rat or rabbit) are available for all of the aliphatic secondary amines. Dermal LD_{50} values ranged from 500 to 1000 mg/kg-bw (**DEA, DPA, DBA, DPeA**; no guideline specified or similar to OECD TG 402) to greater than 1000 (**DIBA**; no guideline specified) or 2000 mg/kg-bw (**DMA**; no guideline specified, and **DIPA**; similar to OECD TG 402). Severe skin necrosis at the site of application was noted in most studies. Similar results including severe skin necrosis would be expected for all substances based on structural similarities. Acute oral LD_{50} values (rat) ranged between 86 (**DPeA**) and 1000 mg/kg-bw (**DMA**) (both similar to OECD TG 401). Clinical signs generally included breathing abnormalities, oral-nasal wetness and/or staining, lethargy, effects on gait, poor condition, tremor/spasm, convulsions, eye closure, atonia and loss of coordination. Site of contact effects (irritation/corrosion) in the gastrointestinal tract were the most common finding noted at gross necropsy. Acute oral studies were not located for **DIPA** or **DIBA**.

All members of the aliphatic secondary amine category are corrosive to the skin (rabbits, primarily in Draize tests or similar to OECD TG 404). No eye irritation data are available for DIBA and DPeA. Based on the available data for the remaining category members (rabbit, no guideline specified or similar to OECD TG 405) and known eye irritation potential of alkyl amines in general, it is expected that all the amines in the category are corrosive to the eye. The aliphatic secondary amines are respiratory irritants in acute inhalation or respiratory irritation studies with rats.

There was no clear evidence of skin sensitization potential for four aliphatic secondary amines in a test with mice (similar to OECD TG 429) or in three guinea pig studies (similar to OECD TG 406). Data were not located for **DMA, DPA,** or **DIBA**, but these would not be expected to be skin sensitizers based on the existing data for other members of the category.

The inhalation or oral repeated dose toxicity has been studied for several of the Aliphatic Secondary Amines category members; no reliable dermal repeated dose toxicity studies are available. Local and systemic LOAECs/NOAECs are determined for these studies, although the distinction is somewhat arbitrary given some of the severe effects observed on the respiratory tract. In 12-month inhalation toxicity studies in rats and mice using **DMA** (no guideline specified), local NOAECs were not established and the local LOAECs were 0.018 mg/L in both rats and mice, based on significant concentration-related lesions in the nasal passages progressing from inflammation to metaplasia, hyperplasia and necrosis in some cases; male and female mice also exhibited decreased body weights. The systemic NOAEC for rats in this study is 0.092 mg/L based on biologically-relevant decreases in body weight at the highest concentration (0.32 mg/L). Changes in hematology and clinical chemistry were also seen at this concentration (although it is not clear whether the effects were seen at 6 or 12 months). Significant non-treatment related mortality in mice precluded setting a systemic NOAEC and LOAEC for mice. For **DEA**, effects on the respiratory tract were observed in a 3-month inhalation study in rats and mice (similar to OECD TG 413) at concentrations of 0.096 mg/L and higher, resulting in a local NOAEC of 0.048 mg/L. In this study, **DEA** also exacerbated clonic seizures of the individually-housed rats (apparently at concentrations of 0.096 mg/L and higher, but data are limited to determine the exact concentrations). In this study, sperm motility was decreased in both rats and mice at 0.096 mg/L and higher, resulting in a systemic NOAEC of 0.048 mg/L for both species. Rats exposed to **DIPA** by inhalation for one month exhibited nasal and corneal lesions and decreased lymphocyte counts at all concentrations, resulting in local and systemic LOAECs at the lowest concentration of 0.1 mg/L. In a 3-month study designed to evaluate respiratory and reproductive effects (no guideline specified), rats exposed to **DBA** for 90 days exhibited nasal lesions and decreased body weights primarily at 0.142 mg/L and higher. A NOAEC for systemic effects could not be determined because the study focused only on the respiratory and reproductive tracts. The LOAEC for local irritation of the upper respiratory tract (nasal cavities) was 0.051 mg/L. In a combined repeated-dose reproduction/developmental toxicity study (OECD TG 422) with **DPeA**, male rats were dosed orally (by gavage) for 32 days including two weeks premating; females were dosed during premating, after the mating period, and during gestation and lactation. The oral NOAEL for **DPeA** was 4 mg/kg bw/day based on signs of aggression at 13 mg/kg bw/day and higher; tremors and piloerection were seen at 40 mg/kg bw/day.

The aliphatic secondary amines were not mutagenic *in vitro* in bacterial reverse mutation (similar to OECD TG 471) using S. *typhimurium*, and mammalian cell assays (mutation at the HGPRT locus of Chinese Hamster Ovary cells (CHO), OECD TG 476). *In vitro*, **DMA** was marginal for chromosomal aberrations with metabolic activation (no guideline), and in a second study did not induce chromosomal aberrations (as DMA-HCl; no guideline). However, the study using **DMA-HCl** did not evaluate conditions with metabolic activation and therefore it is not known whether **DMA-HCl** would induce chromosomal aberrations in the presence of activation. Thus, the positive result from the **DMA** study suggests **DMA** may induce chrosomal aberrations. DIPA did not induce chromosomal aberrations in human lymphocytes in the presence or absence of metabolic activation (guideline not specified). **DBA** was marginal for chromosomal aberrations *in vitro* (CHO, similar to OECD TG 473); this test was conducted only without metabolic activation. DPeA induced chromosomal aberrations *in vitro* (Chinese hamster lung fibroblasts (V79), OECD TG 473) in the presence of metabolic activation. In an *in vivo* chromosome aberration study in rats exposed to **DMA** by inhalation for 90 days (no guideline specified) the incidence of cells with chromosomal breakage did not exceed controls and the incidence of aneuploid cells was significantly higher compared to controls. An *in vivo* micronucleus assay in mice exposed to **DEA** via inhalation (similar to OECD TG 474) and an *in vivo* micronucleus assay in mice exposed orally to **DBA** (OECD TG 475) were both negative.

Two-year inhalation carcinogenicity studies with **DMA** or **DEA** at concentrations up to 0.32 or 0.37 mg/L, respectively, in rats (OECD TG 451 or similar), and with **DEA** at concentrations up to 0.19 mg/L in mice (OECD TG 451) were negative. A 30-month study, in which guinea pigs were exposed to 4000 mg/L **DEA HCl** in drinking water (no guideline specified), was also negative for carcinogenicity.

An increase in relative testis weight and reduced sperm motility were observed in male rats and mice exposed to **DEA** via inhalation for 90 days at 0.096 mg/L or greater in a study similar to OECD TG 413; male mice exhibited increased testes weights at 0.37 mg/L.. Rats exposed to **DIPA** via inhalation for one month exhibited atrophy and decreased secretion of seminal vesicles, and increased relative testes weights at 2.0 mg/L, a dose also associated with a variety of corrosive and other significant effects. Test substance-related microscopic

changes were not observed in the reproductive organs of either males or female rats exposed by inhalation for 91 days to **DBA** concentrations up to 0.448 mg/L (highest concentration tested) in a study similar to OECD TG 413. In an OECD TG 422 study with **DPeA** administered via gavage, there was no effect on reproductive performance of male and female rats, including mating index, gestation index, mean number of implantation sites, post-implantation loss, mean number of pups, or live birth index at doses up to 40 mg/kg-bw (highest dose tested), when exposed for 32 days (males) or, during premating, after mating period, during gestation and lactation (females).

Developmental effects were not observed in an OECD TG 414 with pregnant rats exposed by oral (gavage) to **DMA HCl** at doses up to 1000 mg/kg-bw on GD 6 through GD 19; the NOAEL (developmental toxicity) was 1000 mg/kg bw/day as there was no evidence of an adverse effect on fetal morphology. In an OECD TG 414 study, pregnant Wistar rats were administered **DBA HCl** by oral (gavage) on GD 6 - 19 at doses up to 150 mg/kg bw/day. The NOAEL for maternal toxicity is 15 mg/kg bw/d based on clinical pathological effects at dose levels of 50 mg/kg bw/d and above. At 150 mg/kg bw/day, there was a statistically significant reduction in mean number and mean percent viable male foetuses ($p < 0.05$). Although not statistically significant, post-implantation loss showed a dose-response relationship in this study, with 4.9%, 7.1%, 7.8% and 9.0% in controls, 15, 50 and 150 mg/kg bw/day, respectively. The NOAEL for developmental toxicity is 50 mg/kg-bw/day based on reduced mean number and percent of viable foetuses. In a study conducted according to OECD TG 422, Wistar rats were administered **DPeA** by oral (gavage) at doses up to 40 mg/kg bw/day; substance related effects were not observed and the NOAEL for developmental/teratogenic effects was 40 mg/kg bw, the highest dose tested.

The Aliphatic Secondary Amines category members possess properties indicating a hazard for human health (acute toxicity, irritating/corrosive properties, genotoxicity (chromosomal aberrations), repeated-dose toxicity, effects related to male reproductive toxicity except for DPeA, developmental toxicity in the presence of maternal toxicity for category members except DMA and DPeA). Adequate screening-level data are available to characterize the human health hazard for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Environment

The aliphatic secondary amines are not expected to undergo hydrolysis under environmental conditions. The substances lack functional groups where this process would be relevant. OECD TG 111 studies have not been conducted for the aliphatic secondary amines. In water solution, all of the simple alkyl amines share the property of forming ammonium ions. This is due to the ability of the free electron pair on the amine nitrogen to pick up a proton from water and form a hydroxide ion raising the solution pH. Estimated pKa values of >10.5 indicate that the aliphatic secondary amines will exist primarily as cations in the environment (relevant pH 5.0 – 9.0). However, the EPIWIN modeling program predicts environmental fate endpoints for aliphatic secondary amines in their uncharged form.

In the atmosphere, indirect photo-oxidation by reaction with hydroxyl radicals is predicted to occur with a half-life of <1 day. For the aliphatic secondary amines, EPIWIN Level III fugacity modeling predicts that, when distributed equally to air, water and soil, the aliphatic secondary amines will partition to water and soil with negligible distribution to air and sediment. The substances will partition with higher relative distributions to soil compared to water and this tendency increases proportionally with molecular weight of the aliphatic secondary amine.

Biodegradation data are available for all chemicals in this category. DPeA was tested as a mixture. With the exception of DIPA, these single chemicals are readily biodegradable (OECD TG 301). In an OECD TG 301D, **DIPA** degraded 11% BOD after 28 days (not readily biodegradable).

Predicted BCF values, from BCFBAF Program v3.01 in EPIWIN v4.10, range from 3.16 to 139.7 indicating that they have low bioconcentration potential and are not expected to be bioaccumulative.

The following acute aquatic toxicity test results using buffered/unbuffered conditions have been determined for the aliphatic secondary amines (key and supporting studies are presented; the supporting studies are used to illustrate pH effects). “Estimated” values are based on modelling using the ECOSAR Program (v1.00;

ECOSAR Class used was Aliphatic Amines; all predicted values fall within the applicability domain).

Fish:

Substance	Species	LC50 (96 hr; mg/L)	Remark (measured/nominal; pH adjusted)	Estimated values (ECOSAR 1.0) (96 hr, mg/L)
DMA	*Oncorhynchus mykiss*	118 17	not specified; hard water not specified; soft water	161
	Poecilia reticulate	210	not specified; pH not specified	
	Oncorhynchus mykiss	120 20	not specified; hard water not specified; soft water	
DEA	*Oryzias latipes*	27	Measured; pH not specified	66.8
	Oncorhynchus mykiss	182 25	not specified; hard water not specified; soft water	
	Pimephales promelas	855	nominal; pH adjusted	
	Poecilia reticulate	130	nominal; pH not specified	
DPA	Read across to DEA and DBA 27 – 855 (hard water or unspecified); 5.5 – 25 (soft water)			23.7
DIPA	*Leuciscus idus*	26 >100	nominal, not pH adjusted nominal, pH adjusted	29.1
	Oncorhynchus mykiss	196 37	not specified; hard water not specified; soft water	
	Salmo gairdneri	42	not specified; pH not specified	
	Lepomis macrochirus	75	not specified; pH not specified	
	Pimephales promelas	40	not specified; pH not specified	
	Gasterosteus aculeatus	798	measured; pH not specified	
DBA	*Oncorhynchus mykiss*	37 5.5	not specified; hard water not specified; soft water	7.8
DIBA	*Leuciscus idus*	26 >100	nominal, not pH adjusted nominal, pH adjusted	9.5
DPeA	*Oncorhynchus mykiss*	3.9 mg/L	measured, not pH adjusted	2.4

Aquatic invertebrates:

Substance	Species	EC50 (48 hr; mg/L)	Remark (measured/nominal; pH adjusted)	Estimated values (ECOSAR 1.0) (48 hr, mg/L)
DMA	*Daphnia magna*	88.7	nominal; not pH adjusted	10.3
	Daphnia magna	50	not specified; pH not specified	

DEA	*Ceriodaphnia dubia*	4.6	measured; pH not specified	5.3
	Daphnia magna	56	nominal; pH not specified	
	Daphnia magna	58	measured; pH not specified	
	Daphnia magna	100	not specified; pH not specified	
DPA	*Daphnia magna*	73.34	nominal; not pH adjusted	2.3
DIPA	*Daphnia magna*	110	not specified; pH not specified	2.7
	Daphnia magna	24 hour LC50 = 187	not specified; pH not specified	
DBA	*Ceriodaphnia dubia*	8.4	measured; pH not specified	0.9
	Daphnia magna	65.98	nominal; not pH adjusted	
DIBA	*Daphnia magna*	>71	measured; pH not specified	1.1
	Daphnia magna	35	not specified; pH not specified	
DPeA	*Daphnia magna*	23	measured; not pH adjusted	0.4

Algae:

Substance	Species	EC50 (72 hr; mg/L)	Remark (endpoint; measured/nominal; pH adjusted)	Estimated values (ECOSAR 1.0) (96 hr, mg/L)
DMA	*Pseudokirchneriella subcapitata*	96 hr EC_{50} = 9	growth rate; pH not specified	2.2
	Chlorella pyrenoidosa	96 hr EC_{50} = 30	biomass; not specified; pH not specified	
	Pseudokirchneriella subcapitata/	6.2	growth; not specified; pH not specified	
DEA	*Pseudokirchneriella subcapitata*	54	growth rate; measured, pH not specified	1.5
	Pseudokirchneriella subcapitata	96 hr EC_{50} = 20	growth; not specified; pH not specified	
	Chlorella pyrenoidosa	96 hr EC_{50} = 56	growth; not specified; pH not specified	
	Scenedesmus sp.	96 hr TTC = 4	not specified; pH not specified	
DPA	*Desmodesmus subspicatus*	11.8	growth rate; nominal; not pH adjusted	0.9
DIPA	*Selenastrum sp*.	96 hr EC_{50} = 20	not specified; pH not specified	1.04
DBA	*Desmodesmus subspicatus*	16.91 9.43	growth rate; nominal; not pH adjusted biomass; nominal; not pH adjusted	0.5
	Desmodesmus subspicatus	42.55 5.14	growth rate; nominal; not pH adjusted biomass; nominal; not pH	

			adjusted	
	Desmodesmus subspicatus	16.19 7.17	growth rate; nominal; not pH adjusted biomass; nominal; not pH adjusted	
	Pseudokirchneriella subcapitata	96 hr EC_{50} = 19	not specified; pH not specified	
DIBA	*Pseudokirchneriella subcapitata*	48 hr EC_{50} = 16	growth rate; nominal; pH 7	0.58
DPeA	*Selenastrum capricornutum*	1.7	growth rate; measured; not pH adjusted	0.27

The following chronic toxicity test results have been determined:

Fish

Substance	**Species**	**Result (mg/L)**	**Remark** measured/nominal; pH adjusted
DMA	*Oncorhynchus mykiss*	30 d NOEC = 20 (juvenile) 50 d NOEC = 0.6 (egg fry)	No details specified
DIPA	*Gasterosteus aculeatus*	35 d NOEC (mortality and sublethal effects; growth excluded) = 187 35 d NOEC (embryonic stage) = 582	measured measured

Aquatic invertebrates

Substance	**Species**	**Result (mg/L)**	**Remark** measured/nominal; pH adjusted
DEA	*Daphnia magna*	21 day NOEC = 4.2	measured; pH not specified

The Aliphatic Secondary Amines possess properties indicating a hazard for the environment (acute aquatic toxicity values > 1 and ≤ 100 mg/L). With the exception of DIPA, the aliphatic secondary amines are readily biodegradable, and are not expected to be bioaccumulative. Adequate screening-level data are available to characterize the hazard for the environment for the purposes of the OECD Cooperative Chemicals Assessment Programme.

Exposure

The production volumes for the sponsor country (US) for (2006) were obtained from Inventory Update Reporting.

Substance	**Production Volume (tonnes)**
DMA	45,359 - <226,796
DEA	4536 - < 22,680
DPA	4536 - < 22,680
DIPA	< 227
DBA	4536 - < 22,680
DIBA	No data reported

DPeA	227 – <907

DMA, DEA, DPA, DIPA, **DBA** and **DIBA** are used for the synthesis of other chemical substances; they are consumed in reactions and no longer retain their chemical identities. **DMA, DPA, DBA, DIBA** and **DPeA** are used as solvents in industrial gas manufacturing and other chemical product and preparation manufacturing. **DEA** is used as a processing aid in rubber production; it is consumed in reactions and no longer retains its chemical identity. **DMA**, **DPA, DBA**, **DIBA** and **DPeA** are used in commercial or consumer soaps and detergents.

The most likely route of human occupational exposure is either via dermal contact or inhalation; most of these materials are highly irritating or corrosive to the skin and are respiratory irritants and adequate protective equipment is required if any splash hazard is present. Examples of potential occupational exposure scenarios include sampling for quality control, line breaks, pack-out after manufacturing, and charging reactor vessels for downstream users. **Consumer e**xposure is intended when the category members are used in soaps and detergents. During manufacturing, **DMA** and **DPeA** are vented to the atmosphere through a flare, and aqueous waste streams are biologically treated before being discharged to surface water. Downstream environmental releases of all category members may occur through fugitive air emissions. **DMA, DPA, DBA, DIBA and DPeA** may be released through on-site land disposal. Distribution of **DEA** and **DIPA** to wastewater is expected to be moderate. No monitoring data are available.

ANNEX
Summary of Mammalian Toxicity Data Read Across Approach
(Oral = mg/kg bw/day; Inhalation = mg/L)

Substance	Acute toxicity (inhalation and oral)	Repeated dose (oral)	Repeated dose (inhalation) *	Gene mutation in vitro	Chromosome aberration in vitro	Chromosome aberration in vivo	Effects on fertility (oral) and reproductive organs (inhalation)	Developmental toxicity (oral)
DMA	**LC50 inh = 9.9 (60 min)** **LD50 oral = 1000**	NOAEL = 4 (RA)	**LOAEC (local) = 0.018** **NOAEC (systemic) = 0.092**	**Negative**	**Positive/ Marginal (weight of evidence)**	**Positive**	NOAEL oral = 40 (RA) Dec. sperm motility (inh) >0.096 (RA)	**NOAEL = 1000**
DEA	**LC50 inh = 17.3 mg/l** **LD50 oral = 540**	NOAEL = 4 (RA)	**NOAEC (local) = 0.048** **NOAEC (systemic) = 0.048**	**Negative**	Positive (RA)	**Negative**	NOAEL oral = 40 (RA) **Dec. sperm motility (inh) >0.096**	NOAEL = 50 (RA)
DPA	**LC50 inh > 8.22 (60 min)** **LD50 oral = 495 and 933**	NOAEL = 4 (RA)	LOAEC (local) = 0.018 (RA) NOAEC (systemic) = 0.048 (RA)	**Negative**	Positive (RA)	Positive (RA)	NOAEL oral = 40 (RA) Dec. sperm motility(inh) >0.096 (RA)	NOAEL = 50 (RA)
DIPA	**LC50 inh = 5.35** LD50 oral = 86 (RA)	NOAEL = 4 (RA)	**LOAEC(local) = 0.1** **LOAEC (systemic) = 0.1**	**Negative**	**Negative**	Positive (RA)	NOAEL oral = 40 (RA) **NOAEC=0.6 (inh)** Dec. sperm motility (inh) >0.096 (RA)	NOAEL = 50 (RA)
DBA	**LC50 inh = 1.15 mg/l** **LD50 oral = 550 mg/kg bw**	NOAEL = 4 (RA)	**NOAEC (local) = 0.142** NOAEC (systemic) = 0.048 (RA)	**Negative**	**Positive/ Marginal**	**Negative**	NOAEL oral = 40 (RA) Dec. sperm motility (inh) >0.096 (RA)	NOAEL = 50 (RA)
DIBA	**LC50 inh > 2.6 mg/l** LD50 oral = 86 (RA)	NOAEL = 4 (RA)	LOAEC (local) = 0.018 (RA) NOAEC (systemic) = 0.048 (RA)	**Negative**	Positive (RA)	Positive (RA)	NOAEL oral = 40 (RA) Dec. sperm motility (inh) >0.096 (RA)	NOAEL = 50 (RA)
DPeA	**LC50 inh = 0.238** **LD50 oral = 86**	**NOAEL = 4**	LOAEC (local) = 0.018 (RA) NOAEC (systemic) = 0.048 (RA)	**Negative**	**Positive**	Positive (RA)	**NOAEL oral = 40 [maximum tolerated dose]**	**NOAEL oral = 40**

*Subchronic and chronic studies
RA=Read Across