

SIDS Initial Assessment Report

For

SIAM 22

Paris, France, 18-21 April 2006

Category Name:

Amine Oxides

CAS Numbers:

1643-20-5	1-Dodecanamine, N,N-dimethyl-, N-oxide
3332-27-2	1-Tetradecanamine, N,N-dimethyl-, N-oxide
70592-80-2	Amines, C10-16-alkyldimethyl, N-oxides
68955-55-5	Amines, C12-18-alkyldimethyl, N-oxides
2605-79-0	Decanamine, N,N-dimethyl-, N-oxide
7128-91-8	Hexadecanamine, N,N-dimethyl-, N-oxide
2571-88-2	Octadecanamine, N,N-dimethyl-, N-oxide
61788-90-7	Amine oxides, cocoalkyldimethyl
85408-48-6	Amines, C10-18-alkyldimethyl, N-oxides
85408-49-7	Amines, C12-16-alkyldimethyl, N-oxides
61791-47-7	Ethanol, 2,2'-iminobis-, N-coco alkyl derivs., N-oxides
2530-44-1	Ethanol, 2,2'-(dodecyloxidoimino)bis-
14048-77-2	Ethanol, 2,2'-(octadecyloxidoimino)bis-
61791-46-6	Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides
93962-62-0	Ethanol, 2,2'-[(9Z)-9-octadecenyloxidoimino]bis-

3. Sponsor Country:

United States

4. Shared Partnership with:

Amine Oxides Consortium

5. Roles/Responsibilities of the Partners:

Industry was the main preparer; U.S. EPA was the main reviewer

Name of industry sponsor or consortium

Amine Oxides Consortium

Process used

Industry coalition conducted a comprehensive literature search, including all generally accepted databases, reference books, unpublished studies and data in company files, and prepared first drafts; U.S. EPA reviewed and edited drafts to achieve a final document.

6. Sponsorship History

How was the chemical or category brought into the OECD HPV Chemicals Programme ?

The industry coalition agreed to sponsor AOs in the SIDS-ICCA program, with the U.S. being the sponsor country.

7. Review Process Prior to the SIAM:

Prepared by industry. Reviewed and edited by U.S. EPA to reach a consensus document.

8. Quality check process:

Industry coalition members developed the documents, which were then reviewed by outside third parties.

9. Date of Submission:

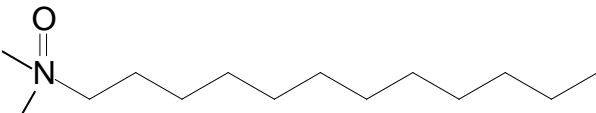
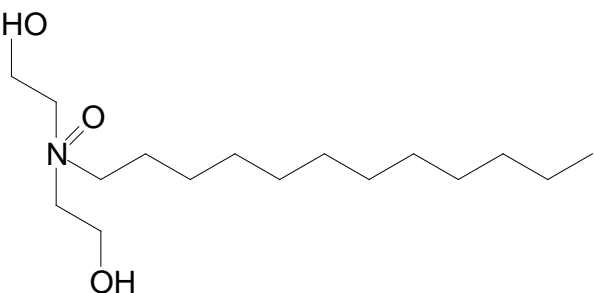
September 2006

10. Comments:

In addition to the sponsored chemicals above, one supporting substance is included that provides data on the genetic toxicity endpoint:

60729-78-4 1-(methyldodecyl)dimethylamine-N-oxide

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	1643-20-5 3332-27-2 70592-80-2 68955-55-5 2605-79-0 7128-91-8 2571-88-2 61788-90-7 85408-48-6 85408-49-7 61791-47-7 2530-44-1 14048-77-2 61791-46-6 93962-62-0	1-Dodecanamine, N,N-dimethyl-, N-oxide 1-Tetradecanamine, N,N-dimethyl-, N-oxide Amines, C10-16-alkyldimethyl, N-oxides Amines, C12-18-alkyldimethyl, N-oxides Decanamine, N,N-dimethyl-, N-oxide Hexadecanamine, N,N-dimethyl-, N-oxide Octadecanamine, N,N-dimethyl-, N-oxide Amine oxides, cocoalkyldimethyl Amines, C10-18-alkyldimethyl, N-oxides Amines, C12-16-alkyldimethyl, N-oxides Ethanol, 2,2'-iminobis-, N-coco alkyl derivs., N-oxides Ethanol, 2,2'-(dodecyloxidoimino)bis- Ethanol, 2,2'-(octadecyloxidoimino)bis- Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides Ethanol, 2,2'-[(9Z)-9-octadecenyloxidoimino]bis-
Chemical Category Name	Amine Oxides (AO)	
Structural Formula	<p>Typical structures for amine oxides are as follows:</p> <p>C12 dimethyl amine oxide</p>  <p>C12 dihydroxyethyl amine oxide</p> 	

SUMMARY CONCLUSIONS OF THE SIAR**Category Identification/Justification**

The justification for grouping the amine oxides (AO) into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl). Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the

nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenylloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-18 alkyl dihydroxy ethyl amine oxides.

Human Health

Substantial data exist for mammalian toxicity by *in vitro* and *in vivo* testing. Amine oxides are produced, and transported in aqueous solutions that are 25-35% concentration and most tests were conducted with aqueous solutions in that concentration range. Sometimes aqueous formulations were tested where the AO was at lesser concentrations than 25-35%. Whatever concentration were tested, results are reported below for the active ingredient, amine oxide, in mg AO/kg bw for dermal and oral acute toxicity results and mg AO/kg bw/day for repeated dose studies.

Toxicokinetic and metabolism studies indicate AO's are extensively metabolized and readily excreted after oral administration. Amine oxide was readily absorbed dermally by rats, mice and rabbits after 24 to 72 hours of exposure. After 8 hours of dermal exposure, humans absorbed <1%.

In rat oral acute toxicity limit tests, no deaths occurred at single doses of 600 mg C₁₀₋₁₆ AO/kg bw or less (for CAS No 70592-80-2). In multi-dose studies, acute oral LD₅₀ values for rats ranged from 846 mg AO/kg bw to 3873 mg AO/kg bw (both values for CAS No 61788-90-7), with several other AO's having rat oral LD50's falling within this range. In single dose acute dermal toxicity limit tests, no deaths occurred at a dose of 520 mg AO/kg bw (CAS No 70592-80-2). This dose was equivalent to 2 mL/kg of a 30% formulation. There were no deaths observed in a rat acute inhalation study to aerosol droplets of a consumer product providing a dose of 0.016 mg AO/L.

In a series of studies on rabbits, AO's of varying chain length showed consistent results and all 1) were not irritating to the skin or eyes at low concentrations (1%), 2) were moderately irritating at 5%, and 3) more severely irritating when tested as produced (e.g., ~30% aqueous solutions). In studies that included rinsing, eye irritation effects diminished with rinsing after 30 seconds of exposure and were slight with rinsing after 4 seconds of exposure. In Draize rabbit eye irritation tests using ~30% AO solutions, rabbits experienced severe to moderate irritation. (The maximum concentration of AO is 10% active in consumer products.) Accidental eye exposure in manufacturing employee incidents and consumer incidents established that eye irritation effects of exposure during manufacturing and use of products containing AO and other surfactants are moderate, transient and reversible.

There is no indication of skin sensitization for the AO category based on the available animal and human data.

In four repeated-dose studies with rats and mice exposed to AO via oral and dermal routes (all with CAS No 70592-80-2), three dermal studies were designed to assess the effect of repeated exposure on skin at maximum doses of 1.5 mg AO/kg-bw/day. Higher doses were tested in a 90-day dietary study with rabbits. No treatment-related clinical chemistry, hematology and histopathological changes were observed. In these studies, LOAELs ranged from 87 to 150 mg AO/kg bw/day with the highest oral NOAEL below the lowest LOAEL as 80 mg AO/kg bw/day. Signs of toxicity observed in the oral study included suppressed mean body weight gain, lenticular opacities and diarrhea; in the dermal studies, local dermal irritation was evident.

In five *in vitro* bacterial (*Salmonella*) mutagenicity studies, AO shows no evidence of mutagenicity either with or without S9 metabolic activation at concentrations up to 250 ug/plate (higher concentrations caused cytotoxicity). Three *in vivo* studies investigated clastogenic effects on a close structural analog of the category, 1-(methyldodecyl)dimethylamine-N-oxide including: a mouse micronucleus, a Chinese hamster micronucleus and a Chinese hamster cytogenetics study. These studies were all negative showing no increase in micronuclei or chromosome aberrations. An *in vivo* mouse dominant lethal assay showed no evidence of heritable effects. Two AOs (CAS No 1643-20-5 and CAS No 3332-27-2) were negative in an *in vitro* cell transformation assay tested at concentrations up to 20 ug/ml.

The carcinogenic potential of amine oxides has been thoroughly investigated in three carcinogenicity studies in rats or mice by dermal, dietary, or drinking water routes. In all cases the substances demonstrated no evidence of a carcinogenic response.

No evidence of reproductive toxicity or fertility effects was observed in a study in which rats were given dietary doses of AO in the diet over two generations (CAS No 1643-20-5). No macroscopic or histopathological changes

were attributable to treatment with the test substance. The maternal NOAEL from this reproductive study was >40 mg AO/kg bw/day, which was the highest dose tested. At all treatment levels, the rate of bodyweight gain for the F1 and F2 offspring was reduced during the lactation period, however, this reduction was not greater than 10%. This effect appeared to be dose-related, but was not statistically significant until after weaning in the mid and high dose levels. This was not considered an adverse effect since the body weight change only reached statistical significance when the rat pups were getting the majority of their calories from solid food (Developmental NOAEL >40 mg/kg bw/day). In three developmental toxicity studies via gavage in rats and rabbits (with CAS No 1643-20-5 & 70592-80-2), effects such as decreased fetal weight or delayed ossification, were most often observed only at maternally toxic doses and were associated with the irritation effects of AO on the gastrointestinal tract. No decreases in litter size, no changes in litter parameters, no malformations or significant differences in skeletal defects were observed at oral doses up to 25 mg/kg bw/day in rats (based on decreased fetal weight at 100 mg/kg bw/day) and >160 mg/kg bw/day in rabbits (the highest dose tested).

Environment

The chemicals of the amine oxides category do not exist as ‘pure’ substances, but are produced, transported and used as aqueous solutions, typically within a range of 25-35% AO/water. Experimental values for melting points of C10 to C16 amine oxides range from 125 to 136°C. Amine oxides undergo Cope elimination, i.e., the formation of an olefin and a hydroxylamine by pyrolysis of an amine oxide, in the temperature range 150-200°C, thus decomposition is likely to occur before the melting point is reached, and all boiling points are predicted to be far above the decomposition temperature. Amine oxides are not volatile: predicted vapor pressure values are < 4.6E-7 hPa. Amine oxides are highly water soluble – measured values for a C12.6 average chain length is ~410g/L. Although it is impossible to accurately measure an octanol-water partition coefficient for surface-active agents like amine oxides, an octanol-water partition coefficient (Log value) of < 2.7 has been calculated for amine oxides of chain length C14 and below. The predicted atmospheric oxidation half lives are of the order of 5 hours, indicating a relatively rapid atmospheric degradation potential.

Amine oxides are removed by conventional sewage treatment systems and biodegrade under aerobic and anaerobic conditions. Of the collected data, four amine oxides meet the “readily biodegradable” OECD criterion, two are “ultimately biodegradable,” and two are “inherently biodegradable.” These studies are conducted on complex mixtures with a high degree of alkyl chain length overlap. Further, biodegradation is not dependent on chain length. Removal of amine oxides in biological wastewater treatment has been studied in laboratory simulation studies (>99.8% removal, OECD 303A study) as well as through monitoring activities in different geographies; the main removal mechanism can be attributed to mineralization and an average removal number of 98% can be assumed as applicable for secondary activated sludge treatment. Level III fugacity modeling, using loading rates for air, soil, and water of 1000 kg/h for each media, shows water receiving compartment receiving 99.5%; the other compartments are negligible. The bioconcentration factor for amine oxides <C14, is predicted to be <87, based on log Kow data, indicating low potential for bioaccumulation in aquatic organisms.

Extensive aquatic toxicity data are available for commercially representative amine oxides (C10 to C18) that are single chain length as well as mixtures. Based on hazard data, freshwater green algae are considered the most sensitive species, for acute and chronic endpoints. Acute toxicity is affected by chain length for fish and invertebrates. Chain length affects hydrophobicity, wherein longer chain-lengths increase the rate of uptake and decrease depuration. All but four supporting AO’s have been tested for acute toxicity in fish, daphnia, and algae. The range of acute LC₅₀/EC₅₀/ErC₅₀ values based on a review of the aquatic toxicity data on AO were 0.60-32 mg/L for fish, 0.50-10.8 mg/L for *Daphnia magna* and 0.010-5.30 mg/L for algae. Chronic toxicity data were normalized to a chain length of 12.9 carbon atoms, as this average chain length represents the largest volume product for North America (CAS No 70952-80-2). Chronic toxicity (NOEC, EC20) for an amine oxide of average chain length of C12.9 ranged as follows for the different trophic levels: 0.010-1.72 mg/L for algae, 0.28 mg/L for *Daphnia* (flow through) and 0.31 mg/L for fish (flow through). These are based on geometric mean values, and a dataset of 21 chronic toxicity studies. Based on a chronic periphyton microcosm bioassay that included 110 taxa of algae (most sensitive species), a NOEC value of 0.050 mg/L was derived when normalized for a C12.9 amine oxide.

Exposure

For the AO category as a whole, current production is approximately 26,000 metric tonnes in the US (sponsor country), 16,000 tonnes in Europe and 6,800 tonnes in Japan. In the production phase, manufacturing processes have been designed to maximize production yield and minimize potential releases. The potential for human exposure to AO is minimized by a water solubility of 409.5 g/L, having volatility below 4.6E-5 Pa and being produced in aqueous solutions. Engineering controls (e.g., closed system operations, exhaust ventilation, dust collection) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and

formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for AO. A limited amount of AO in aqueous solution may be released as a dilute solution from washing and rinsing operations in the manufacturing process and is discharged to wastewater treatment.

Labeling of consumer products containing AO and other surfactants include warnings of the potential for eye irritation and first aid instructions to rinse with water.

Amine oxides are amphoteric surfactants used at active concentrations between 0.1 and 10% in consumer cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing and laundry detergents, liquid hard surface cleaners, shampoos, hair conditioners, creams, moisturizers, bar soaps, cleansing and other personal care products. There are no known commercial uses or industrial process intermediate uses of the amine oxides.

Data suggest that inhalation of AO-containing products during use will be low. Spray cleaning products containing AO are designed to produce the large particle sizes needed for efficient delivery of the spray to the surface being cleaned. In laboratory simulations with six spray nozzles representing those used in spray cleaning products, less than 0.1% of the total volume sprayed consists of respirable particles (particles under 10 microns in diameter) and air concentrations in the breathing zone are in the 0.13-0.72 mg/m³ range. Based on these data, it is expected that inhalation exposures to AO in respirable particles are low.

Results of environmental field monitoring in the United States and the Netherlands indicate that surface water concentrations downstream from sewage treatment plant mixing zones range from <0.1 to <1 µg/L. Results of a four season monitoring program in major urban rivers of Japan found concentrations ranging from non-detect (< 0.01 µg/L) to 0.34µg/L, with a median concentration of 0.04µg/L.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: This category is currently of low priority for further work. The chemicals in this category present properties indicating a hazard for human health (skin and eye irritation). However, these hazards do not warrant further work as they are related to reversible, transient and non-lasting effects. Nevertheless, these hazards should be noted by chemical safety professionals and users.

Environment: The chemicals in this category are candidates for further work. The chemicals in this category have properties indicating a hazard for the environment (aquatic toxicity <1 mg/L for fish, aquatic invertebrate and/or algae). This category is anticipated to biodegrade and has a limited potential for bioaccumulation. Member countries are invited to perform an exposure assessment and, if necessary, a risk assessment.

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1 IDENTITY

Surfactants known as amine oxides (AO) contain even numbered linear alkyl chains ranging from C₈ to C₂₀. Also known as fatty alkyl dimethyl AOs, they are usually produced by reacting alkyl dimethyl amines with hydrogen peroxide in water. The AOs are produced, transported and used in water solutions, typically at a 25-35% activity level. The AOs are produced and used either as single chain length substances (e.g., C₁₂) or as a mixture of different chain lengths (e.g., C₁₂ to C₁₈). The most common AO in commerce is the alkyl dimethyl AO, where the alkyl group contains 10 to 16 carbon atoms, predominately C₁₂ and C₁₄, and the average chain length is C_{12.9}. There is a high degree of overlap between the chain length ranges represented in several AOs that have High Production Volume (HPV) status in one or more OECD country: C₁₀₋₁₆ alkyl dimethyl AO (CAS No. 70592-80-2) and C₁₂₋₁₈ alkyl dimethyl AO (CAS No. 68955-55-5) predominantly contain the C₁₂ and the C₁₄ dimethyl AOs (CAS Nos. 1643-20-5 and 3332-27-2, respectively). The other AOs in this category include both individual chain length as well as mixed chain length substances.

1.1 Identification of the Substance Category

CAS Numbers:	1643-20-5	1-Dodecanamine, N,N-dimethyl-, N-oxide (C ₁₂ AO)
	3332-27-2	1-Tetradecanamine, N,N-dimethyl-, N-oxide (C ₁₄ AO)
	70592-80-2	Amines, C10-16-alkyldimethyl, N-oxides (C ₁₀₋₁₆ AO)
	68955-55-5	Amines, C12-18-alkyldimethyl, N-oxides (C ₁₂₋₁₈ AO)
	2605-79-0	Decanamine, N,N-dimethyl-, N-oxide
	7128-91-8	Hexadecanamine, N,N-dimethyl-, N-oxide
	2571-88-2	Octadecanamine, N,N-dimethyl-, N-oxide
	61788-90-7	Amine oxides, cocoalkyldimethyl
	85408-48-6	Amines, C10-18-alkyldimethyl, N-oxides
	85408-49-7	Amines, C12-16-alkyldimethyl, N-oxides
	61791-47-7	Ethanol, 2,2'-iminobis-, N-coco alkyl derivs., N-oxides
	2530-44-1	Ethanol, 2,2'-(dodecyloxidoimino)bis-
	14048-77-2	Ethanol, 2,2'-(octadecyloxidoimino)bis-
	61791-46-6	Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides
	93962-62-0	Ethanol, 2,2'-[(9Z)-9-octadecenylloxidoimino]bis-

Category Name: Amine Oxides

Description: AOs are used in cleaning and personal care products as foam stabilizers, thickeners, emollients, emulsifying and conditioning agents. Primary uses are in liquid hard surface cleaners, laundry and dishwashing detergents, shampoos and hair conditioning products.

Molecular Formula: CH₃.(CH₂)**R**.N(CH₃)₂:O
Where **R** is 9-17

Molecular Weight: 237 (70% C₁₂: 30% C₁₄) (molecular weight will vary depending on structure)

Synonyms:

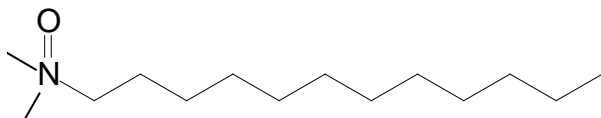
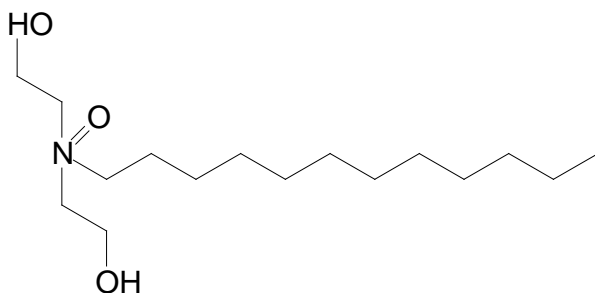
General:	dimethyl alkyl amine oxide, AO, DDAO, N,N-dimethyl alkyl amine oxide, amine oxides, fatty alkyl dimethyl amine oxides, ADAO, alkyl dimethyl amine oxide
1643-20-5:	Dimethyloctylamine oxide, Dimethyldodecylamine oxide, Lauramine oxide, Lauryldimethylamine N-oxide
3332-27-2:	Myristamine oxide, Myristyldimethylamine oxide, N,N-Dimethyl 1-tetradecanamine N-oxide, N,N-Dimethylmyristylamine oxide, Tetradecyldimethylamine oxide
70592-80-5:	Alkyl (C ₁₀₋₁₆) dimethyl amine oxide, N,N-dimethyl alkyl amine oxide
68955-55-5:	Alkyl (C ₁₀₋₁₈) dimethyl amine oxide, N,N-dimethyl alkyl amine oxide

Category Justification for AOs

The AO Consortium has identified fifteen AO substances that are included in this category. The justification for grouping the AOs into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the AO) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial AOs are either alkyl dimethyl AOs or alkyl dihydroxyethyl AOs which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 (Table 1) with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound. It should be noted that the nomenclature and CAS identifications for these AOs are based on historical and geographical considerations, not on significant differences in the structure and composition of the commercial substances. Table 1 illustrates the analogous nature of the substances.

Typical structures for AOs are as follows:

C12 dimethyl AOC12 dihydroxyethyl AO

Note: In the structure diagrams, the N-O bond that is typically depicted as double, covalent (N=O), is really a polar coordination-covalent bond (N(+)-O(-)). A tertiary nitrogen atom “shares” two electrons with oxygen; the oxygen is a powerful hydrogen bond acceptor.

The AOs and their typical chain length distributions compiled from commercial product information and test articles are shown in Table 1. All names are 9th Collective Index (CI) or CA Index name.

Table 1 : Typical Alkyl Chain Length Distribution of AOs in Category (%)*

CAS No.	Chemical Name	Avg. Chain Length	C ₈	C ₁₀	C ₁₂	C ₁₄	C ₁₆	C ₁₈	C ₂₀
1643-20-5	1-Dodecanamine, N,N-dimethyl-, N-oxide	12.0		0-1	98-100	0-1			
70592-80-2	Amines, C10-16-alkyldimethyl, N-oxides	12.9		<1	41-75	22-51	4-9	<1	
68955-55-5	Amines, C12-18-alkyldimethyl, N-oxides	13.5		0-3	50-64	18-26	9-17	6-14	0-2
3332-27-2	1-Tetradecanamine, N,N-dimethyl-, N-oxide	14.0			2-6	86-97	1-10		
2605-79-0	1-Decanamine, N,N-dimethyl-, N-oxide	10.0		96-100	0-4				
61788-90-7	Amine oxides, cocoalkyldimethyl	13.0		<1-3	64-74	21-30	2-13	<1-9	
85408-48-6	Amines, C10-18-alkyldimethyl, N-oxides	13.2		2	58	24	10	6	
85408-49-7	Amines, C12-16-alkyldimethyl, N-oxides	13.4		0-3	40-62	20-50	9-13	5-9	
7128-91-8	1-Hexadecanamine, N,N-dimethyl-, N-oxide	16.0				<3	>94	<2	
2571-88-2	1-Octadecanamine, N,N-dimethyl-, N-oxide	18.0					<5	>94	<5
2530-44-1	Ethanol, 2,2'-(dodecyloxidoimino)bis-	12.0			> 98				
61791-47-7	Ethanol, 2,2'-iminobis-, N-coco alkyl derivs., N-oxides	13.1	5	6	50	19	10	10	
61791-46-6	Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides**	17.2			1	4	31	64	
14048-77-2	Ethanol, 2,2'-(octadecyloxidoimino)bis- **	18.0						> 95	
93962-62-0	Ethanol, 2,2'-[(9Z)-9-octadecenylloxidoimino]bis-**	18.0						> 80	

*Chain length distributions based on a survey of Industry Consortia members that summarized the relevant data for sponsored materials. This distribution is a condensation of the AOs described by a particular CAS No. that are commercially available. There are some differences in industry nomenclature practice and/or use patterns across geographical regions that, in some cases, lead to differences in how some substances are identified on national and regional chemical inventories.

** The long alkyl chain may contain one or two double bonds (i.e., unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl)

The chemical behaviors of the AOs are expected to be very similar (Kirk Othmer, 2001). Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant and this may have flow-on effects on properties. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyl oxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl AO.

These substances share similar physical chemical properties, environmental fate characteristics, ecotoxicity and mammalian toxicity. A data matrix of available studies is presented in Tables 2 and 3.

Table 2 : Matrix of Available and Adequate Phys Chem, Fate and Ecotoxicity Data for the AO Category

PHYSICAL CHEMICAL CHARACTERISTICS															
	1643-20-5	70592-80-2	68955-55-5	3332-27-2	2605-79-0	61788-90-7	85408-48-6	85408-49-7	7128-91-8	2571-88-2	2530-44-1	61791-47-7	61791-46-6	14048-77-2	93962-62-0
EPISuite	CM	CM	R	CM	CM	R	R	R	CM	R	CM	R	R	CM	CM
Melting Point	A	R	R	A	A	R	R	R	A	R	R	R	R	R	R
Dissociation Const	R	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Boiling Point	A	A	A	A	CM	R	R	R	CM	R	CM	R	R	CM	CM
Vapor Pressure	CM	A-	R	CM	CM	R	R	R	CM	R	CM	R	R	CM	CM
Partition Coefficient	CM	A	R	CM	CM	R	R	R	CM	R	CM	R	R	CM	CM
Water Solubility	CM	A	R	CM	CM	R	R	R	CM	R	CM	R	R	CM	CM
ENVIRONMENTAL FATE															
Photodegradation	CM	R	R	CM	CM	R	R	R	CM	R	CM	R	R	CM	CM
Stability in Water	R	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Transport (Fugacity)	R	CM	R	R	R	R	R	R	R	R	R	R	R	R	R
Biodegradation	A	A	A	R	A	A	R	A	A-	R	R	A	A	R	A
Monitoring Data	R	A	R	R	R	R	R	R	R	R	R	R	R	R	R
ECOTOXICITY															
Acute Fish	A	A-	A	A	R	A	R	A-	A	A	A	A	A	R	A
Acute Invertebrates	A	A-	R	R	R	R	R	R	R	R	R	R	R	R	R
Acute Aquatic Plants	A	A	R	A	R	A	R	R	A	R	R	A	A	R	A
Chronic Fish	R	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Chronic Aquatic Invertebrates	A	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Terrestrial Plants	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Soil Dwelling Organisms	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
A = Reliable study data available A- = Data available, considered inadequate CM = Data requirement filled by EPIWIN computer modeling (Note EPIWIN cannot be run for mixtures. It has been applied to those endpoints where considered applicable.) R = Read across from other category members or supporting substance - = No data available															

Table 3 : Matrix of Available and Adequate Mammalian Toxicity Data for the AO Category

	1643-20-5	70592-80-2	68955-55-5	3332-27-2	2605-79-0	61788-90-7	85408-48-6	85408-49-7	7128-91-8	2571-88-2	2530-44-1	61791-47-7	61791-46-6	14048-77-2	93962-62-0
Toxicokinetics	A	R	R	R	R	R	R	R	R	R	R	R	R	R	R
Acute Oral	A	A	R	R	R	A	R	R	R	R	R	R	R	R	R
Acute Inhalation	A	R	R	R	R	R	R	R	R	R	R	R	R	R	R
Acute Dermal	R	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Skin Irritation	A	A	R	R	R	A	R	R	R	A	R	R	R	R	R
Eye Irritation	A	A	R	R	R	A	R	R	R	A	R	R	R	R	R
Sensitization	A	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Repeat Dose Toxicity	A	A	R	R	R	R	R	R	R	R	R	R	R	R	R
In vitro Genetic Toxicity	A	R	R	A	R	A	R	R	R	R	R	R	R	R	A
In vivo Genetic Toxicity	A-	R	R	R	R	R	R	R	R	R	R	R	R	R	R
Chronic / Carcinogenicity	A	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Reproductive Toxicity	A	A	R	R	R	R	R	R	R	R	R	R	R	R	R
Developmental Toxicity	A	A	R	R	R	R	R	R	R	R	R	R	R	R	R
A = Reliable study data available A- = Data available, considered inadequate CM = Data requirement filled by computer modeling R = Read across from other category members or supporting substance															

1.2 Purity/Impurities/Additives

The chemicals of the amine oxides category do not exist as ‘pure’ substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

1.3 Physico-Chemical properties

Vapor pressure: The AOs in this category are not volatile. Predicted vapor pressure values for the dimethyl AOs are in the range 4.6E-5 to 2.6E-7 Pa for increasing chain length moving from C10 to C16 (based on EPIWIN), while the predictions for the C12 to C18 dihydroxyethyl AOs range between 3.4E-12 to 7.5E-15 Pa for increasing chain length (based on EPIWIN). These EPIWIN predictions are available as robust summaries in the SIDS dossier. A measured value also exists for C10-16 AO, showing an unusually high vapor pressure of 1200-2300 Pa at 20oC (TSCA ITC, 1983). This is likely due to the fact that the substance was tested “as is”, i.e. in a 32% aqueous solution, and the value relates to the vapor pressure of water in the substance.

Partition coefficients: Although a measured logKow value exists for C10-16 AO, with a result of – 1.08 (The Procter & Gamble Co, 2002C), the accurate measurement of Kow is difficult if not impossible for surface active substances, because they tend to accumulate at the octanol/water interface, forming octanol-water emulsions. LogKow values between 0.95-2.7 have also been predicted by comparing published Critical Micellar Concentration (CMC) values of C10 to C14 AOs, in water, with measured octanol solubility values; CMC’s can be considered as a conservative measure of water solubility for surface active substances (published CMC values were obtained from Mukerjee & Mysels, 1971). Thus, AOs with alkyl chain length less than C14 can be considered as having LogKow < 2.7.

Water solubility: AOs behave as typical surfactants in aqueous solutions: below the critical micelle concentration (CMC), they exist as single molecules, while above this concentration, micellar (spherical) aggregates predominate in solution. The measured water solubility for a C12.6 average chain length was ~410 g/L (see table 4a). When compared to measured data, EPIWIN results were found to be of limited accuracy for water solubility. This is attributed to the inherent limitations of the algorithms with surface active materials.

Dissociation constant: AOs are weak bases, showing either nonionic or cationic behavior in aqueous solution depending on pH. In acid solution, the cationic form $[R(CH_3)_2 N^+-OH]$ is observed while in neutral and alkaline solution the nonionic form predominates as the hydrate $[R(CH_3)_2 NO \cdot H_2O]$. A measured pKa value of 4.1 was obtained for a C12.6 average chain length AO, which is in line with literature data on pKa values of aliphatic AOs (Kirk Othmer, 2001).

Table 4a: Physico-Chemical Properties of C₁₀₋₁₆ AO, average chain length 12.6*

Property	Values	Reference ^ψ
Molecular weight (g/ mole)	237	Calculated using EPIWIN
Melting point (°C)**	C ₁₀ AO 133 – 136 C ₁₂ AO 130 – 134 C ₁₄ AO 125 – 129 C ₁₆ AO 126 – 130 [Average: 130.5]	Devinsky et al, 1985. [2]
Boiling point (°C)	Decomposes before boiling**	TSCA ITC, 1983 [4]; Kirk Othmer, 2001 [2]
Vapor pressure (Pa)***	4.6E-5	Calculated - EPIWIN [2]; TSCA ITC, 1983 [4]
Dissociation constant	4.1	The Procter & Gamble Company, 2002B [1]
Water solubility (g/L)	409.5	The Procter & Gamble Co, 2002C [2]
Partition coefficient n-octanol/water (log value)	< 2.7	The Procter & Gamble Co, 2002C [2]

* Except Melting Point

** Aliphatic AOs undergo thermal decomposition between 90 and 200°C, and Cope elimination in the temperature range 150-200° C (formation of an olefin and a hydroxylamine by pyrolysis of an AO). As a consequence, melting is likely to be accompanied by decomposition, and all boiling points are predicted to be far above the decomposition temperature.

***predicted for a pure, dry state AO

^ψ Klimisch scores are indicated in square brackets

Table 4b EPIWIN Predictions of Physico-Chemical Properties of Single Chain Length AOs

CAS #	Chain Length	MW (g/mole)	BP (°C)	MP (°C)	VP (Pa)	Atmospheric Oxidation half-life (hours)
N,N-Dimethyl AOs						
2605-79-0	C10	201.4	403.4	152.6	4.6E-5	5.3
1643-20-5	C12	229.4	426.6	168.0	2.1E-5	4.7
3332-27-2	C14	257.5	449.8	183.3	1.5E-6	4.3
7128-91-8	C16	285.5	473.0	198.7	2.6E-7	3.9
N,N-Dihydroxyethyl AOs						
2530-44-1	C12	289.5	536.7	229.8	3.4E-12	2.4
14048-77-2	C18	373.6	606.4	262.3	7.5E-15	2.0
93962-62-0	C18:1	371.6	609.9	264.0	5.4E-15	3.0

Predictive modeling of the physical/chemical properties of the even numbered, single chain length AOs has been carried out using EPIWIN version 3.0 (see Table 4b). When compared with measured data obtained for C₁₀₋₁₆ AO (see Table 4), the EPIWIN estimates were found to be of limited accuracy for partition coefficient and water solubility. This is attributed to inherent limitations of the algorithms with surface-active substances, which have a tendency to partition to interphases between oils/fats and water and whose phase behavior is a function of temperature and concentration, characterized by a phase diagram. EPIWIN outputs for the melting point, boiling point, vapor pressure, molecular weight can be considered as useful predictors for pure, dry state, AO, however, AOs are always produced, transported, marketed and used in aqueous solutions of approximately 25-35% active substance.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Approximately 26,000 metric tonnes of total AO are produced annually in the U.S. (sponsor country). Total annual production in Europe and Japan is approximately 16,000 and 6,800 tonnes,

respectively. AOs are amphoteric surfactants that are used at active concentrations between 0.1 and 10% in consumer cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing and laundry detergents, liquid hard surface cleaners, with minor uses in personal care products like shampoos, hair conditioners, creams, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the AOs. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in industrial, institutional and commercial applications.

2.2 Environmental Exposure and Fate

Based on its use pattern, the predominant disposal route following use of the products that contain AO is via wastewater. AOs are highly water soluble (C_{10-16} AO = 409.5g/L). AO is fully biodegradable under both aerobic and anaerobic conditions and is effectively removed during wastewater sewer transport (“pipe loss” >90%) and in biological wastewater treatment (~98%). It has low potential for bioaccumulation (BCF <87 L/kg). These characteristics help to minimize the potential for environmental exposure, and for indirect human exposures via drinking water and/or fish consumption.

2.2.1 Sources of Environmental Exposure

Environmental

Production Releases

Manufacturing and formulation processes have been designed to maximize production yield and minimize potential releases. A limited amount of AO in aqueous solution may be released as a dilute solution from washing and rinsing operations in the manufacturing process. Any minimal release from manufacturing plants that produce or formulate AO is discharged to wastewater treatment. Monitoring data from a major AO manufacturing site in the U.S. which produces one of the sponsored HPV substances are available: in this study, AO levels were measured in effluents of the municipal waste water treatment plant designated to treat the production facility’s wastewater, as stipulated by an industrial discharge permit (The Procter & Gamble Company, 2003B). The range of AO concentration in effluent was 0.02 µg/L to 0.11 µg/L, measured over a 3-day period (The Procter & Gamble Company, 2005). These observations are in line with modelling predictions (U.S. EPA E-FAST) of manufacturing facility effluent discharges for high end to bounding conditions (see also “Use and Exposure Information on Amine oxides”, available from the U.S. SDA website at <http://www.sdahq.org/AMINEOXIDES/>) – output results for estimated mean and low flow (7Q10) stream concentrations were 0.046 µg/L and 0.19 µg/L, respectively, for the high end scenario.

Releases to the Environment following consumer use:

AOs are used primarily in detergent-based cleaning and personal care products. Following use, these substances are discharged down the drain and transported via the sewage system to wastewater treatment plants. Upon discharge, >90% pipe loss occurs during transport in the sewers, after which an average 98% of AO is removed by conventional wastewater treatment systems (see section 2.2.4). AOs are highly water-soluble, non-volatile and readily biodegradable under aerobic and anaerobic conditions, thus environmental concentrations are expected to be low. This has been confirmed by field monitoring studies in the United States (The Procter & Gamble Company, 2001;

The Procter & Gamble Company, 2003B). The Netherlands (The Procter & Gamble Company, 1996A; Soap and Detergent Association, Report, 2005) and Japan (The Japanese Soap and Detergent Association, Human Safety and Environment Task Force, 2003). AO concentrations in sewage treatment plant effluents were found to be in the <0.3 to 3.0 µg/L range, and river water concentrations were below 1 µg/L. In concurrence with field monitoring results, E-FAST, a U.S. EPA model to predict environmental concentrations, estimated harmonic mean and 7Q10 surface water concentrations of 0.066 and 0.34 µg/L, respectively, for down-the-drain release the United States (see also “Use and Exposure Information on Amine oxides”, available from the U.S. SDA website at <http://www.sdahq.org/AMINEOXIDES/>).

2.2.2 Photodegradation

Photodegradation rates were estimated for single chain length AOs using AOPWIN (EPIWIN version 3.1). The predicted atmospheric oxidation half lives were of the order of 5 hours, indicating a relatively rapid atmospheric degradation potential. This information is of limited relevance to this assessment, since AOs are not volatile and photodegradation in surface waters plays only a minor role as a removal mechanism.

2.2.3 Stability in Water

C₁₀₋₁₆ AO was shown to be hydrolytically stable in water over a pH range of 4 to 9 (The Procter & Gamble Company, 2002D).

2.2.4 Transport between Environmental Compartments

Fugacity modelling has been conducted to determine the theoretical distribution of AOs in various environmental compartments (Table 5). Based on EQC Level III modelling (version 2.8, 2002), using loading rates for air, soil, and water of 1000 kg/h for each media, water is quantitatively the most important receiving compartment for AOs; their predicted partitioning to water is approximately 99.5%; the other compartments are negligible. Input parameters used for the simulation are those of a C₁₀₋₁₆ AO.

Table 5 : EQC Level III - C₁₀₋₁₆ AO (70% C₁₂: 30% C₁₄ AO)

MW	Water Solubility (mg/L)	Octanol-Water Partition Coefficient (Log Kow)	Melting Point (°C)	Vapor Pressure (Pa)*	Fraction in Soil (%)	Fraction in Air (%)	Fraction in Water (%)	Fraction in Sediment (%)
237.83	409500	< 2.7	132	4.6E-05	Negligible	Negligible	99.5	0.5

* Vapor pressure used is that predicted for a pure, dry state AO; the only existing measured value reflected the water content in the sample, therefore was not considered valid for modeling purposes.

2.2.5 Biodegradation

AOs are highly removed by conventional sewage treatment systems and biodegrade rapidly and completely under aerobic and anaerobic conditions. The results of biodegradability studies are summarized in Table 6.

Commercial AOs are regarded as being readily biodegradable according to OECD criteria (CESIO, 2003). In ready aerobic biodegradation OECD screening studies, up to 93% theoretical oxygen (ThO₂) consumption and 97% dissolved organic carbon (DOC) removal was observed. Eight ready

biodegradation studies of Klimisch reliability 2 and above are summarized in Table 6: of these studies, four meet the “readily biodegradable” OECD criterion – these span C10 to C17 chain length; two studies meet the “ultimately biodegradable,” and two meet the definition of “inherently biodegradable”. One of the studies indicating ultimate biodegradability was for CAS# 70592-80-2, and was conducted pre-GLP (The Procter & Gamble Company, 1977). This same substance was later tested under GLP in a removability simulation study using radiolabel detection (The Procter & Gamble Company, 1996E): mineralization rates of 125 h⁻¹ were observed, which are 100 times faster than the 1 h⁻¹ default for a ready biodegradable material (European Commission, 2003; OECD 2005; US EPA, 2000). These rapid measured biodegradation rates are consistent with observations in field monitoring where >90% pipe loss occurs during sewer system transport and >98% of AO is removed by conventional wastewater treatment systems (see 2.2.7).

Parent AO molecules reaching surface waters are expected to undergo further mineralization. This has been shown by laboratory studies simulating biodegradation of C₁₀₋₁₆ AO on leaving an activated sludge unit and entering receiving river water (The Procter & Gamble Company, 1996D). Based on ¹⁴CO₂ measurements, AOs present in effluent derived from a continuous activated sludge (CAS) simulation study underwent extensive mineralization in river water, as indicated by the measured 63% CO₂ production in 14 days, and a mineralization half life of ~4 days.

Based on studies by Van Ginkel on fatty amine derivatives (Van Ginkel, 2004), the biodegradation pathway of AOs is expected to involve an initial cleavage of the C alkyl -N bond (N-dealkylation). The central fission leads to the formation of alkanals and hydrophilic nitrogen-containing molecules, which essentially detoxifies the molecule. The alkanals are readily converted to fatty acids and undergo beta-oxidation, resulting in shortening of the alkyl chain. Van Ginkel (2004), indicated that degraders of fatty amine derivatives have a broad substrate specificity with respect to the alkyl chain length of the fatty amine derivatives, and because of this, it is unlikely that the biodegradation rates differ significantly with various alkyl chain lengths. This is consistent with the measured data on screening studies, where ready biodegradability was observed for AO average chain lengths ranging from C10 to C17.

Table 6 : Summary of ready aerobic OECD biodegradation screening tests on AO*

Average Chain length	CAS No.	OECD Guideline or equivalent	Biodegradation in 28 days	Comments	Reference
C10	2605-79-0	OECD 301E	97% DOC removal	Readily biodegradable	Th. Goldschmidt AG (1997) Report# 970303GS
C12.9	70592-80-2	OECD 301B	63.1% ThO ₂	Ultimately biodegradable; Pre-OECD study; value is for 26day	The Procter & Gamble Company (1977B) Report# TDR-77008
C13.0	61788-90-7	OECD 301D	93% ThO ₂	Readily biodegradable	Akzo Chemie (1987) Report# SDA102
C13.4	85408-49-7	OECD 301D	48% ThO ₂	Inherently biodegradable; Value is for 30day; does not meet biodegradation criteria	Henkel KGaA (2000) Report# R0001279
C13.1	61791-47-7	OECD 301D	57% ThO ₂	Inherently biodegradable	Akzo Nobel Chemicals (1990) Report# CRL F90055
C13.5	68955-55-5;	OECD 301D	82% ThO ₂	Readily biodegradable	Akzo Nobel Chemicals (1990I) Report# CRL F90054
C17.2	61791-46-6	OECD 301D	79% ThO ₂	Readily biodegradable	Akzo Nobel Chemicals (1990G) Report# CRL F90066
C18	93962-62-0	OECD 301D	60% ThO ₂	Ultimately biodegradable	Akzo Chemicals International B.V. (1990G) Report# CRL F90067

* All studies in table have Klimisch reliability of 1 or 2.

During an anaerobic mineralization study, C10-16 AO produced 78.9% of the theoretically expected biogas (CO₂/ CH₄) in 28 days (greater than 85% was measured after 62 days). These rates support the conclusion that AOs degrade readily under anaerobic conditions (The Procter & Gamble Company (1996B, F).

2.2.6 Bioaccumulation

BCFWIN predictions using the calculated logK_{ow} value of < 2.7 as input parameters (derived for C₁₀₋₁₆ AO), calculated bioconcentration factor < 87 for C₁₂₋₁₄ AO (The Procter & Gamble Company, 2002C). Thus the potential for bioaccumulation of AOs in aquatic organisms is considered to be low.

2.2.7 Other Information on Environmental Fate

Removal of AOs by sewage treatment processes is greater than 99.8% removal as observed in a CAS study (The Procter & Gamble Company, 1996E). The laboratory simulation studies were corroborated by U.S., Netherlands and Japan monitoring data, where >96% removal in activated sludge plants was observed (The Procter & Gamble Company, 2001, The Procter & Gamble Company, 1996A, and The Japanese Soap and Detergent Association, Human Safety and Environment Task Force, 2003; see Table 7). Based on CAS data, the main removal mechanism can be attributed to mineralization (see Table 7). An average removal number of 98% can be assumed as applicable for secondary activated sludge treatment.

In the U.S. monitoring study, average AO levels in raw sewage ranged from 2.3 to 27.8 µg/L while treated effluent concentrations ranged between 0.4 and 2.91 µg/L (oxidation ditches and trickling filters effluents representing the high end values (The Procter & Gamble Company, 2001). For The Netherlands, average AO levels in raw sewage ranged from 9 to 130 µg/L (geometric mean concentration of 32 µg/L), while treated effluent concentrations were below 0.43 µg/L (The Procter & Gamble Company, 1996A).

River water concentrations have not been specifically measured for the United States however they are expected to be below 1 µg/L, based on the high end, measured effluent concentrations recorded following secondary treatment and considering a surface water dilution factor of 3 (Rapaport, 1988). Based on the monitoring data from The Netherlands, and using a surface water dilution factor of 3, surface water concentrations are expected to be below 0.14µg/L. Use of the 3 dilution factor is conservative (protective) approach compared to the standard default dilution of 10 (European Commission, 1998). Surface waters been monitored directly in four major urban rivers in Japan, determining an annual, median surface water concentration of 0.04 µg/L (The Japanese Soap and Detergent Association, Human Safety and Environment Task Force, 2003).

Table 7 : Removability and Monitoring studies on AOs*

CAS No.	Chain length	Type	Results	Reference
1643-20-5 70592-80-2	C ₁₂ C ₁₀₋₁₆	Removability	<u>Continuous Activated Sludge simulation</u> (OECD 303, CAS): 69.2% ¹⁴ CO ₂ ; >99.8% removal of parent in 33 days	The Procter & Gamble Company , 1996E
1643-20-5	C ₁₂	Removability	<u>Effluent in River water die-away simulation:</u> 69.2% ¹⁴ CO ₂ ; >99.8% removal of parent in 33 days	The Procter & Gamble Company , 1996D
70592-80-2	C ₁₀₋₁₆	Monitoring	<u>U.S.:</u> wastewater treatment plant effluent concentrations : 0.4 - 2.9 µg/L Average removal of AO in AS treatment (effluent vs. influent): >96% <u>The Netherlands:</u> wastewater treatment plant effluent concentrations : <0.43 ug/L Average removal of parent molecule in AS treatment (effluent vs. influent): >94.9 to >99.5%. <u>Japan:</u> Surface water concentrations : < 0.01 µg/L to 0.34 µg/L (median concentration = 0.04 µg/L, 95th percentile high = 0.25 µg/L).	The Procter & Gamble Company, 2001 The Procter & Gamble Company, 1996A The Japanese Soap and Detergent Association, Human Safety and Environment Task Force, 2003

* All studies in table have Klimisch reliability of 1 or 2

A less well understood mechanism that appears to contribute significantly to elimination of parent AO molecules from the environment is degradation in the sewers prior to wastewater treatment, also

referred to as “pipe-loss” (Matthijs et al., 1995). The mechanisms likely involve settling/flocculation of the substances with other waste components followed by biodegradation of the parent molecules. Comparisons of monitoring results with theoretically expected concentrations of AOs in wastewater treatment influent (based on national consumption volume) indicate that pipe-losses account for pre-wastewater treatment losses of ~98% of parent in the U.S. monitoring (The Procter & Gamble Company, 2003B) and ~91% in The Netherlands (Soap and Detergent Association, Report # SDA121bis).

2.3 Human Exposure

2.3.1 Occupational Exposure

Three AOs were included in a broad-scale National Occupational Exposure Survey (1981-1983) conducted by NIOSH (NIOSH, 1983). NIOSH conducted exposure survey to collect data on potential occupational exposures to chemical, physical, and biological agents. The survey involved on-site visits to 4,490 establishments in 522 industry types employing approximately 1,800,000 workers in 377 occupational categories (<http://www.cdc.gov/noes/default.html>). Exposure to C₁₂ AO (CAS # 1643-20-5), was reported in many occupations. The top five occupational groups where exposure occurred were, in order of decreasing numbers of employees exposed: personal services, health services, automotive dealers and service stations, communication, and chemicals and allied products. Exposure C₁₄ AO (CAS # 3332-27-2), was reported in just one group, namely health services. Exposure to C₁₈ AO (CAS # 2571-88-2), also was reported in one occupation group, namely personal services.

The potential for human exposure to AO is minimized by a water solubility of 409.5 g/L, having volatility below 4.6E-5 Pa and being produced in aqueous solutions. Engineering controls (e.g., closed system operations, exhaust ventilation, dust collection) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for AO.

2.3.2 Consumer Exposure

AOs are used in consumer cleaning and personal care products, which may be used as is, or diluted prior to or during use. Dermal contact is expected with these products. There is some potential for incidental or accidental ingestion of, inhalation of, and/or eye contact with products during handling and use. Exposure to AO in formulated consumer products is mitigated by following use and precaution instructions on product labels. Product labels reflect the hazard potential of the chemical ingredients in the product. These product labels also include first aid instructions to accompany each hazard warning. For example, products may include eye and skin irritancy warnings along with instructions to rinse thoroughly if dermal or other exposure occurs.

Spray cleaning products containing AO are designed to produce large particle sizes. These large particles are needed for efficient delivery of the spray to the surface being cleaned. This results in particle sizes that are much larger than the respirable particle sizes used in non-clinical testing. These particles are therefore not able to reach deep into the lungs where effects could occur. A study conducted for the Soap and Detergent Association (Battelle, 1999) measured the “under 10 micron” fraction delivered from 6 representative cleaning product trigger spray nozzles. The overall mean (n=30) was 0.11% particles under 10 microns and the standard deviation was 0.21. The very highest observation was 0.80%. This testing only captured the spray particles that were under 600 microns, so the actual respirable particle percent of total volume sprayed was less than 0.1%. The Battelle (1999) study also reported that for spray products in normal use conditions, the peak

breathing zone concentration under 10 microns ranged from 0.13-0.72 mg/m³. HERA (2002) measured aerosol particles less than 6.4 microns in size generated upon spraying with typical surface cleaning spray products, resulting in a product concentration of 0.35 mg/m³. These estimates of exposure to respirable particles from consumer spray products indicate that inhalation is not a route of concern for human exposure (see also “Use and Exposure Information on Amine oxides”, available from U.S. SDA).

Human exposure will be mitigated by the fact that residues from many of these products are washed or rinsed off. Dermal exposure modeling for use of products containing AO estimates exposures ranging from 0.000009 to 3.2 mg/kg/day, based on an assumption of 100% absorption (see U.S. SDA website for more details on the exposure assessment). This is likely an overestimate of exposure as actual dermal absorption is < 1% of product (Rice, 1977, discussed in 3.1.1). Inhalation modeling of trigger-spray products indicates an estimated exposure of 0.000016 to 0.00032 mg/kg/day. Environmental releases from down-the-drain discharges following product use may lead to potential environmental exposures in surface waters and indirect human exposures via drinking water and/or fish consumption. Modeled indirect human exposure estimates range from 0.00000013 to 0.00000027 mg/kg/day.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

The chemicals of the AO category do not exist as ‘pure’ substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. There is no need to test the pure compound for acute toxicity or irritation since it is not available in that form and workers and consumers will never be exposed to this concentration.

3.1.1 Toxicokinetics, Metabolism and Distribution

Absorption, elimination and distribution studies have been conducted for orally and dermally administered C₁₂ AO (CAS No. 1643-20-5) in multiple animal species. Absorption and elimination studies have been conducted in human volunteers (Rice, 1977).

Studies in Animals

In vivo Studies

The absorption, distribution, metabolism and elimination of C¹⁴-radiolabeled AOs have been studied in several species, including rats, mice and rabbits (Rice, 1977; Turan and Gibson, 1981). C₁₂ AO (CAS No. 1643-20-5), was administered topically (i.e., dermally) or orally and the distribution to skin and urine was determined.

Dermal administration (rats/rabbits). In rats, 14.2% of the topically administered AO was recovered in the urine, 1.8% in the feces, 2.5% in expired CO₂, while 48% was recovered from the application site. In mice, 11.6% of the topically administered AO was recovered in the urine, 1.4% in the feces, 2.2% in expired CO₂, while 49% was recovered from the application site. In rabbits, 42% of the topically administered AO was recovered in the urine, 2.2% in the feces, 1.4% in expired CO₂, while 39% was recovered from the application site.

Oral administration (rats/rabbits). After oral administration to male and female rats, ~75% of the radioactivity was excreted within 24 hours primarily to urine (>50%), followed by feces and expired CO₂. In rats, 1.1 – 1.5% of the orally administered AO was recovered in the liver and 1.9 – 4.8% in

the carcass; all other tissues retained $\leq 0.1\%$. Rabbits were more efficient than rats in degrading the alkyl chain to compounds containing 4-carbon acids.

Studies in Humans

In vivo Studies

Dermal administration. In humans, 10 mg radiolabeled, C₁₂ AO (CAS No. 1643-20-5) was applied to an area of the forearm (4 x 15 cm). After drying, the area was covered with a non-occlusive dressing and after 8 hours, the skin area was cleaned and the percentage of radioactivity in the stratum corneum was assayed by skin stripping (10 times). The extent of absorption was determined by appearance of radioactivity in excretion products over the next 144 hours. In humans, less than 1% (0.01 and 0.23%) of the administered AO was recovered in the excretion products, while 92% was recovered from the application site. This suggested to the authors that $<1\%$ was absorbed through the skin of humans (Rice, 1977).

Oral administration. In humans the absorption from the gastrointestinal tract and subsequent excretion of C₁₂ AO (CAS No. 1643-20-5) was rapid, as determined by the appearance of radioactivity in excretion products over the next 144 hours. Absorption and excretion were rapid with 37 - 50% of the administered radioactivity collected in the urine and 18 - 22% collected in expired carbon dioxide within 24 hour after dose administration to two volunteers. Humans were more efficient than rats in degrading the alkyl chain to compounds containing 4-carbon acids (Turan and Gibson, 1981).

Conclusion

Toxicokinetic and metabolism studies indicate AOs are extensively metabolized and rapidly excreted after oral administration. AO was readily absorbed dermally by rats, mice and rabbits after 24 to 72 hours of exposure. After 8 hours of dermal exposure, humans absorbed $<1\%$.

3.1.2 Acute Toxicity

AOs demonstrate a low to moderate order of acute oral and dermal toxicity (Table 8). Limited inhalation data are available, the available data and coincident low exposure by this route are supportive that the endpoint is addressed.

Studies in Animals

Dermal

Three reliable acute dermal toxicity studies are available on C₁₀₋₁₆ AO (CAS No. 70592-80-2). C₁₀₋₁₆AO was tested for acute dermal toxicity in separate studies in New Zealand White rabbits at limit doses of 2 mL/kg (corresponding to 520 mg active AO/kg bw) according to EPA OPP 81-2. Marked skin irritation was observed. There were no substance related deaths, establishing an acute dermal LD₅₀ of $> 2\text{mL/kg}$ bw test substance or $>520\text{ mg AO/kg bw}$ (The Procter & Gamble Company, 1978B; 1978C and 1978D).

Oral

Eight acute oral toxicity studies are available on AOs in rats. C₁₀₋₁₆ AO (The Procter & Gamble Co, 1978A, TSCA ITC, 1983, Hoechst AG, 1987A), C₁₂ AO (CAS No. 1643-20-5) (Onyx Chemical, 1985A; 1985B), C₁₀₋₁₈ AO (CAS No 61788-90-7) Hoechst AG, 1978A; 1983C) and CAS No. 93962-62-0 (Akzo Chemicals International BV, 1990F), have been tested for acute oral toxicity according to OCED 401 or equivalent in Wistar and Sprague-Dawley rats, and the results have been recalculated to reflect the toxicity of the active AO in the preparation. The substances demonstrate

a low to moderate acute oral toxicity profile. In rat oral acute toxicity limit tests, no deaths occurred at single doses of 600 mg C₁₀₋₁₆ AO/kg bw or less. In multiple dose studies, acute oral LD₅₀ values for rats ranged from 846 mg AO/kg bw to 3873 mg AO/kg bw (both values for CAS# 61788-90-7), with several other AO's having rat oral LD₅₀'s falling within this range. Symptoms noted in most of the studies included piloerection, hunched posture, abnormal gait (waddling), lethargy, decreased respiratory rate, and diarrhea.

Two formulations containing C₁₂ AO (CAS No. 1643-20-5) (Pang, 1994) are included in the dossier, though are of limited value due to the low level of AO in the formulation (0.3% AO in the formula) and the availability of reliable studies on the HPV substance as raw substances discussed above.

Inhalation

The only inhalation study identified was with a formulation containing 0.3% C₁₂ AO (CAS No. 1643-20-5), was tested in a 4 hour acute inhalation study in Sprague Dawley rats (International Research and Development Corp, 1990A; summarized in Pang, 1994). Five male and five female rats were exposed to liquid droplets aerosol of the test product at a nominal concentration of 5.3 mg product/L for 4 hours, which corresponds to 0.016 mg AO/L. The formulation was a hairspray containing 85-95% water and other ingredients. There were no deaths in the study. There were no exposure-related pharmacotoxic signs in any organs (International Research and Development Corp, 1990A; summarized in Pang, 1994)

Conclusion

In rat oral acute toxicity limit tests, no deaths occurred at single doses of 600 mg C₁₀₋₁₆ AO/kg bw or less. In multiple dose studies, acute oral LD₅₀ values for rats ranged from 846 mg AO/kg bw to 3873 mg AO/kg bw. There were no deaths observed in acute dermal toxicity studies at doses up to 2 mL/kg test substance (corresponding to 520 mg active AO/kg bw). The oral and dermal toxicity data indicate low to moderate hazard potential. There were no deaths observed in an acute inhalation study to product containing 0.3% AO with an exposure of 5.3 mg test product / L (corresponding to 0.016 mg AO/L). Less than 0.1% of the total volume sprayed from cleaning product spray nozzles consists of respirable particles and resulting estimates of exposures indicate that inhalation is not a route of concern.

Table 8 : Acute Toxicity to Mammalian Species

Species	Route of Exposure	CAS No.	LD ₅₀ (mg AO/kg bw)	Doses (mg AO/kg bw)	Reference
Rabbit	Dermal	70592-80-2	>520	520	The Procter & Gamble Co, 1978B
Rabbit	Dermal	70592-80-2	>520	520	The Procter & Gamble Co, 1978C
Rabbit	Dermal	70592-80-2	>530	530	The Procter & Gamble Co, 1978D
Rat	Oral	70592-80-2	>600	600	Hoechst AG, 1987A
Rat	Oral	70592-80-2	1330	554, 776, 1080, 1497, 2107	The Procter & Gamble Co, 1978A
Rat	Oral	93962-62-0	2394	757, 1397, 2444	Akzo Chemicals Intl BV, 1990F
Rat	Oral	61788-90-7	1236 (males) 846 (females)	375, 600, 750, 945, 1200, 1500	Hoechst AG, 1983
Rat	Oral	70592-80-2	1610 – 1850	Not available	TSCA ITC, 1983
Rat	Oral	1643-20-5	1080	1500	Onyx Chemical Co, 1985B
Rat	Oral	1643-20-5	>1275	1275	Onyx Chemical Co, 1985A
Rat	Oral	61788-90-7	3873	3000, 5000	Hoechst AG 1978

* Reliable studies shown first, above the bold line. Studies are only summarized where AO was a predominant component of the tested article, i.e., formulation studies where AO was <1% of the mixture are not included in the table.

3.1.3 Irritation

Several skin and eye irritation studies have been conducted on AOs as prepared and showed consistent, moderate to severe irritation effects (Pang, 1994). Studies are also available on formulations containing the HPV substances. There is no need to test the pure compound for acute toxicity or irritation since it is not available in that form and the consumer will never be exposed to this concentration.

Skin Irritation

Studies in Animals

C₁₀₋₁₆ AO (CAS No. 70592-80-2), C₁₂ AO (CAS No. 1643-20-5), C₁₀₋₁₈ AO (CAS No. 61788-90-7), and C₁₈ AO (CAS No. 2571-88-2), were evaluated for primary skin irritation in rabbits. The substances are moderate to severe skin irritants when tested as produced (i.e., 30% active AO). C₁₂ AO was tested as a 5% active AO aqueous solution on rabbit skin and found to be irritating with a primary skin irritation index of 2.58 (Onyx Chemical Co, 1986) or non-irritating with a primary skin irritation index of 0 or 1.41 (Onyx Chemical Co, 1973A; 1973B).

Three formulations containing 30% C₁₂ AO, 30% cocamidopropyl betaine (also a surfactant - CAS# 61789-40-0) and 40% water were tested in 24 hour rabbit skin irritation tests (Stepan, 1988). All three mixtures caused severe erythema and edema 72 hours after patch removal with a primary skin irritation index of 7.3 / 8.0.

Cocoalkyldimethyl AO (CAS No. 61788-90-7), was tested in a 4 hour rabbit skin irritation test according to OECD 404, 'as produced' (i.e. 30% active AO), under semi-occlusive patch (Hoechst

AG, 1983E) and reported to result in skin irritation. In another study, the same substance (CAS No. 61788-90-7), was tested in a 24 hour rabbit skin irritation test, at 3 concentrations: 'as produced' (i.e. 30% active AO), 10% (i.e. 3% active AO) and 1% (i.e. 0.3% active AO), under occlusive patch (Hoechst AG, 1978B). The 'as produced' treatment resulted in well defined erythema and moderate-strong edema. The 10% test substance was also irritating, with the resulting irritation decreasing with dilution of the test substance, with only light erythema and minimal edema evident at 1% (Hoechst AG, 1978B).

Four skin lotions, containing 2.5% C₁₈ AO (CAS No. 2571-88-2), were tested for skin irritation in rabbits according to the Draize method (Like et al, 1975). The authors demonstrated the minimal to moderate skin irritation observed with two of the four formulas was due to the presence of 35% mineral oil with a single variable substitution with 35% isopropyl palmitate; all of the skin lotions contained 2.5% C₁₈ AO, only those with mineral oil were skin irritants (Like et al, 1975).

C₁₀₋₁₆ AO (CAS No. 70592-80-2) was tested in rabbits and reported to be irritating (TSCA ITC, 1983). There are no additional details for this study available. CAS No. 61788-90-7 was tested 'as produced' for 3 min or 4 hours on rabbit skin. The 'as produced' test substance was corrosive to rabbit skin (Hoechst, 1987B).

Studies in Humans

C₁₂ AO was tested in a human cumulative irritation test to determine the highest non-irritating concentration that could be used in a Human Repeat Insult Patch Test (HRIPT) (The Stepan Co, 1992; Pang, 1994). The cumulative irritation screening test included 0.3, 0.6, 0.9, 1.2 and 1.5% active AO in water and included sodium dodecyl sulfate at 0.2 and 0.5% as the positive control. The 0.3% active AO was found to be non-irritating. Higher concentrations were shown to result in mild cumulative irritation; the authors selected 0.45% as the appropriate test concentration for the planned HRIPT.

C₁₀₋₁₆ AO was tested at 0.2% in humans and shown to be non-irritating (TSCA ITC, 1983). Pang (1994) summarized clinical studies on C₁₂ AO (CAS No. 1643-20-5) where volunteers were exposed to up to 5% AO in skin irritation studies. They reported a slight potential for mild cumulative irritation (Pang, 1994)

Eye Irritation

Studies in Animals

C₁₀₋₁₆ AO, C₁₂ AO, C₁₀₋₁₈ AO and C₁₈ AO were evaluated for eye irritation in the rabbit according to the Draize method. Consistent with other surfactants, the substances are severe eye irritants when tested 'as produced.' The irritation is reduced upon dilution.

C₁₂ AO was tested 'as produced' (i.e. 30% active AO) in a rabbit eye irritation study. There were no effects on the cornea or iris with only slight redness and swelling observed (Hoechst AG, 1983A). C₁₀₋₁₆ AO was tested according to the Draize method and found to be severely to moderately irritating to the rabbit eye when tested 'as produced' (i.e. 28% active AO), to unrinsed or rinsed eyes, respectively (The Procter & Gamble Co, 1978F; 1978G). The same study also included a 10% dilution of the test substance (i.e. 2.8% active AO) and demonstrated eye irritation, though less than the 'as produced' substance. In another study, C₁₀₋₁₆ AO was tested according to the Draize method and found to be moderately irritating to rabbit eye when tested 'as produced' (i.e. 27.84% active AO) to rinsed or unrinsed eyes (The Procter & Gamble Co, 1978H).

C₁₀₋₁₈ AO (CAS No. 61788-90-7) was tested 'as produced' (i.e. 30% active AO) according to OECD 405 and found to be an eye irritant (Hoechst AG, 1983B). The same substance was tested in a separate study and included dilutions of the test substance for evaluation (Hoechst AG, 1978B). In

this study, the 'as produced' substance (i.e. 30% active AO) produced slight corneal opacity, redness, swelling and discharge. The 10% test substance (i.e. 3% active AO), produced slight corneal opacity, redness, swelling and discharge. At 1%, only slight conjunctival effects were observed (Hoechst AG, 1978B).

A hair mousse formulation containing 0.3% C₁₂ AO was tested for rabbit eye irritation according to the Low Volume modification to the Draize method and found to be non-irritating (Hazelton Labs, 1986; Pang, 1994). Four skin lotions containing 2.5% C₁₈ AO were tested for eye irritation in rabbits according to the Draize method and shown to be non irritating (Like et al, 1975).

Comparisons between animal test results and human eye irritation experiences indicate that the rabbit eye irritation test is not well correlated to human responses for surfactant-based substances. Human experience with eye exposure to surfactants was reported by Freeberg and coworkers (Freeberg et al., 1984; Freeberg et al., 1986; Cormier et al., 1995) for manufacturing employees and for consumers using cleaning products, indicating that in accidental exposure situations, the effects were moderate, transient and reversible. The investigators evaluated 514 incidents and demonstrated that 88.1% of the eyes cleared in 4 days or less with no reported permanent eye damage (Freeberg et al., 1984). All eyes cleared in 28 days. Depending on the product profile and level of surfactant, labeling of consumer products containing AO and other surfactants may include warnings of the potential for eye irritation and generally provide first aid instruction to rinse with water.

Sensory Irritation

A product containing 0.3% C₁₂ AO (CAS No. 1643-20-5) was tested in an upper airway irritation study in mice (International Research and Development Corp, 1990B; summarized in Pang, 1994). Three groups of four Swiss Webster mice were exposed to liquid droplet aerosol concentrations of 0.2, 1.0 or 5.2 mg product/L, corresponding to 0.00006, 0.003, and 0.016 mg AO/L, respectively. Breathing rate was measured before, during and after the 10 minute exposure. A decrease in respiratory rate would be indicative of upper airway respiratory irritation. There were no dose related changes in respiratory rate observed in the study. There were no deaths under the conditions of this study. There was no evidence of sensory irritation under the conditions of the study.

Conclusion

When tested 'as produced' (i.e., approximately 30% active AO), AOs are moderate to severe skin and eye irritants. In multiple studies, dilution reduces the irritation response with only very minimal irritation evident with 1% aqueous solutions. In studies that included rinsing, eye irritation was not diminished when rinsing was conducted after 30 seconds of exposure and was slight with rinsing after 4 seconds of exposure. Human experience suggests that irritation effects of consumer products containing AO and other surfactants are moderate, transient and reversible.

3.1.4 Sensitization

Studies in Animals

Skin

C₁₀₋₁₆ AO (27.72% active) was evaluated for sensitization according to the Buehler method. For induction, patches of test article "as is" (i.e. 27.72% active AO) were reapplied to the same site once per week for three applications. A screening study was conducted with 10, 5, 2 and 1% (v/v) to determine the highest non-irritating concentration for challenge. After a two-week rest, a 10% (v/v) solution was used during challenge on a fresh application site for a 6-hour exposure. There was no

evidence of sensitization observed in guinea pigs exposed to AO under the conditions of this study (The Procter & Gamble Co, 1978E).

Studies in Humans

Skin

As reviewed by the Cosmetic Ingredient Review (CIR) (Pang, 1994), several studies with formulations containing AO have been conducted with no evidence of delayed contact hypersensitivity. A few similar studies on formulations containing very low levels of C₁₀₋₁₆ AO were summarized (TSCA ITC, 1983) and reported a lack of sensitization potential. A liquid hand cleanser containing 10% active C₁₂ AO (also containing chlorhexidine gluconate and 4% n-propanol) was tested in human patch tests with questionable reactions observed in 2 subjects (Muston et al, 1977; and summarized in Pang, 1994). The CIR noted that other components in the hand cleanser resulted in allergic contact dermatitis. A formulation containing 0.75% AO was tested at 1.5% under patch for 6 induction patches, then 0.75% under patch for the remaining applications due to local irritation effects. Local, primary irritation was observed during induction and challenge. There was no evidence of delayed contact hypersensitivity (Pang, 1994). Cosmetic formulations containing 0.3% active AO were tested as 50% aqueous solutions in Human Repeat Insult Patch Tests with no evidence of delayed contact hypersensitivity (Harris, 1987; summarized in Pang, 1994). After their review, the CIR concluded that dodecyl dimethyl AO (C₁₂ AO) and octadecyl dimethyl AO (C₁₈ AO) were acceptable for use in “leave-on” products up to 3.7% and 5.0%, respectively, to limit the possibility of skin irritation.

Conclusion

AOs are not skin sensitizers in animal studies or in humans.

3.1.5 Repeated Dose Toxicity

Nine oral and dermal subchronic/chronic repeat dose toxicity studies conducted in rats, mice and rabbits are available on the AOs. The results are summarized below and in Table 9. Also, of note, the carcinogenicity studies available on AOs also discuss chronic toxicity and these results are summarized in section 3.1.7.

Studies in Animals

Dermal

A 28-day rabbit percutaneous study, similar to OECD 410, and two 91-day rabbit percutaneous studies, similar to OECD 411, were conducted on liquid dishwashing detergents that contained 3% or 5% active C₁₀₋₁₆ AO (CAS No. 70592-80-2) (The Procter & Gamble Co, 1986; The Procter & Gamble Co, 1987; Petersen, 1988). These studies were conducted to assess the overall dermal profile of formulations containing AO, rather than toxicity of AO specifically. Doses were selected to provide a substantial exaggeration from the consumer use concentration of approximately 0.12% dishwashing detergent in water. The detergents were applied dermally to the shaved backs of New Zealand White rabbits at a dose volume of 2 mL/kg bw/day at concentrations of 0, 0.5, 1.0, and 2.5% dishwashing detergent in distilled water for 6 hr/day. Each test group contained 5 males and 5 females. No treatment-related deaths occurred in either study. These subchronic percutaneous toxicity studies on liquid dishwashing detergents that contained up to 5% AO showed no evidence of systemic effects in animals exposed to exaggerated concentrations. The highest formula concentration tested in either study, 2.5% detergent, lacked systemic toxicity, leading to a NOEL of 2.5% detergent (or 2.5 mg AO/kg bw/day) (The Procter & Gamble Co, 1986; The Procter & Gamble Co, 1987; Petersen, 1988).

A 28-day percutaneous toxicity study was conducted in rabbits exposed to a hair spray formulation containing 0.3% C₁₂ AO (CAS No. 1643-20-5) (6 mg AO/kg bw/day) or to vehicle control. This study was conducted to assess the overall dermal profile of the formulation, rather than toxicity of AO specifically. Nonetheless, it is included as AO was a component of the formulation that was tested. There were no treatment related deaths or systemic effects. Local irritation was observed. The study established a NOEL for the formulation that corresponds to 6 mg AO/kg bw/day (The Procter & Gamble Co, 1990; Pang, 1994).

Oral

A 91-day subchronic feeding study in rats was conducted with C₁₀₋₁₆ AO (CAS No. 70592-80-2), according to EPA OPP 82-1, to assess the potential for toxicity after repeated exposure and to determine the Maximum Tolerated Dose (MTD) for a 2-year chronic feeding study (The Procter & Gamble Co, 1980). AO was administered in diet for 13 weeks to 4 groups of rats (40 per group, 20 male and 20 female) at levels of 0, 0.1, 0.2 and 0.4% (equivalent to 0, 63, 112, and 236 mg AO/kg bw for males and 0, 80, 150, and 301 mg AO/kg bw for females).

Animals were observed daily for overt signs of toxicity and mortality and weekly for systemic effects. Body weight and food consumption were recorded weekly throughout the study. Clinical chemistry laboratory studies were performed on blood and urine collected at weeks 7 and 13 and included hematology, blood chemistry and urinalysis. Ophthalmoscopic examinations were performed on all animals prior to study, at week 6, and at study end. Complete necropsies were performed on surviving animals at study end. Histopathological examinations were performed on the major organs/tissues.

No treatment-related clinical chemistry, hematology and histopathological changes were observed. Statistically significant decreases in mean body weight were noted in group 4 males (236 mg AO/kg bw) and group 3 and 4 females (150 and 301 mg AO/kg bw, respectively). Ophthalmoscopic examination revealed lenticular opacities pertaining to the posterior cortex of the lens in males at the mid- and high-dose.

The study established 0.1% in diet (63 mg/kg bw/day for males and 80 mg/kg bw/day for females) as the no observed adverse effect level (NOAEL) and 0.2% (112 mg/kg bw for males and 150 mg/kg bw/day for females) in diet as the LOAEL based on decreased body weight in females (The Procter & Gamble Co, 1980).

A 32 week subchronic feeding study in rabbits, with interim sacrifice at 13 weeks, was conducted with C₁₀₋₁₆ AO (CAS No. 70592-80-2) (The Procter & Gamble Co, 1977A). AO was administered in diet to 4 groups of rabbits (50 per group, 25 male and 25 female) at levels of 0, 0.1, 0.5 and 1.0% for 32 weeks. An interim sacrifice was conducted at 13 weeks with all of the surviving high dose animals and 5 animals per group for the other dose levels. Doses were equivalent average daily doses of 0, 40, 196, and 390 mg AO/kg bw for males and 0, 39, 195, and 380 mg AO/kg bw for females.

Animals were observed daily for overt signs of toxicity and mortality and weekly for systemic effects. Body weight and food consumption were recorded weekly throughout the study. Clinical chemistry studies were performed at weeks 0, 13 and 32 and included hematology and blood chemistry. Ophthalmoscopic examinations were performed on all animals prior to study, at weeks 6, 9, 13, 18, 22 and at study end. Complete necropsies were performed on surviving animals at study end. Histopathological examinations were performed on the major organs/tissues.

Decreased alkaline phosphatase levels and an increased liver/body weight ratio were noted in the mid-dose (0.5% AO) males. No compound-related gross pathological or histopathological findings were noted in the treated animals compared to controls. There were no ophthalmoscopic effects.

The study established 0.1% in diet (40 mg/kg bw/day for males and 39 mg/kg bw/day for females) as the no observed adverse effect level (NOAEL) and 0.5% (196 mg/kg bw for males and 195 mg/kg bw/day for females) in diet as the LOAEL based on decreased alkaline phosphatase and increased liver/body weight ratio in males (The Procter & Gamble Co, 1977A).

Conclusion

The AOs have been well examined for repeated dose toxicity in rats and rabbits by the oral route in studies of 90 days to 2 years duration. The major findings were decreased body weight and lenticular opacities, observed in the 90-day study at doses of 112 mg/kg bw/day and above with the highest NOAEL below the lowest LOAEL as 80 mg AO/kg bw/day.

The dermal studies on finished products containing AOs demonstrated a lack of systemic effects with local irritation evident at the high doses of the products. It should be noted that several of the studies are finished product mixtures containing AO and therefore had a relatively low concentration of AO in the test matrix. Nonetheless, these studies provide information about the dermal effects of products containing AO.

Table 9 : Summary of Subchronic and Chronic Toxicity Tests

Species	CAS No. Route of Exposure	Study Duration	NOAEL (mg AO/kg bw)	LOAEL (mg AO /kg bw)	Doses (mg AO/kg bw)	Reference
Rat	70592-80-2 Oral feed	91 days	63 (m) 80 (f)	112 (m) based on lenticular opacity 150 (f) based on decreased body weight	Males: 0, 63, 112 and 236; Females 0, 80, 150, and 301	The Procter & Gamble Company, 1980
Rabbit	70592-80-2 Oral feed	32 weeks Interim sacrifice at 13 weeks	40 (m) 195 (f)	196 (m) based on increased liver: bw ratio	Males: 0, 40, 196 and 390; Females 0, 39, 195, and 380	The Procter & Gamble Company, 1977A
Rat	1643-20-5 Drinking water	93 weeks	There was no effect on life span. For AO exposed, no increase in any tumor compared to untreated controls	-	0.1% in drinking water corresponding to ~250 mg/kg bw	Lijinsky, 1984
Rat	70592-80-2 Oral feed	2 years	42.3 (males) 52.6 (females)	87.4 (m) 107 (f) based on decreased mean body weight	Males: 0, 4.24, 42.3, 87.4 Females: 0, 5.23, 52.6, 107	Cardin et al, 1985; The Procter & Gamble Co, 1979B
Mouse	70592-80-2 Dermal	2 years	No systemic effects. High dose: skin irritation observed microscopically. No skin tumors. No compound-related skin or systemic tumors.	-	0.1 mL aqueous solution of AO at 0, 0.05%, 0.13%, or 0.26%; corresponds to average daily dose of 0, 1.1, 2.8 or 5.6 mg AO/kg bw/day	Cardin et al, 1985; The Procter & Gamble Co, 1979A
Rabbit	70592-80-2 Dermal	28 days	No systemic effects; high dose provides 1 mg AO/kg/day*	-	<i>formula</i> providing 0, 0.1, 0.5, 1.0 mg AO/kg bw/day	The Procter & Gamble Co, 1986; Petersen, 1988
Rabbit	70592-80-2 Dermal	91 days	No systemic effects; high dose provides 2.5 mg AO/kg/day*	-	<i>formula</i> providing 0, 0.5, 1, 2.5 mg AO/kg bw/day	The Procter & Gamble Co, 1986; Petersen, 1988
Rabbit	70592-80-2 Dermal	91 days	No systemic effects; high dose provides 1.5 mg AO/kg/day*	-	<i>formula</i> providing 0, 0.3, 0.6, 1.5 mg AO/kg bw/day	The Procter & Gamble Co, 1987; Petersen, 1988
Rabbit	1643-20-5 Dermal	28 days	No systemic effects; high dose provides 6 mg AO/kg/day*	-	<i>formula</i> providing 6 mg AO/kg bw/day	The Procter & Gamble Co, 1990; Pang, 1994

* Of limited value for NOAEL determination due to low level of AO in tested formulations.

3.1.6 Genetic Toxicity

AOs have been assessed for mutagenic potential in a variety of *in vitro* and *in vivo* assays (see Table 10). In addition, a supporting substance, 1-methyl-C₁₂AO (CAS No. 60729-78-4), that provides relevant *in vivo* genetic toxicity data was identified.

Ames assays in *Salmonella typhimurium* (Andrews et al., 1984 and Inoue et al., 1989), cell transformation assays in Syrian Hamster embryo cells (Inoue et al., 1989), and a dominant lethal assay in mice (The Procter & Gamble Co, 1983) have been reported on AOs. The supporting substance was negative in a mouse micronucleus assay (Szabova and Devinsky, 1988), a Chinese hamster micronucleus and an *in vivo* cytogenetics studies (Karasova et al, 1987). The existing AO genetic toxicity dataset provides information to address the potential to cause transmissible damage to the genetic material of somatic cells (with potential carcinogenic or other consequences) and germ cells (which may result in heritable damage to the offspring).

In vitro Studies

Ames Assays: The mutagenic potential of C₁₂ AO (CAS No. 1643-20-5) (29.1% active ingredient) and C₁₄ AO (CAS No. 3332-27-2) (26.7% active ingredient) were evaluated in the bacterial reverse mutation assay using *Salmonella typhimurium* strains TA100 and TA 98 (Ames Test) (Inoue et al, 1980). There was no evidence of mutagenicity observed with C₁₂ AO (CAS No. 1643-20-5) or C₁₄ AO (CAS No. 3332-27-2) with or without PCB-induced rat liver S-9 activation.

Andrews et al (1984), evaluated the mutagenic potential of eight amine or amide drugs and their N-nitroso derivatives formed after interactions with nitrous acid, including C₁₂ AO (CAS No. 1643-20-5) and nitrosated dimethyl dodecyl AO. The mutagenic potential was evaluated in the bacterial reverse mutation assay using *Salmonella typhimurium* strains TA1535, TA1538, TA100 and TA 98 (Ames test). No evidence of mutagenicity was observed with C₁₂ AO with and without Aroclor-induced rat liver S-9 activation. Nitrosated dimethyl dodecyl AO was positive to strain TA1535.

CAS No. 93962-62-0 was also tested for mutagenic potential in a reliable Ames assay according to OECD 471 (Akzo Chemicals International BV, 1990A). There was no evidence of mutagenicity observed with or without metabolic activation.

Cocoalkyldimethyl AO (CAS No. 61788-90-7) was also tested for mutagenic potential in an Ames assay according to OECD 471 (Hoechst AG, 1989A) with no evidence of mutagenicity observed with or without metabolic activation.

Cell Transformation (SHE assay): Inoue et al. (1989) exposed cell lines from Syrian golden hamster embryos to C₁₂ AO (CAS No. 1643-20-5) (29.1% active ingredient) and C₁₄ AO (CAS No. 3332-27-2) (26.7% active ingredient) at concentrations of 0.1, 1, 5, 10, and 20 µg/mL. AOs did not induce cell transformation under the conditions of the assay.

In vivo Studies

Dominant Lethal Assay: The potential of C₁₂ AO (CAS No. 1643-20-5) to induce heritable genetic effects was evaluated in a Dominant Lethal Assay in mice (The Procter & Gamble Co, 1983). Treated males (20 per treatment group) received 10, 100, or 1000 mg/kg bw AO in the drinking water. After last treatment, males were mated with untreated females for a period of 7 days. To study successive germ cell stages of the males, each male was then housed with two additional females for a period of seven weeks. Pregnant females were sacrificed on day 13 or 14 of pregnancy and total implantations, resorptions and dead embryos were counted and recorded. Pregnancy rate was not significantly affected by treatment of male mice with AO. There was no significant reduction in average number of implants per pregnancy, average number of resorptions or dead embryos detected in any treatment group. While this study only evaluated seven weeks of

sequential matings, and could be faulted for not allowing the least mature cells adequate opportunity to "express" any genetic damage, it does provide useful information that can be evaluated in the weight-of-evidence against heritable gene mutation for AOs.

No mutagenic effects were detected in any treatment group.

Mammalian Erythrocyte Micronucleus test: Szabova and Devinsky (1988) evaluated the effect of AO on micronuclei in mice exposed to the supporting substance 1-methyl-C₁₂AO (CAS No. 60729-78-4). 1-methyl-C₁₂AO, dissolved in water, was administered to 8 week old male and female mice weighing 25-30 g as 0.1 mL/10g single dose p.o.

There was no statistical increase in micronuclei (t-test at $p < 0.05$).

Karasova et al (1987) evaluated the effect of AO on micronuclei in Chinese hamsters exposed to the supporting substance 1-methyl-C₁₂AO (CAS No. 60729-78-4). 1-methyl-C₁₂AO, at doses of 160, 300, and 700 mg/kg i.p. was administered to animals 8-10 weeks old weighing 25-30 g. The study included 2 administrations, 24 hr apart, 6 hr harvest after last dose and included negative (water) and positive control (cyclophosphamide). Bone marrow was collected from both femurs, prepared separately for each animal. 1000 PCE analyzed for the incidence of micronuclei.

There was no increase in micronuclei formation; the positive control showed an appropriate response.

Mammalian Bone Marrow Chromosome Aberration Test: Karasova, et al (1987) evaluated the cytogenetic effect of AO in Chinese hamsters exposed to the supporting substance 1-methyl-C₁₂AO (CAS No. 60729-78-4). 1-methyl-C₁₂AO, at doses of 160, 300, and 700 mg/kg i.p. was administered to animals 8-10 weeks old weighing 25-30 g. Colchicine was administered two hours prior to sacrifice. The authors analyzed 250 metaphase cells / concentration.

There was no increase in chromosome aberrations for 1-methyl-C₁₂AO; the positive control showed an appropriate response.

Table 10 : Summary of *in vitro* and *in vivo* Genetic Toxicity Studies

Test Type	Strains/ Species	CAS No / Test Substance*	Doses	Conclusion	Reference
Ames	TA100 & TA98	1643-20-5 C ₁₂ AO	10-200 µg/plate	No evidence of mutagenicity with or without S9 activation	Inoue et al, 1989
Ames	TA100 & TA98	3332-27-2 C ₁₄ AO	10-200 µg/plate	No evidence of mutagenicity with or without S9 activation	Inoue et al, 1989
Ames	TA100, TA98, TA1535, TA1538	1643-20-5 C ₁₂ AO	250 µg/plate	No evidence of mutagenicity with or without S9 activation	Andrews et al, 1984
Ames	TA1535, TA1537, TA98, TA100	93962-62-0	-S9: 0.33 - 33.3 µg a.i./plate. +S9: 1.0 - 100.0 µg a.i./plate.	No evidence of mutagenicity with or without S9 activation	Akzo Chemicals International BV, 1990A
Ames	TA98, TA100, TA1535, TA1537, TA1538	61788-90-7	0.8 - 2500 µg/plate	No evidence of mutagenicity with or without S9 activation	Hoechst AG, 1989A
Cell Transformation	Cell lines from Syrian golden hamster embryos	1643-20-5 C ₁₂ AO	0.1 – 20 µg/mL	No evidence of cell transformation	Inoue et al, 1989
Cell Transformation	Cell lines from Syrian golden hamster embryos	3332-27-2 C ₁₄ AO	0.1 – 20 µg/mL	No evidence of cell transformation	Inoue et al, 1989
Dominant Lethal	Mouse	1643-20-5 C ₁₂ AO	10, 100, 1000 mg/kg bw (drinking water)	No effects on pregnancy rate, number of implants per pregnancy, average # resorptions or dead embryos	The Procter & Gamble Co, 1983
Micronucleus	Mouse	60729-78-4* 1Me-C ₁₂ AO	235 mg/kg (gavage)	No increase in micronuclei; negative	Szabova and Devinsky, 1988
Micronucleus	Chinese hamster	60729-78-4* 1Me-C ₁₂ AO	160, 300, 700 mg/kg (i.p.)	No increase in micronuclei; negative	Karasova et al, 1987
Cytogenetics	Chinese hamster	60729-78-4* 1Me-C ₁₂ AO	160, 300, 700 mg/kg (i.p.)	No increase in chromosome aberrations; negative	Karasova et al, 1987

*CAS # 60729-78-4 is a supporting substance for the AO category providing reliable *in vivo* genetic toxicity information for the category.

Conclusion

The available studies for AOs support the conclusion that there is not a concern for carcinogenicity or genotoxicity. Several studies are available to address genetic toxicity and heritable damage: genetic toxicity (*in vitro* and *in vivo*) (Table 10), carcinogenicity studies (Table 9), developmental and reproductive toxicity (Table 11) studies are available.

Further, there are no structural alerts for these chemicals. The identification of structural features of electrophiles and their precursors has been a centerpiece for structure-activity relationship (SAR)

prediction of genotoxic carcinogens (Lai and Woo, 2001). Lai and Woo identified ten general structural criteria of potential mutagenic and carcinogenic chemicals that are electrophiles or that may generate electrophiles after metabolic transformation – AOs do not contain these alerts.

In summary, the above summary of the available information on AOs supports the conclusion that there is not a concern for carcinogenicity or genotoxicity.

3.1.7 Carcinogenicity

Chronic toxicity/carcinogenicity data exist on C₁₀₋₁₆ AO (CAS No. 70592-80-2) in rats orally exposed and mice dermally exposed (The Procter & Gamble Company, 1979A; The Procter & Gamble Company, 1979B; Cardin et al, 1985). A chronic drinking water study with C₁₂ AO (CAS No. 1643-20-5) in rats is also available (Lijinsky, 1984). These chronic studies provide compelling data to demonstrate that the AOs are not carcinogenic.

Dermal (Cardin et al, 1985; The Procter & Gamble Company, 1979A)

Seventy-five male and 75 female ICR Swiss mice received a 0.1 mL dermal application of an aqueous solution of C₁₀₋₁₆ AO (CAS No. 70592-80-2) at concentrations of 0, 0.05%, 0.13%, or 0.26% (on a 100% active basis) to the clipped dorsal skin once daily three times per week for 104 weeks; this corresponds to an average daily dose of 0, 1.1, 2.8 or 5.6 mg AO/kg bw/day. Compound related skin irritation limited the dose selection for chronic exposure, though the highest dose exceeds the exposure consumers experience via hand dishwashing (a main use of the AO that was considered for this study; www.sdahq.org/amineoxides provides additional details on consumer exposure).

There were no statistical differences in group average body weight, organ weights, and organ to body weight ratios among treated animals compared to controls.

Compound-related skin irritation was observed microscopically in the high dose group of mice. No skin tumors were observed in any group. There were no compound-related skin effects or systemic neoplasms in the study.

There was no evidence of a carcinogenic response at any dose level.

Oral (Cardin et al, 1985; The Procter & Gamble Company, 1979B; Lijinsky, 1984)

Oral Feed Study: Sixty male and 60 female rats per group were exposed to 0, 0.01, 0.1 or 0.2% C₁₀₋₁₆ AO (CAS No. 70592-80-2), corresponding to 0, 4.24, 42.3, or 87.4 mg/kg bw/day for males and 0, 5.23, 52.6, or 107 mg/kg bw/day for females, in their diet for 104 weeks.

There were no treatment related effects on survival, clinical chemistry, ophthalmoscopic exams, gross observations, histopathologic exams or clinical signs. The high dose animals demonstrated >10% decreases in mean body weight. There were no compound-related effects on histopathologic examination. This study established 0.1% (42.3 mg AO/kg bw for males and 52.6 mg AO/kg bw for females) in diet as the NOAEL for systemic effects. The LOAEL was 87.4 (males) and 107 (females) mg AO/kg bw/day based on decreased mean body weight.

There was no evidence of a carcinogenic response after chronic dietary administration of AO to rats.

Drinking water: Lijinsky (1984) studied the administration of a variety of amines, including C₁₂ AO (CAS No. 1643-20-5), in the presence and absence of sodium nitrite for the ability to cause a tumorigenic response. The author was investigating “environmentally important” materials that could interact with nitrites. Twenty four male and 24 female F344 rats were exposed to drinking water containing 0.1% C₁₂ AO, or to 0.1% C₁₂ AO with 0.2% sodium nitrite for 93 weeks. The

authors noted that while the 0.1% C₁₂ AO was not designed to be a MTD, it was marginally toxic. Controls received untreated feed or water. Nitrite-treated controls were given 0.2% sodium nitrite in drinking water.

There was no effect on life span for either treatment group.

For animals exposed to C₁₂ AO alone, there was no evidence of an increase in the incidence of any tumor compared to the untreated controls.

For males exposed to AO with 0.2% sodium nitrite, an increased incidence of liver carcinomas compared to sodium nitrite only-treated animals was observed.

Conclusion

AOs have been assessed for carcinogenicity in three studies by dermal and oral (feed and drinking water) routes of exposure in rats and mice. In all cases the substances demonstrated no evidence of a carcinogenic response.

3.1.8 Toxicity for Reproduction

Development toxicity and reproductive toxicity studies are available for AO.

Effects on Fertility

In a two-generation reproduction study, rats received 0, 750, 1500, and 3000 ppm of C₁₂ AO (CAS No. 1643-20-5) in diet for 6.5 weeks; doses were reduced to 0, 188, 375 and 750 ppm for the remainder of the study due to toxicity (inhibition of body weight gain) at the mid and high dose (Lion Corp, 1979B). The F1 generation received 0, 188, 375, and 750 ppm in diet. Doses were converted from ppm in the diet to chemical intake based on the actual feed consumption, by reviewing recorded food consumption and animal body weights.

750 ppm corresponds to 40 mg/kg bw/day; 375 ppm corresponds to 20 mg/kg bw/day; and 188 ppm corresponds to 11 mg/kg bw/day.

Slight reductions in weight gain of both parents and offspring were evident, but were without adverse effect on mating performance and fertility. At all treatment levels, the rate of bodyweight gain for the F1 and F2 offspring was reduced during the lactation period, however, this reduction was not greater than 10%. This effect appeared to be dose-related, but was not statistically significant until after weaning in the mid and high dose levels. This was not considered an adverse effect since the body weight change only reached statistical significance when the rat pups were getting the majority of their calories from solid food (i.e., suggestive of a palatability effect) and was not associated with any other effects. Mating performance, fertility, and conception rate were not affected by treatment in either generation. There was a slight reduction in the number of F2 offspring born at the 750 ppm level, however, there were no adverse effects of treatment on litter size at birth, live birth index and birth weight in either generation. Further, this slight reduction in mean viability index in treatment groups (91% to 93%, 4 and 25 days post partum, respectively) and viability index in control group (99% to 99%, 4 and 25 days post partum, respectively) was within normal variation and was not considered an adverse effect. No macroscopic or histopathological changes were attributable to treatment with the test substance.

Based on the lack of adverse reproductive effects in the study, the maternal NOAELs was > 750 ppm, which corresponds to > 40 mg/kg bw/day (Lion Corp, 1979B). The NOAELs for the F1 and F2 offspring was >40 mg/kg bw/day (Lion Corp, 1979B).

Developmental Toxicity

There are three developmental toxicity studies available on AOs (Lion Corp, 1979A; 1980; The Procter & Gamble Co, 1999)

C₁₂ AO (CAS No. 1643-20-5) was administered via gavage at 0, 50, 100, or 200 mg/kg bw/day to female Charles River CD rats during days 7 to 17 of gestation (Lion Corp, 1979A). Approximately two-thirds of the animals in each group were sacrificed on Day 20 of gestation and the uterine contents examined, including number of *corpora lutea* in each ovary, number of implantation sites, number of resorption sites (early or late), number of live and dead fetuses in each uterine horn, including an estimation of time of death of non-viable fetuses, weight and sex of fetuses, individual placental weights, and external abnormalities. Extensive skeletal examinations were also performed on approximately half of each litter, and visceral examinations were performed on the remainder of the fetuses.

The remaining one-third of the females in each treatment group was permitted to deliver their young naturally and rear their own offspring until weaning on Day 25 post-partum. F1 animals were paired at 10 weeks of age. On Day 20 of gestation, the females were killed and uterine contents were examined macroscopically and examined as above.

At 200 mg/kg/day, slight reductions (<10%) in body weight and water consumption were observed. In females killed on Day 20 of gestation, mean fetal weight was depressed at the highest dose level, and this was associated with a slight retardation of fetal ossification. However, in females allowed to litter, parturition, survival, and growth and development of F1 offspring were unaffected by previous treatment with the test substance. The subsequent growth, mating performance, and fertility of F1 animals was similar in all groups, but in F1 females derived from F0 females that received 200 mg/kg/day, fetal and placental weights were slightly elevated compared with concurrent controls. Dosages of 50 and 100 mg/kg/day were tolerated without discernible influence upon the dam or upon the course and outcome of pregnancy. At terminal necropsy of F1 animals, no macroscopic changes were observed that could be related to treatment of F0 females.

In this study, the maternal NOEL was 100 mg/kg/day based on decreased body weight and water consumption in the 200 mg/kg bw/day group. The NOEL for adverse developmental effects (decreased fetal weight) was 100 mg/kg/day (Lion Corp, 1979A).

C₁₂ AO (CAS No. 1643-20-5) was administered to New Zealand White rabbits via gavage at 0, 40, 80 or 160 mg/kg bw/day during days 6 to 18 (inclusive) of gestation (Lion Corp, 1980). On Day 29 after insemination, animals were sacrificed and examined macroscopically for evidence of disease or adverse reaction to treatment. The following was recorded: number of corpora lutea in each ovary, number of implantation sites, number of resorption sites (early or late), number of live and dead fetuses in each uterine horn, including an estimation of time of death of non-viable fetuses, weight and sex of fetuses, individual placental weights, and external abnormalities. Extensive skeletal examinations were also performed on all fetuses from each litter.

There were no adverse effects upon survival and development *in utero*. Maternal condition was generally unaffected by treatment with the test substance; however, maternal bodyweight gain was depressed in all treated groups, although at 40 mg/kg bw/day terminal bodyweights similar to those of controls were achieved. Three females receiving 80 mg/kg bw/day and three females receiving 160 mg/kg/day died or were killed in extremis, but no direct involvement of the test substance was apparent. Food intake, when compared with pre-treatment values, was reduced during the second half of the treatment period in groups receiving 40 and 80 mg/kg bw/day, and from the commencement of treatment in animals receiving 160 mg/kg bw/day. Water intake was also decreased in all treated groups. Reductions in body weight gain, food intake and water intake did not exceed 10%. Litter response was unaffected by any treatment with the test substance. No

adverse effects upon litter responses and development were recorded. No teratogenic responses were observed.

The maternal NOEL was >160 mg/kg bw/day based on decreased body weight. No developmental toxicity was observed; the NOEL for developmental effects was >160 mg/kg bw/day (Lion Corp, 1980).

Table 11 : Summary of Oral Reproductive and Developmental Toxicity Studies

Species	Material CAS No. Route	Exposure in Pregnancy	NOAEL Maternal (mg AO/kg bw/day)	NOAEL Fetal (mg AO/kg bw/day)	Doses (mg AO/kg bw/day)	Reference
Rat	C ₁₂ AO 1643-20-5 Oral feed	continuous	>40	>40	0, 750, 1500, 3000 ppm for 6.5 wks; then 0, 188, 375 and 750 ppm (750 ppm corresponds to 40 mg/kg bw/day)	Lion Corp, 1979B
Rat	C ₁₂ AO 1643-20-5 Gavage	Days 7-17	100	100	0, 50, 100, or 200	Lion Corp, 1979A
Rabbits	C ₁₂ AO 1643-20-5 Gavage	Days 6-18	>160	>160	0, 40, 80 or 160	Lion Corp, 1980
Rat	C ₁₀₋₁₆ AO 70592-80-2 Gavage	Days 6-19	25	25	0, 25, 100 or 200	The Procter & Gamble Co, 1999

C₁₀₋₁₆ AO, was tested according to EPA OTS 798.4900 in Sprague Dawley rats (The Procter & Gamble Co, 1999). Animals received 0, 25, 100, and 200 mg a.i./kg bw by gavage on days 6 through 19 gestation. One treatment related death occurred in the high dose group. Reduced weight gain and relative food consumption were seen in mid and high dosage groups. Fetal body weights and live litter sizes were decreased, and early resorptions were increased in high dose animals. Fetal variations consisting of delays in skeletal ossification were associated with reduced fetal body weights in high dose animals. Some delays in fetal ossification were also noted in mid dose animals. Delays in ossification observed in the low dose animals were within laboratory historical control information and was not supported by an increase in the more relevant parameter, the percentage of litters with this variation and was considered non-adverse developmental variation. No fetal malformations were observed at any dose level. No maternal toxicity, alterations in pregnancy rates, fetal toxicity or fetal effects were attributed to treatment in the low dose groups.

The maternal NOAEL was 25 mg/kg bw/day and the maternal LOAEL was 100 mg/kg bw/day based on decreased body weight (The Procter & Gamble Co, 1999). The developmental NOAEL was 25 mg/kg bw/day and the developmental LOAEL was 100 mg/kg/day based on a decrease in fetal weight which occurred in the presence of maternal toxicity.

Conclusion

AOs have been evaluated for the potential to cause reproductive toxicity in rats and rabbits and were not developmental toxicants, nor did they demonstrate reproductive toxicity.

3.2 Initial Assessment for Human Health

Toxicokinetic and metabolism studies indicate that the AOs are extensively metabolized and rapidly excreted after oral administration. AO was readily absorbed dermally by rats, mice and rabbits after 24 to 72 hours of exposure. After 8 hours of dermal exposure, humans absorbed <1%. In rat oral acute toxicity limit tests, no deaths occurred at single doses of 600 mg C₁₀₋₁₆ AO/kg bw or less. In multiple dose studies, acute oral LD₅₀ values for rats ranged from 846 mg AO/kg bw to 3873 mg AO/kg bw. The dermal acute toxicity LD₅₀ value was > 520 mg AO/kg bw. There were no deaths observed in an acute inhalation study with a product at a dose of 0.016 mg AO/L. Less than 0.1% of the total volume sprayed from consumer product spray nozzles consists of respirable particles and estimates of exposure indicate that inhalation is not a route of concern for human exposure.

In a series of studies on rabbits, the AOs were found to be not irritating to the skin or eyes at low concentrations (1%), moderately irritating at 5%, and severely irritating when evaluated 'as produced' (i.e. ~30% active AO). In studies that included rinsing, irritation effects were not appreciably attenuated when rinsing was conducted after 30 seconds of exposure and were only slightly attenuated with rinsing after 4 seconds of exposure. The maximum concentration of AO in consumer products is less than 10% and human experience has established that irritation effects of consumer products containing AOs and other surfactants are mild to moderate, transient and reversible. There is no indication of skin sensitization for the AO category based on the available animal and human data.

In repeated dose exposures to AOs via oral and dermal routes, LOAELs ranged from 87 to 150 mg/kg bw/day. The highest NOAEL below the LOAEL was 80 mg/kg bw/day. Effects observed included suppressed body weight gain.

No evidence of genetic toxicity was observed. There are three reliable carcinogenicity studies available that show no evidence of cancer by oral feed, drinking water or dermal routes of exposure. The highest dose tested in the oral feed carcinogenicity studies was 107 mg AO/kg bw/day. Effects observed included suppressed body weight gain.

Similarly, no evidence of reproductive effects was observed in any of the available developmental or fertility toxicity studies in which rats or rabbits were exposed to AOs. The NOAEL from this reproductive study was obtained at the high dose level of 40 mg/kg bw/day (750 ppm dose level). In the developmental toxicity studies, effects such as decreased fetal weights and increased incidence of skeletal variations secondary to maternal toxicity were observed at oral doses up to 100 mg/kg bw/day. Maternal toxicity was observed and was associated with the irritation effects of AO on gastrointestinal tract.

The most appropriate overall NOAEL from the mammalian toxicity studies was determined to be 80 mg/kg bw/day based on a weight of evidence approach. This value comes from a 91-day rat feeding study on C₁₀₋₁₆ AO, and represents the highest NOAEL value below the lowest LOAEL from all studies.

E-FAST modeled estimates of environmental concentrations leading to indirect human exposure from drinking water and fish consumption range from 0.000000064 to 0.00000018 mg/kg/day. Similarly, the results of modeling dermal exposure during consumer use range from 0.0000094 to 3.2 mg/kg/day. Inhalation modeling of trigger-spray products indicates an estimated exposure of 0.000016 to 0.00032 mg/kg/day. These human exposure evaluations include conservative (protective) input assumptions, e.g. all dermally modeled exposures use of a default assumption of 100% absorption vs. a measured value of <1%.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Data on SIDS endpoints for aquatic effects are available for a wide range of taxonomic groups and include dimethyl- as well as dihydroxyethyl- AOs. Acute toxicity studies are available for single chain length AOs as well mixtures. Twenty-one chronic toxicity studies were conducted with fish, daphnid invertebrates and algal species. In the case of mixtures, the chain length shown is the average chain length of the AO that was tested.

Acute Toxicity Test Results

Based on hazard data, freshwater green algae are considered the most sensitive species, for acute and chronic endpoints. Acute toxicity is affected by chain length for fish and invertebrates. Chain length affects hydrophobicity, which likely increases the rate of uptake and decreases depuration.

Toxicity to fish: The acute toxicity to fish increases is a function of alkyl chain length. The data is presented in Table 12. Since there is only a marginal influence of the substituents on the nitrogen (whether methyl or hydroxyethyl groups) on toxicity, data for dimethyl and dihydroxyethyl AOs have been combined. For AOs with average chain lengths ≤ 14 , the 96h LC₅₀ values were in the 2 to 32 mg/L range. AOs with chain lengths > 14 were more toxic, with LC₅₀ values ranging from 0.6 to 1.4 mg/L.

Table 12 summarizes the range of acute toxicity data for different fish species. Data for dimethyl and dihydroxyethyl AOs have been combined, and the combined dataset separated based on average chain length. All studies in the table have Klimisch reliability of 1 or 2.

Table 12 : Fish Acute Toxicity Values for AOs Table

Average Chain length	Species	96h LC ₅₀ (mg/L)	Number of Records	CAS#
< C13	<i>Brachydanio</i> *	10.5 - 32	2	1643-20-5; 2530-44-1
	<i>Oryzias</i>	29.9	1	1643-20-5
	<i>Pimephales</i>	2.6 - 3.5	1	70592-80-2
C13 \leq x \leq C14	<i>Brachydanio</i> *	1.0 - 3.4	4	61788-90-7; 68955-55-5; 3332-27-2; 61791-47-7;
	<i>Salmo</i> *	13.0	1	61788-90-7
\geq C16	<i>Brachydanio</i> *	0.6 - 1.4	4	7128-91-8; 2571-88-2; 61791-46-6; 93962-62-0

* Genus names *Brachydanio* and *Salmo* have recently been changed to *Danio* and *Oncorhynchus*.

Toxicity to invertebrates: As with fish, the acute toxicity of AOs to invertebrates increases as a function of chain length. The data are presented in Table 13. Here again, because the nature of the substituents on the nitrogen (whether methyl or hydroxyethyl groups) only affects the toxicity marginally, data for dimethyl and dihydroxyethyl AOs were combined. For AOs with predominant chain lengths ≤ 14 , the 48h EC₅₀ values ranged from 1.0 to 11.0 mg/L. AOs with chain lengths greater than 14 were more acutely toxic to daphnids, with LC₅₀ values ranging from 0.5 to 0.7 mg/L.

Table 13 summarises the range of acute toxicity data for *Daphnia magna* species. Data for dimethyl and dihydroxyethyl AOs have been combined, and the combined dataset separated based on average chain length. The number of available records is indicated in the table. All studies in the table have a Klimisch reliability of 1 or 2.

Table 13 : Acute toxicity of AOs to invertebrates (*Daphnia magna*) .

Average Chain length	Species	48h EC ₅₀ – range of values (mg/L)	Number of Records	CAS#
< C13	Daphnia	1.0 – 10.8	5	1643-20-5; 70592-80-2; 2530-44-1
C13 ≤ x ≤ C14	Daphnia	1.1 – 2.9	3	61788-90-7; 3332-27-2; 61791-47-7
≥C16	Daphnia	0.5 – 0.7	3	7128-91-8; 61791-46-6; 93962-62-0

Toxicity to bacteria: The 3h EC₅₀ of AO for microorganisms present in the aerobic activated sludge was experimentally measured as 214 mg/l for a C₁₂₋₁₈ AO (average chain length of 13.5) Hoechst AG, 1993B). A 16h EC₁₀ value of >1000 mg/l, was measured for *Pseudomonas putida* in a growth inhibition test with C₁₆ AO (Hoechst AG, 1994C). No direct inhibition by AO of the microbial population present in STP activated sludge digesters has been reported during monitoring activities. Therefore, AO is not considered to interfere with the operations of treatment facilities.

Toxicity to algae: Based on the hazard data, the most sensitive freshwater species are green algae (*Selenastrum* and *Scenedesmus*). As described above, the data for dimethyl and dihydroxyethyl AO have been combined in this assessment.

Toxicity data suggest that green algae are more sensitive to the AOs than blue-greens or diatoms. The results of testing different algal species are presented in Table 14. For *Scenedesmus* and *Selenastrum*, the EC₅₀ values range between 0.01 and 0.4 mg/l for C₁₂ and longer chain length AOs. For *Anabaena* and *Diatoma*, the EC₅₀ values range between 2 and 5 mg/L (data based on a C₁₀₋₁₆ AO, a mixture of predominantly C₁₂ and C₁₄ AO, of average chain length C_{12.6}).

Table 14 : Acute Toxicity of algae to AOs*

Average Chain length	Species	72h EC ₅₀ (mg/L)	Number of Records	CAS#
<C13	<i>Selenastrum</i>	0.01 – 0.4	5	70592-80-2; 1643-20-5; 2530-44-1;
	<i>Scenedesmus</i>	0.04 – 0.28	2	70592-80-2; 1643-20-5
	<i>Chlorella</i>	1.7	1	70592-80-2
	<i>Diatoma</i>	2.16	1	70592-80-2
	<i>Anabaena</i>	5.3	1	70592-80-2
C13 ≤ x ≤ C14	<i>Selenastrum</i>	0.08 – 0.29	3	61788-90-7; 3332-27-2; 61791-47-7
≥C16	<i>Selenastrum</i>	0.06 – 0.3	4	7128-91-8; 2571-88-2; 93962-62-0; 61791-46-6

* All studies in the table have a Klimisch reliability of 1 or 2.

Chronic Toxicity Test Results

All chronic toxicity data were normalized to a chain length of 12.9 carbon atoms as this average chain length represents the largest volume for North America. The resulting geometric mean values per species are shown in Table 15.

Chronic toxicity to fish: A chronic study was conducted with fish for an AO of average chain length of C_{12.6} (The Procter and Gamble Company, 1976; Maki, 1979). This study includes a 302-day survival, growth and reproduction study as well as a 60-day larval survival and growth study on larvae produced during the 302-day study. The result was a measured NOEC of 0.42 mg/L. Normalization of the data to a C_{12.9} AO resulted in a predicted NOEC of 0.31 mg/L.

Chronic toxicity to invertebrates: Two chronic studies are available for *Daphnia magna*: one with an AO of average chain length of 12.6 (Maki, 1979), and the second with average chain length of 12.0 (Environment Agency of Japan, 1999B). Based on the available data, reproduction was observed to be the most sensitive indicator of chronic toxicity, measured as a 21day NOEC and EC₁₀ value. Normalization of the data to a C_{12.9} AO resulted in a predicted EC₁₀ value of 0.28 mg/L. This finding is consistent with the anticipated close similarity between invertebrates and fish in terms of their sensitivity to AOs, which has also been described in Maki (1979).

Chronic toxicity to algae: As noted with acute toxicity, green algae are the most sensitive for chronic endpoints, with lowest geometric mean 72h EC₂₀ value of 0.011 mg/L. For *Anabaena* and *Diatoma*, the chronic toxicity values indicate <5-fold less sensitivity to AOs compared to *Selenastrum* and *Scenedesmus*.

A 28-day freshwater periphyton microcosm assay has been conducted for an AO of average chain length C_{12.6}: this microcosm was composed of a complex consortia of bacterial, cyanobacterial, algal, and fungal species, and included 110 taxa of algae (notably 87 diatom, 12 green, 7 blue-green, 2 euglenoid, 1 chrysophyte and 1 red). A NOEC value of 0.067 mg/L was derived, protective of all autotrophic and heterotrophic periphyton communities tested (The Procter & Gamble Company, 1999B).

Table 15 : Chronic Toxicity of C_{12.9} AO to Fish, Invertebrates and Algae*, **

Taxonomic group	Species	Endpoint	Chronic geometric mean (mg/L)	Number of Records	CAS# from which data are based
Fish	<i>Pimephales</i>	(302d NOEC-hatchability)	0.31	1	70592-80-2
Invertebrates	<i>Daphnia</i>	(21d EC ₁₀ , NOEC)	0.28	2	1643-20-5; 70592-80-2
Algae	<i>Selenastrum</i>	(72h EC ₂₀ , EC ₁₀)	0.11	12	70592-80-2; 1643-20-5; 2530-44-1; 61788-90-7; 3332-27-2; 61791-47-7; 7128-91-8; 2571-88-2; 93962-62-0; 61791-46-6
	<i>Scenedesmus</i>	(72h EC ₂₀)	0.01	2	70592-80-2; 1643-20-5
	<i>Anabaena</i>	(240h EC ₁₀)	1.72	1	70592-80-2
	<i>Diatoma</i>	(240h EC ₂₀)	0.13	1	70592-80-2
	<i>Navicula</i>	(120h, NOEC)	0.075	1	70592-80-2
	<i>Chlorella</i>	(120h, EC ₂₀)	0.58	1	70592-80-2

* All studies in table have Klimisch reliability of 1 or 2

** See Annex 7.2 for the process used to normalize the chronic toxicity data for an average chain length of 12.9.

4.2 Terrestrial Effects

There were no terrestrial toxicity studies found for the AOs. Although components with longer alkyl chain lengths are predicted to be more sorptive to soil, the considerations below suggest that there is

a low potential for AO to persist in terrestrial environments, and are therefore unlikely to pose a toxicity hazard to terrestrial organisms:

- fugacity modelling predicts that soil will not be an important fate compartment
- rapid biodegradation under aerobic conditions (measured data available covers a range of average alkyl chain lengths, C10 to C17) and ultimate degradability of AOs under anaerobic conditions
- low potential for bioaccumulation in aquatic tissues can be extrapolated to low potential for bioconcentration in terrestrial organisms

4.3 Other Environmental Effects

4.4 Initial Assessment for the Environment

The AOs are highly water-soluble, non-volatile and readily biodegradable under aerobic and anaerobic conditions. Thus, environmental levels are expected to be low. They are used primarily in consumer cleaning and personal care products. Following use, these substances are discharged down the drain and transported via the sewage system to wastewater treatment plants. Greater than 90% pipe loss occurs during transport in the sewers, and ~98% of the remaining AO is removed by wastewater treatment systems. This has been confirmed by field monitoring studies in the United States, The Netherlands and Japan—AO concentrations in sewage treatment plant effluents were found to be in the <0.3 to 3.0 µg/L range, and river water concentrations were below 1 µg/L. In concurrence with the field monitoring results, E-FAST, a U.S. EPA model used to predict environmental concentrations, estimated harmonic mean and 7Q10 surface water concentrations of 0.066 and 0.34 µg/L, respectively, for the high-end to bounding consumer use scenario. E-FAST modelling of manufacturing facility effluent discharges resulted in estimated mean and low flow (7Q10) stream concentrations of 0.046 µg/L and 0.19 µg/L, respectively for bounding conditions. In areas in the where discharges from consumer use and discharges from manufacturing come together, stream concentrations would still be expected to be below 0.12 and 0.53 µg/L under mean flow and low flow conditions, respectively. These data indicate that aquatic hazard levels for AOs are not likely be reached in normal conditions of manufacture or use under mean and low flow conditions.

5 RECOMMENDATIONS

Human Health: This category is currently of low priority for further work. The chemicals in this category present properties indicating a hazard for human health (skin and eye irritation). However, these hazards do not warrant further work as they are related to reversible, transient and non-lasting effects which may become evident only at high exposure levels. They should be noted by chemical safety professionals and users.

Environmental: The chemicals in this category are candidates for further work. The chemicals in this category have properties indicating a hazard for the environment (aquatic toxicity <1 mg/L for fish, aquatic invertebrate and algae). This category is anticipated to biodegrade and has a limited potential for bioaccumulation. Member countries are invited to perform an exposure assessment and, if necessary, a risk assessment.

6 DATA SEARCH STRATEGY AND REFERENCES

Search Strategy: Consortium member companies contributed in-house studies of physical-chemical properties, environmental fate and transport, ecotoxicity, and animal toxicity for the chemicals and mixtures in the category. To supplement the industry data, literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases. These databases include:

- Registry of Toxic Effects of Chemical Substances (RTECS)
- Hazardous Substances Database (HSDB)
- Aquatic Toxicity Information Retrieval (AQUIRE)
- Toxic Substances Control Act Test Submissions (TSCATS)
- Integrated Risk Information System (IRIS)
- The Environmental Teratology Information Center (ETIC)
- The Developmental and Reproductive Toxicology Database (DART)
- The Catalog of Teratogenic Agents (CTA)
- ENVIROFATE, DATALOG, AQUIRE, PHYOTOX and TERRATOX
- Chemical Carcinogenesis Research Information (CCRIS)
- The Environmental Mutagen Information Center (EMIC)
- GENETOX
- Sax's Dangerous Properties of Industrial Materials
- Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles
- International Uniform Chemical Information Database (IUCLID)
- Environmental Chemical Data Information Network (ECDIN)
- TOXLINE
- Beilstein Abstracts
- www.chemfinder.com
- Standard scientific data compendia such as Verschueren (1996), CRC Handbook of Chemistry and Physics and The Merck Index.

CAS Registry Numbers in Table 1 were used to match records available in each database. All reports identified were subject to a reliability check for determining adequacy in developing the Robust Summaries.

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Van Ginkel (2004). Metabolic studies enable ready biodegradability classification of classes of fatty amine derivatives characterized by hydrophilic moiety. Poster presentation at SETAC EUROPE 14th Annual Meeting (Prague, 2004) and oral presentation at 6th World Surfactants Congress, CESIO 2004 (Berlin, 2004).

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7 ANNEXES

7.1 Glossary of abbreviations and terms

ADAO	Alkyl Dimethyl Amine Oxide
AO	Amine Oxide
BCF	Bioconcentration Factor
CAS	Chemical Abstract Service
CMC	Critical Micellar Concentration
DDAO	Dodecyl Dimethyl Amine Oxide
HPV	High Production Volume
ICCA	International Council of Chemical Associations
SIAM	SIDS Initial Assessment Meeting
SIAR	SIDS Initial Assessment Report
SIDS	Screening Information Data Set
ThCO ₂	Theoretical carbon dioxide (produced)
ThO ₂	Theoretical oxygen (consumed)

7.2 Normalization of chronic toxicity data for a C_{12.9} AO

Available chronic toxicity single species data (21 records in total) on dimethyl and dihydroxyethyl AOs of alkyl chain lengths ranging between C₁₀ to C₁₈ were normalized to reflect toxicity of an AO of average C_{12.9} chain length. Based on annual tonnages, C_{12.9} average chain length (dimethyl) AOs represent the highest US tonnages.

Normalization of measured toxicity data followed the methods described in Fendinger et al. (1994):

- the following equation was used to extrapolate from toxicity data on AOs of different average chain lengths, to predict toxicity on C_{12.9} AO for the same chronic toxicity endpoint:

$$\log_{10} \text{ chronic value of C}_{12.9} = (\log_{10} \text{ chronic value of C}_n) - [0.42 \cdot (12.9 - n)]$$

[where C_n = AO with n carbons in the alkyl chain, where observed toxicity data is available ; n is the number of carbons in the alkyl chain of the AO where toxicity data is available]

The C_{12.9} normalized values were then subjected to a geometric mean calculation, shown in Table 1 below.

Annex Table 1 : Chronic Toxicity Values for C_{12.9} AO

This table summarizes the geometric mean values of chronic toxicity data normalized for a C_{12.9} AO. Where multiple toxicity datapoints were extrapolated for the same species and toxicity endpoint, a geometric mean was calculated – the number of records used for the derivation of the geometric mean is indicated in the table.

Chain length	Taxonomic group	Species	Endpoint	Chronic geometric mean (mg/L)	No. Of Records	CAS# from which data are based
C _{12.9}	Algae	<i>Selenastrum</i>	(72h EC ₂₀ , EC ₁₀)	0.11	12	70592-80-2; 1643-20-5; 2530-44-1; 61788-90-7; 3332-27-2; 61791-47-7; 7128-91-8; 2571-88-2; 93962-62-0; 61791-46-6
	Algae	<i>Scenedesmus</i>	(72h EC ₂₀)	0.01	2	70592-80-2; 1643-20-5
	Algae	<i>Anabaena</i>	(240h EC ₁₀)	1.72	1	70592-80-2
	Algae	<i>Diatoma</i>	(240h EC ₂₀)	0.13	1	70592-80-2
	Algae	<i>Navicula</i>	(120h, NOEC)	0.075	1	70592-80-2
	Algae	<i>Chlorella</i>	(120h, EC ₂₀)	0.58	1	70592-80-2
	Invertebrates	<i>Daphnia</i>	(21d EC ₁₀ , NOEC)	0.28	2	1643-20-5; 70592-80-2
	Fish	<i>Pimephales</i>	(302d NOEC-hatchability)	0.31	1	70592-80-2

References

Fendinger NJ, Versteeg DJ, Weeg E, Dyer SD, Rapaport RA (1994). Environmental Chemistry of lakes and Reservoirs. ACS Advances in Chemistry Series No. 237. American Chemical Society.

SIDS DOSSIER

CAS NO. 1643-20-5

1-Dodecanamine, N,N-dimethyl-, N-oxide

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

2571-88-2
2530-44-1
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

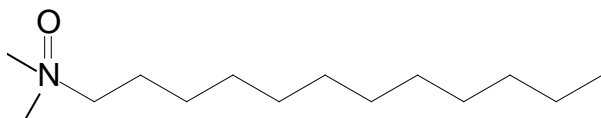
Sponsor Country: United States
Date: July, 2006

1. GENERAL INFORMATION**1.01 SUBSTANCE INFORMATION**

- A. CAS number** 1643-20-5
- B. Name (IUPAC name)**
- C. Name (OECD name)** 1-Dodecanamine, N,N-dimethyl-, N-oxide
- D. CAS Descriptor**
- E. EINECS-Number** 2167006
- F. Molecular Formula** C₁₄H₃₁NO
- G. Structural Formula**

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

C₁₂ dimethyl amine oxide



- H. Substance Group** Amine Oxides category
- I. Substance Remark** None
- J. Molecular Weight** 230 grams/mole
- 1.02 OECD INFORMATION**
- A. Sponsor Country:** United States
- B. Lead Organization:** Environmental Protection Agency (EPA)

Contact person: Oscar Hernandez
Address U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460
U.S.A.

Tel: (202) 564-7641
Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of

these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyl oxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic []; petroleum product []

B. Physical State (*at 20°C and 1.013 hPa*)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

Dimethylaurylamine oxide,
Dimethyldodecylamine oxide,
Lauramine oxide,
Lauryldimethylamine N-oxide

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

- (a) United States
26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)
Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.
- (b) Europe
(i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tones (AISE, 2002)
- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in industrial, institutional and commercial applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS

A. Options for Disposal

Remarks: Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

Remarks: 2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

2.0 PHYSICAL CHEMICAL PROPERTIES

2.0.1 EPISuite™ ESTIMATION OF PHYSICAL/CHEMICAL PROPERTIES

Test Substance

CAS Number: 1643-20-5
 Identity: Dodecyldimethylamine oxide
 Purity: not relevant
 Chain Length Distribution: C12

Method

GLP: n/a
 Report/Study Number: SDA122
 Method/Guideline Followed: EPIWIN
 Remarks: All estimates apply to the pure, dry substance and not their solutions in water.

Results

	Estimate	Exp. Database Match
Molecular Weight (grams/mole):	229.41	
Water Solubility (mg/l):	3.13	n/a
Octanol Water Partition Coefficient (Log K _{ow}):	4.67	n/a
Bioconcentration Factor (Log BCF):	2.392	
Boiling Point (°C):	426.62	n/a
Melting Point (°C):	167.95	n/a
Vapor Pressure (Pa):	2.09E-5	n/a
Henry's Law Constant (atm/(mole/m ³)):	1.513E-8	n/a
Atmospheric Oxidation Half-Life (hours):	4.71	n/a
Soil Adsorption Coefficient (Log K _{oc}):	4.271	

Remarks Trends analysis, based on the N,N-Dimethyl Amine Oxides:
 For every extension of two –CH₂– units to the alkyl chain

- Water solubility decreases by 1 order of magnitude.
- The Log K_{ow} increases by ~ 1 unit [or the octanol/water partition coefficient increases by 1 order of magnitude].
- The Log BCF increases by ~ 0.25 units [or the BCF nearly doubles; it increases by a factor of 1.8].
- The boiling point increases by ~ 23°C, although these are theoretical values, as most surfactants decompose before they boil.
- The melting point increases by ~ 15°C.
- The Log K_{oc} increases by ~ 0.5 unit [or the soil adsorption coefficient increases

by a factor of 3].

Trends are similar for the N,N-Dihydroxyethyl Amine Oxides - The substitution of the nitrogen with two hydroxyethyl groups (vs. the two methyl groups of the N,N-Dimethyl Amine Oxides) increases the hydrophilicity of the hydrophilic head group of the surfactant. This results in a higher water solubility, a lower Log Kow and a lower Koc.

CAS #	Chain Length	MW (g/mole)	Water Sol. (mg/l)	Log Kow	Log BCF	BP (°C)	MP (°C)	VP (Pa)	Log Koc	Atm Oxidation half-life (hours)
N,N-Dimethyl Amine Oxides										
2605-79-0	C10	201.36	30.35	3.69	2.142	403.41	152.60	4.57E-5	3.739	5.26
1643-20-5	C12	229.41	3.13	4.67	⁽¹⁾ 2.392	426.62	167.95	2.09E-5	4.271	4.71
3332-27-2	C14	257.46	0.32	5.66	2.655	449.82	183.30	1.48E-6	4.803	4.27
7128-91-8	C16	285.52	0.032	6.64	2.911	473.03	198.65	2.59E-7	5.334	3.90
N,N-Dihydroxyethyl Amine Oxides										
2530-44-1	C12	289.46	29.89	3.13	1.712	536.73	229.76	3.39E-12	2.360	2.36
14048-77-2	C18	373.63	0.029	6.08	2.481	606.35	262.28	7.45E-15	3.955	2.04
93962-62-0	C18:1	371.61	0.045	5.86	2.815	609.93	263.95	5.43E-15	3.955	2.95

⁽¹⁾The Log BCF value obtained by KOWWIN is 1.989, which is an outlier. The expected value, based on linear extrapolation between C10, C14 and C16 AO, is 2.392.

Data Quality

Reliability
(Klimisch): 2D

Remarks: Reliable with restrictions. Predictive modeling of the physical/chemical properties of the C10-18 even numbered, single chain length amine oxides has been carried out using EPIWIN V. 3.0. When compared with measured data obtained for CAS# 70592-80-2, EPIWIN results were found to be of limited accuracy for these endpoints: partition coefficient, BCF and water solubility. This is attributed to the inherent limitations of the algorithms with surface-active materials, which have a tendency to partition to interphases between oils/fats and water and whose phase behavior is a function of temperature and concentration, characterized by a phase diagram. EPIWIN outputs for the melting point, boiling point and vapor pressure can be considered as useful predictors for pure, dry state amine oxides, although it must be remembered that the commercial grade amine oxides are always produced, marketed and used in water solutions of approximately 25-35% active substance.

Reference

Source Reference: EPIWIN, Version 3.0.

2.1 MELTING POINT

Test Substance

CAS Number: 1643-20-5

Identity: C12 amine oxide; dodecylamine oxide

Carbon Chain Length Distribution: C12

Method

GLP: n/a

Report/Study Year: 1985

Report/Study Number: SDA628

Results

Value:		Lower (°C)	Upper (°C)
	=	130	134

Data Quality

Reliability (Klimisch): 2A

Remarks: Reliable with restrictions. Acceptable, well-documented publication/study report, meets basic scientific principles.

Reference

Source Reference: Devinsky et al, 1985.

2.2 BOILING POINT**Test Substance**

CAS Number: 1643-20-5

Identity: Dodecyldimethylamine oxide

Purity: unknown

Carbon Chain Length Distribution: C12

Method

GLP: no

Report/Study Year: 2001

Method/Guideline Followed: other

Results

Remarks: Amine oxides undergo thermal decomposition between 90 and 200°C.

Data Quality

Reliability (Klimisch): 2D

Remarks: Reliable with restrictions ; Secondary literature source

Reference

Source Reference: Kirk Othmer Encyclopedia of Chemical Technology, 2001.

3.0 ENVIRONMENTAL FATE AND PATHWAYS

3.5 BIODEGRADATION

(a)

Test Substance

CAS Number: 1643-20-5
Identity: ¹⁴C-labeled dodecyldimethylamine oxide
Purity: 100% radio-pure
Carbon Chain Length Distribution: C12
Remarks: Specific activity 6.8 uCi/mg. Unlabeled test substance 32% pure, balance is water. The ¹⁴C-labeled material was the tracer in the experiment. The unlabeled carrier substance was C10-16 dimethyl amine oxide (CAS # 70592-80-2, 32% in water).

Method

GLP: yes
Report/Study Year: 1996
Report/Study Number: SDA131
Test Type: aerobic
Method/Guideline Followed: other
Inoculum: activated sludge, domestic, non-adapted
Inoculum Acclimated: no

Results

Half Life: *Mineralization:* Mineralisation rate = 125 h-1
Primary Biodegradation: n/a
Result: Rapidly, Ultimately biodegradable
Degradation Products: Yes, polar intermediates. Identity not investigated.
Remarks: Continuous activated sludge (CAS) study; sludge from domestic sewage treatment plant of Bocholt; average COD 128 mg/l, enriched with synthetic sewage to obtain COD ≥ 350 mg/l. Final, average COD was 422 mg/l. Hydraulic retention time 8 hours. Sludge retention time 10 days. pH 7.15 (unit 1) and 7.01 (unit 2). Temp. 22.8°C (unit 1) and 22.6°C (unit 2). Oxygen in aerator 7.01 mg/l (unit 1) and 7.07 mg/l (unit 2).

Test period:
Unit 1: 33 day running-in period; 21 day test period with labeled DDAO (110 µg/l) only; 7 day test period with unlabeled and labeled DDAO (990 µg/l); total 61 days.
Test unit 2: 33 day running-in period; 21 day test period with labeled DDAO (110 µg/l) only; total 54 days.
Sampling influent/effluent/wasted sludge 5x/week.
Analysis by LSC and radio-TLC.

Radioactivity remaining in effluent and wasted sludge determined by LSC. Effluents subjected to flashfreezing and lyophilization (TLC). Residues extracted with chloroform/methanol/formic acid.

Removal of DDAO was $\geq 99.8\%$ for both units. Effluents contained 2 or 3 intermediates. Wasted activated sludge from both test units contained 5 intermediates. Mass balance for test unit 1 was 100.2% (76.3% $^{14}\text{CO}_2$; 7.6% released with effluent; 16.3% associated with solids, 93% of which was incorporated into biomass). Mass balance for test unit 2 was 97.5% (69.2% $^{14}\text{CO}_2$; 15.5% released with effluent; 12.9% associated with solids, 93% of which was incorporated into the biomass).

Biodegradation kinetics: the mineralisation rate can be calculated from the following equation, using input data from the test:

$$C_{\text{effluent}} = \frac{C_{\text{influent}}}{1 + (Kd)(SS_{\text{reactor}})(HRT/SRT) + (k_1)(HRT)}$$

Where, C_{effluent} (concentration in effluent) = 0.1% of that in influent

HRT (Hydraulic retention time) = 8 hrs

SRT (sludge retention time) = 10 days = 240 hrs

Kd (adsorption coefficient) = 459 L/kg [based on Koc, organic carbon partitioning, assuming 40% Carbon in sludge]

Reactor solids = 2.1 g/L = 0.0021 kg/L (average)

Mineralization rate $K_1 = 125 \text{ h}^{-1}$

Conclusion: the removal of parent dimethyldodecylamine oxide averaged $\geq 99.9\%$, 99.8% and $\geq 99.9\%$ for a test concentration of 110, 384 and 990 $\mu\text{g/l}$, respectively. The mineralization rate was 125 hour^{-1} . Very small amounts (low $\mu\text{g/l}$) of polar intermediates are present in the treated effluent. The concentration of DDAO and degradation intermediates in activated sludge is in the low $\mu\text{g/g}$ range. The identity of intermediates was not investigated.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2A

Remarks: Experimental protocol (e.g. number and identity of traps) not detailed in the report. Test procedure described in protocol "Biodegradation study. Activated sludge simulation test with ^{14}C ." Lisec Laboratories, The Netherlands. Protocol # WG-01 ECMETS 537/01. No deviations from protocol were reported, but conformity of test to stated protocol could not be confirmed.

Reference

Source Reference: The Procter & Gamble Company, 1996E.

(b)

Test Substance*CAS Number:* 1643-20-5*Identity:* ¹⁴C-labelled dodecyldimethylamine oxide*Purity:* > 98% radio-pure*Carbon Chain Length Distribution:* C12*Remarks:* Radiolabeled test substances are highly radio-pure (98.6%) meaning 98.6% of the radiolabel is in the test substance. Radiolabel in a carbon of the alkyl side chain.**Method***GLP:* no*Report/Study Year:* 1996*Report/Study Number:* SDA201*Test Type:* aerobic*Method/Guideline Followed:* Effluent in River Die Away Test (Procter & Gamble protocol, study # ECM ETS 553)*Inoculum:* river water from Zenne at Tubize (Belgium), activated sludge and effluent from municipal sewage treatment plant at Hofstade (Belgium)*Inoculum Acclimated:* no

<i>Test Substance Initial Concentration:</i>	Value	Unit	Expressed as
	1	µg/l	Test substance
	2	µg/l	Test substance

Remarks: Ten liters of test solution prepared as follows: 3.3 l of effluent (from either unit 1 or 2 from CAS study with amine oxide, see report # SDA 131 of this dataset), were mixed with 6.6 l of river water and 0.1 l of activated sludge. Abiotic controls had 0.1 g/l HgCl₂ added.

Sampling times: 15 and 30 min and 1, 1.5, 2, 3, 4, 5, 6, 8, 24, 48, 72, 120, 168, 240 and 336 hours.

Sample preservation: lyophilization (flash-freezing).

Analysis for radiolabeled species in solution by TLC-RAD (Thin Layer Chromatography with Radioactive Detection) and LSC (Liquid Scintillation Counting). Sample preparation for TLC-RAD as follows: 200 ml sample extracted with chloroform/methanol/formic acid/water (80:20:1:3). Residue further extracted with 5 ml methanol and 2 ml water. Detection limit 0.33 µg/l.

Sample preparation of liquid samples for LSC as follows: acidify a 10 ml sample with 1 ml 0.5% HCl, incubate 24 h at room temp. and add 10 ml Ultima Gold XR.

Results*Kinetics Measured* CO₂

as:

Kinetics of Test Substance:

Exposure Period	Exposure Unit		Lower (%)	Upper (%)
14	days	=	46	63

*Half Life:**Mineralization:* 2 - 4 days*Primary Biodegradation:* n/a*Result:*

Rapidly, Ultimately biodegradable

Degradation Products:

yes

Remarks:

Results of analysis for radiolabeled species in starting solutions:
 Test solution prepared with CAS unit 1 effluent:
 2 µg/l test substance and non-detectable levels of intermediates
 Test solution prepared with CAS unit 2 effluent:
 1 µg/l test substance and 2.9 µg/l of polar intermediates
 Results after 14 days:
 Unit 1: ¹⁴CO₂ production averaged 43%; 0.78 µg/l test substance and non-detectable levels of intermediates.
 Unit 2: ¹⁴CO₂ production averaged 63%; 1 µg/l test substance and non-detectable levels of intermediates.
 Radiochemical mass balances 87 and 99% in units 1 and 2, respectively.
 After 14 days approx. 20% of radioactivity was associated with the solids in both units.

Data Quality*Flags:*

Critical study for SIDS endpoint

Reliability (Klimisch):

2A

Remarks:

Reliable with restrictions. Acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Source Reference: The Procter & Gamble Company, 1996D.

Other Reference: The Procter & Gamble Company, 1996E.

(c)

Test Substance*CAS Number:*

1643-20-5

*Identity:*¹⁴C-labeled dodecyldimethylamine oxide*Purity:*

not given

Carbon Chain Length

C12

*Distribution:**Remarks:*

Radiolabeled materials are usually highly radio-pure (>95%)

Method*GLP:* no data*Report/Study Year:* 1999*Report/Study Number:* SDA125*Test Type:* aerobic*Method/Guideline Followed:* OECD Guideline 303 A*Inoculum Acclimated:* no*Control Substance:* other

Remarks: Unacclimated inoculum. Method essentially same as EEC 79/831 Part C. The radiolabeled test substance was added to real wastewater in 2 duplicate test systems at concentrations of 110 and 480 µg/l. No control substance needed with radiolabeled test substance. Overall removal was 89%, measured as total radioactivity in the ¹⁴CO₂ and in sludge solids. Major removal mechanism was mineralization (73%) followed by sorption (14%) to the sludge. Removal of parent compound with same CAS # was also analyzed by G. Debaere (1996) in same CAS system at LISEC Laboratories, with influent concentrations of 110, 384 and 990 µg/l. Parent removal there was 99.8%.

Results

Half Life: *Mineralization:* n/a
Primary Biodegradation: n/a

Result: other*Degradation Products:* not measured**Data Quality***Reliability (Klimisch):* 3B**Reference**

Source Reference: The Procter & Gamble Company, 1999A.

(d)

Test Substance*CAS Number:* 1643-20-5*Identity:* dodecyldimethylamine oxide, lauryl dimethyl amine oxide*Purity:* Not available*Carbon Chain Length Distribution:* C12*Remarks:* CAS # assigned by reviewer based on name.**Method**

GLP: no
Report/Study Year: 1965
Report/Study Number: SDA105
Test Type: aerobic
Method/Guideline Followed: other
Inoculum: activated sludge, adapted
Inoculum Acclimated: yes
Acclimated to what Concentration: 30 mg/l test substance
Acclimated for what Duration: 9 days
Control Substance: other

Value	Unit	Expressed as
30	mg/l	test substance

Remarks: Method is referred to as "shake culture test". No control substance. Activated sludge culture (1% inoculum into the test medium) was adapted to test substance by 3 successive 72-hour transfers in shake flask system. Temp. 25 °C. Biodegradation measured as surface tension.

Test substance completely biodegraded after 72 hours.

Results

Kinetics Measured as: other

Kinetics of Test Substance:

Exposure Period	Exposure Unit	Operator	%
0	hour(s)	=	47
24	hour(s)	=	47
48	hour(s)	=	48
72	hour(s)	=	50
144	hour(s)	=	72

Half Life: *Mineralization:* not determined

Primary Biodegradation: n/a

Result: Ultimately biodegradable

Degradation Products: no

Data Quality

Reliability (Klimisch): 3C

Remarks: Units of surface tension not specified, assumed to be mN/m. Not a generally accepted, validated method given today's standards. No control flasks (positive control, abiotic control, toxicity control). Insufficiently documented.

Reference

Source Reference: Soap and Chemical Specialties, 1965.

4.0 ENVIRONMENTAL TOXICITY

4.1.1 TOXICITY TO FISH (ACUTE)

(a)

Test Substance

CAS Number: 1643-20-5
Identity: N,N-dimethyldodecylamine N-oxide; N,N-dimethyl-N-oxidedodecylamine
Purity: 93%
Carbon Chain Length Distribution: C12
Remarks: Aldrich lot # 10102TG

Method

GLP: yes
Report/Study Year: 1999
Report/Study Number: NMMP/E98/4100
Method/Guideline Followed: OECD Guideline 203
Test Type: acute, semi-static, renewal at 24 hrs
Analytical Monitoring: yes
Limit Test: no
Species: *Oryzias latipes*

Exposure Period:

Value	Unit
96	hour(s)

Remarks: Killifish; 10 fish per concentration; water quality parameters: pH 6.9; Temp. 23.4-24.1 °C; O₂ 5.9-10.7 mg/l; hardness 30 mg/l expressed as CaCO₃. Nominal test conc. 0.0 - 9.5 - 17.1 - 55.6 - 100.0 mg/l; test conc. measured at 0 h and 24 h each interval; geom. mean of actual test conc. 0.0 - 6.3 - 13.0 - 24.2 - 41.4 - 66.9 mg/l.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	13	n/a
LC0:	m	=	13	n/a
LC50:	c	=	24.2	41.4
LC100:	m	=	41.4	n/a
LC10	c	=	18.9	n/a
LC20	c	=	21.7	n/a

LC50	c	=	29.9	n/a
------	---	---	------	-----

Remarks: LC50 calculation method: TOXDAT Multi-Method Program of US EPA. Geometric means of m concentrations used to calculate results. LC10 and LC20 values calculated using linear regression function on HP-11C calculator for the 13.0 - 41.4 mg/l conc. interval; correlation coefficient = 0.95.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; comparable to guideline study.

Reference

Source Reference: Environment Agency of Japan, 1999C.

(b)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide

Purity: 23.7%

Carbon Chain Length Distribution: C12

Remarks: Balance is water

Method

GLP: yes

Report/Study Year: 1992

Report/Study Number: CRL F92043

Method/Guideline Followed: Directive 92/69/EEC, C.1; OECD Guideline 203

Test Type: acute, semi-static, renewal at 48 hrs

Analytical Monitoring: no

Limit Test: no

Species: *Brachydanio rerio*

Exposure Period:	Value	Unit
	96	hour(s)

Remarks: Method essentially identical to OECD Guideline 203. 7 fish per vessel and 1 vessel per conc. Nominal test concentrations 0 - 23.7 - 42.7 - 76.8 - 138.2 - 248.9 mg/l (active ingredient). Aeration. Renewal after 48 hours. Temp. 21-22 °C. Hardness 210 mg/l as CaCO₃. pH 7.8-8.2. O₂ > 80% of saturation. Fish not fed. Statistical method Trimmed Spearman-Kärber.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
LC50:	c	=	32	n/a
LC50	c	=	24	43

Remarks: No analyses. Test substance believed to be stable during the test, but possibly the test concentrations would have decreased somewhat over time.

Data Quality

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 2B

Remarks: No information on frequency of physical measurements (pH, O₂, temp.). No information on biodegradation during the test.

Reference

Source Reference: Akzo Chemicals B.V., 1992.

4.2.1 AQUATIC INVERTEBRATES TOXICITY (ACUTE)

(a)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide

Purity: 35.5%

Carbon Chain Length Distribution: C12

Remarks: test substance from batch # 3425; balance is water

Method

GLP: yes

Report/Study Year: 2000

*Report/Study
Number:* SPL 140/1028

*Method/Guideline
Followed:* OECD Guideline 202

Test Type: acute, static

*Analytical
Monitoring:* no

Limit Test: no

Species: *Daphnia magna*

Exposure Period:

Value	Unit
-------	------

48	hour(s)
----	---------

Remarks: Reconstituted water; no solvent aids used; 2 replicates of 10 daphnids at each concentration; nominal concentrations 1.0 - 1.8 - 3.2 - 5.6 - 10 - 18 - 32 - 56 - 100 mg/l (active ingredient); water quality parameters pH [7.9-8.0] O₂ 7.5-8.0 mg/l; temp. 20-21 °C; hardness 250 mg/l as CaCO₃

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	c	~ =	1.8	n/a
EC0:	c	=	1.8	n/a
EC50:	c	=	3.6	4.3
EC100:	c	=	5.6	n/a
EC10	c	=	2.5	n/a
EC20	c	=	2.9	n/a

Remarks: EC50 = 3.9 mg/l (95% confidence interval listed). Statistical analysis by trimmed Spearman-Kärber method of Hamilton *et al.* (1977) (1) using a ToxCalc software package (2). EC10 and EC20 calculated by reviewer using linear regression function on HP-11C calculator. Correlation coefficient (r) = 0.97.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; comparable to guideline study.

Reference

Source Reference: Kao Corporation, 2002.

Other References: Hamilton et al, 1977.

(b)

Test Substance

CAS Number: 1643-20-5

Identity: N,N-dimethyldodecylamine N-oxide; dimethyl laurylamine oxide

Purity: > 93 %

Carbon Chain Length C12

Distribution:

Remarks: test substance from Aldrich lot # 07116DR

Method

GLP: yes

Report/Study Year: 1999

Report/Study Number: NMMP/E98/2100
 Method/Guideline Followed: OECD Guideline 202
 Test Type: acute, static
 Analytical Monitoring: yes
 Limit Test: no
 Species: *Daphnia magna*

Exposure Period:	Value	Unit
	48	hour(s)

Remarks: Reconstituted water as prescribed by OECD Guideline 211; daphnids fed with 0.1-0.2 mg C per day per daphnid of *Chlorella vulgaris*; no solvent aids used; 4 replicates of 5 daphnids per concentration; nominal concentrations 0.5 - 0.9 - 1.7 - 3.1 - 5.6 - 10.0 mg/l (active ingredient); measured concentrations (geometric mean, active ingredient) 0.26 - 0.75 - 1.28 - 2.23 - 5.76 - 11.41 mg/l; water quality parameters pH 7.1-7.7 ; O₂ 7.8-8.6 mg/l ; temperature 20.1-20.7 °C; hardness 227 mg/l as CaCO₃.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	1.28	n/a
EC0:	m	=	1.28	n/a
EC50:	c	=	1.28	5.76
EC100:	m	=	5.76	n/a
EC10	c	=	1.09	n/a
EC20	c	=	1.6	n/a
EC50	m	=	2.23	n/a

Remarks: EC50 = 2.23 mg/L; 95% confidence interval listed; statistical analysis: EC50 using TOXDAT Multi-METHOD PROGRAM Binomial method of US EPA. Geometric mean values of measured concentrations at 0 hours and 48 hours were used for the calculations. EC10 and EC20 calculated by reviewer using linear regression function on HP-11C calculator in 1.28 - 5.76 mg/l conc. interval; regression coefficient (r) = 0.95.

Data Quality

Flags: Critical study for SIDS endpoint
 Reliability (Klimisch): 1A
 Remarks: Reliable without restriction; comparable to guideline study

Reference

Source Reference: Environment Agency of Japan, 1990.

(c)

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine oxide
Purity: 23.7%
Carbon Chain Length Distribution: C12
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1994
Report/Study Number: CRL F94173
Method/Guideline Followed: OECD Guideline 202
Test Type: static
Analytical Monitoring: no
Limit Test: no
Species: *Daphnia magna*

Exposure Period:

Value	Unit
48	hour(s)

Remarks: Nominal test conc. 0.0 - 1.2 - 2.1 - 3.8 - 12.4 mg/l; 20 daphnids per concentration; no vehicle. Trimmed Spearman-Kärber statistics. Temp. 19-20°C; hardness 210 mg/l CaCO₃; pH 8.0-8.2; O₂ 88-97% sat.; 16 h light; unfed.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC50:	c	=	3.5	5.2
EC50	c	=	4.2	n/a

Remarks: No analyses. Results based on nominal conc. Test conc. may have decreased during test.
No information about feeding.
EC50 = 4.2 mg/l (3.5 - 5.2 mg/l confidence limit).

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2B
Remarks: No analyses.

Reference

Source Reference: Akzo Nobel Central Research, 1994.

4.2.2 AQUATIC INVERTEBRATES TOXICITY (PROLONGED)**Test Substance**

CAS Number: 1643-20-5
Identity: N,N-dimethyldodecylamine N-oxide; N,N-dimethyl-N-oxidedodecylamine
Purity: >= 93%
Carbon Chain Length Distribution: C12
Remarks: Aldrich lot # 07116DR

Method

GLP: yes
Report/Study Year: 1999
Report/Study Number: NMMP/E98/3100
Method/Guideline Followed: other
Test Type: chronic, semi-static
Analytical Monitoring: yes
Limit Test: no
Species: *Daphnia magna*

Exposure Period:

Value	Unit
21	day(s)

Remarks: OECD Guideline 211; test solution renewal 3x per week; nominal test conc. 0.0 - 0.12 - 0.21 - 0.38 - 0.68 - 1.22 - 2.20 mg/l (active ingredient); 10 daphnids per conc. in 80 mL of test solution; actual test conc. was 95.2-144% of nominal at 0 h and 50.5-125% of nominal at 48 h. Time weighted averages of actual conc. was used to calculate results. Water quality parameters pH 7.5-8.4; O₂ 7.1-8.7 mg.l; Temp. 19.8-20.9 °C; Hardness 223-238 mg/l CaCO₃.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	0.36	n/a
EC50:	c	=	1.4	n/a
EC50	c	=	1.2	1.5
LC50	c	>	2.6	n/a

Remarks: LC values based on mortality of parent daphnids. EC values based on cumulative number of living offspring. Various statistical methods used by the laboratory (1). EC10 and EC20 computed using method by Bruce and Versteeg (2) for use in probabilistic risk assessment.

Results:
 21 day NOEC = 0.36 measured

21 day EC10 = 0.354 [0.221 - 0.566] computed
 21 day EC20 = 0.549 [0.383 - 0.787] computed
 21 day EC50 = 1.27 [0.950 - 1.53] computed
 21 day LC50 = > 2.6 computed

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Reference

Source Reference: Environment Agency of Japan, 1999B.

Other Reference: Bruce and Versteeg, 1992.

4.3 TOXICITY TO AQUATIC PLANTS e.g. ALGAE

(a)

Test Substance

CAS Number: 1643-20-5
Identity: Dodecyldimethylamine oxide
Purity: 35.5%
Carbon Chain Length Distribution: C12
Remarks: Balance is water (64.5%)

Method

GLP: yes
Report/Study Year: 2000
Report/Study Number: SPL 140/1029
Method/Guideline Followed: OECD Guideline 201
Analytical Monitoring: no
Species: *Scenedesmus subspicatus*
Endpoint: other

Exposure Period:

Value	Unit
72	hour(s)

Remarks: Endpoints are biomass (b) and growth rate (r); no solvent aids used. Standard OECD algal growth medium (OECD Guideline 201); hardness (Ca + Mg) dH 0.6 mmol/l. Nominal test conc. 0.000 - 0.005 - 0.01 - 0.02 - 0.04 - 0.08 mg/l (active ingredient). Three flasks per concentration. pH range [7.5-7.7] at 0 h and [7.8-9.4] at 72 h. Temp. 20-22 °C. Continuous illumination 7000 lux. Constant aeration. Standard algal growth medium. Algal cell counts daily by Coulter Counter.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	0.005	n/a
EC10:	c	=	0.008	0.017
EC50:	c	=	0.031	0.034
EC20	c	=	0.013	0.023

Remarks: EbCx = effect on biomass. ErCx = effect on growth rate.

Growth inhibition data were read from graph of % inhibition vs. log conc. Curve-fitting was done by eye. Biomass was the most sensitive endpoint. Unless otherwise indicated, endpoints listed are for total biomass. One-way analysis of variance incorporating Bartlett's test for homogeneity of variance and Dunnett's multiple comparison procedure for comparing several treatments with control carried out on biomass data at 72 h to determine statistically significant differences. There were no significant differences between the control and the 0.0050 mg/l test conc.

Results calculated according to Bruce & Versteeg (1992) in mg/l:

EbC10 = 0.012 [0.008 - 0.017] computed

EbC20 = 0.018 [0.013 - 0.023] computed

EbC50 = 0.036 [0.031 - 0.034] computed

ErC10 = 0.030 [0.024 - 0.038] computed

ErC20 = 0.050 [0.044 - 0.057] computed

ErC50 = 0.129 [0.111 - 0.151] computed

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Reference

Source Reference: Kao Corporation, 2000.

Other Reference: Bruce and Versteeg, 1992.

(b)

Test Substance

CAS Number: 1643-20-5

Identity: N,N-dimethyl-N-oxidedodecylamine; N,N-dimethyldodecylamine N-oxide

Purity: 93%

Carbon Chain Length Distribution: C12

Remarks: Aldrich Lot # 07116DR

Method

GLP: yes
 Report/Study Year: 1999
 Report/Study Number: NMMP/E98/1100
 Method/Guideline Followed: OECD Guideline 201
 Analytical Monitoring: yes
 Species: *Selenastrum capricornutum*
 Endpoint: other

Exposure Period:	Value	Unit
	72	hours

Remarks: Nominal test conc. 0.0 - 0.001 - 0.002 - 0.004 - 0.008 - 0.016 - 0.032 - 0.064 - 0.128 mg/l (active ingredient).
 Measured test conc. 0.0 - 0.0008 - 0.0023 - 0.004 - 0.008 - 0.015 - 0.030 - 0.060 - 0.123 mg/l. (active ingredient).
 Standard OECD algal growth medium (OECD Guideline 201); hardness (Ca + Mg) dH 0.6 mmol/l. Water quality parameters: pH 7.3-7.7; Temp. 22.0-23.1 °C.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC10:	c	=	0.0031	0.0059
EC50:	c	=	0.0190	0.0260
EC20:	c	=	0.0058	0.0098

Remarks: Biomass was the most sensitive endpoint in this test. Various statistical methods used by the testing laboratory and the method of Bruce and Versteeg (1992) were used to derive ECxx values. These values were found to be in good agreement with one another and with results from other algal growth inhibition studies with amine oxide, suggesting that the low NOEC was not a result of an unusually sensitive algal culture or unusual exposure conditions but rather due to the high precision of the test. Results were calculated based on measured concentrations:

Results according to Bruce & Versteeg (1992) in mg/l:

	EC50	EC20	EC10
Biomass	0.022 [0.019-0.026]	0.0075 [0.0058-0.0098]	0.0043 [0.0031-0.0059]
Growth Rate	0.11 [0.1-0.12]	0.029 [0.025-0.035]	0.015 [0.011-0.019]

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Reference

Source Reference: Environment Agency of Japan, 1999A.

Other Reference: Bruce and Versteeg, 1992.

(c)

Test Substance

CAS Number: 1643-20-5

Identity: Dodecyldimethylamine oxide; laurylamine oxide

Purity: 23.7%

Carbon Chain Length Distribution: C12

Method

GLP: no

Report/Study Year: 1992

Report/Study Number: CRL F92119

Method/Guideline
Followed: OECD Guideline 201

Analytical Monitoring: no

Species: *Selenastrum capricornutum*

Endpoint: other

Exposure Period:

Value	Unit
72	hour(s)

Remarks: Endpoints are biomass and growth rate. 3 reps./conc. and 6 controls. Standard OECD algal growth medium (OECD Guideline 201); hardness (Ca + Mg) dH 0.6 mmol/l. Nominal conc. 0.0 - 0.014 - 0.028 - 0.057 - 0.114 - 0.227 mg/l (active ingredient).

Results

Unit: mg/l

	Measured/Computed		Lower
EC10:	c	=	0.008
EC50:	c	=	0.064
EC20:	c	=	0.016

Remarks: NOEC was not determined. No analyses were conducted. Test substance is expected to be stable during the test; some degradation is possible. Individual cell counts not reported. No pH measurements reported. Growth in controls not reported.

Calculated results by Bruce & Versteeg (1992) in mg/l:

	EC50	EC20	EC10
Growth Rate	0.204	0.051	0.025
Biomass	0.064	0.016	0.008

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2B

Reference

Source Reference: Akzo Nobel Chemicals, 1992C.

Other Reference: Bruce and Versteeg, 1992.

(d)

Test Substance

CAS Number: 1643-20-5
Identity: Dodecyldimethylamine oxide
Purity: not given
Carbon Chain Length Distribution: C12
Remarks: n/a

Method

GLP: no
Report/Study Year: 1990
Report/Study Number: SDA142
Method/Guideline Followed: other
Analytical Monitoring: yes
Species: *Vicia sativa*
Remarks: Regression of Quantitative Structure Activity Relationships (QSAR), based on IC50 values.
Observation(s): growth. No dosage information given. *V. sativa* was exposed to various concentrations of a series of N-alkyl dimethylamine oxides of different chain lengths. The study was conducted for 72 hours in an environmental chamber maintained at 25+/- 1°C.

Results

Unit: mg/l

	Measured/Computed		
EC50:	c	=	15

Remarks: Phytotoxicity was significantly dependent on carbon chain length. Lipophilicity did not significantly influence phytotoxicity.

Data Quality

Reliability (Klimisch): 4A

Remarks: Abstract is in English. Paper is in Russian, no translation available.

Reference

Source Reference: Murin et al, 1990.

5. TOXICITY

5.0 TOXICOKINETICS, METABOLISM and DISTRIBUTION

(a)

Test Substance

CAS Number: 1643-20-5
Identity: [Methyl-¹⁴C] dodecylamine, N,N-dimethyl-, N-oxide
[1-dodecyl-¹⁴C] dodecylamine, N,N-dimethyl-, N-oxide
Purity: >98.5%
Carbon Chain Length
Distribution: C12
Remarks: Radiochemical purity is given.

Method

GLP: not stated
Report/Study Year: 1977
Report/Study Number: SDA130
Method/Guideline Followed: other
Vitro/Vivo: *In vivo*
Species: human, rat, rabbit and mouse
Number of Animals: See remarks
Doses Male: See remarks
Doses Female: See remarks
Vehicle: n/a
Route of Administration: oral, dermal, intraperitoneal
Exposure Time: See remarks
Remarks: Test 1 (rats): Excretion study. Single oral dose at 100 mg/kg bw (methyl-¹⁴C) to 4 males (mean weight 205 g) and 4 females (mean weight 202 g) and at 100 mg/kg bw (1-dodecyl-¹⁴C) males only (n=5, mean weight 185 g); in stainless steel metabolism cages for 72 h; collection of urine, feces and CO₂ (24, 48 and 72 h). At study termination ¹⁴C determination from cage wash, contents of safety traps and contents of GI, tissues and carcass.

Test 2 (rats): Tissue distribution study. Single oral dose at 100 mg/kg bw (methyl-¹⁴C) to 4 males (mean weight 205 g) and 4 females (mean weight 202 g) and at 100 mg/kg bw (1-dodecyl-¹⁴C) males only (mean weight 185 g); in stainless steel metabolism cages for 72 h; sacrifice at 48 (females) and 72 h (males); sampling of tissues and organs listed in table below.

Test 3 (rats): Bile duct cannulation study. Single oral dose at 40 or 100 mg/kg bw (methyl-¹⁴C) to 3 male cannulated rats (mean weight 263 g); in stainless

steel metabolism cages for 72 h; collection of bile, urine, feces (24 and 48 h and total) and carcass (72 h).

Test 4 (rats): Dermal excretion study. Administration of 20 mg/mL (methyl-¹⁴C) (18 cm²/rat, 4 males, mean weight 188 g) on the clipped skin. Animals were restrained in stainless steel metabolism cages for 72 h; collection of urine, feces and CO₂ (24, 48 and 72 h). The amount of radio activity was determined in liver, kidney and carcass.

Test 5 (rats, mice and rabbits): Dermal tissue distribution study
Administration of 20 mg/ml (methyl-¹⁴C) (18 cm²/rat, n=4), 10 mg/ml (methyl-¹⁴C) (6 cm²/mouse, n=3) and 20 mg/ml (methyl-¹⁴C) (40 cm²/rabbit, n=4) on the clipped skin. Animals were restrained in stainless steel metabolism cages for 72 h; collection of, urine, feces and CO₂. Sampling of tissues and organs listed in table below.

Test 6 (humans): Two volunteers (fasted for 12 h) were dosed orally with 50 mg test substance (1-dodecyl-¹⁴C labeled). Urine was collected over intervals 0-6 and 6-24 h and over 24 h intervals until 144 h. Feces were collected individually. CO₂ was collected for 15 minutes at 0, 1, 2, 3, 4, 5, 6, 8, 12, 24, 36, 48 and 72 h after dosing.

Test 7 (humans): Two volunteers received 10 mg test substance (1-dodecyl-¹⁴C-labeled) on an area of 4x15 cm of the forearm (clipped). After drying the area was covered with a non-occlusive dressing. After 8 hours the skin was cleaned and the percentage radioactivity retained in the *stratum corneum* was assayed by repeatedly (10x) stripping the skin. Sampling procedures were equal to those of test 6.

Results

Remarks: Test 1 (rats)

Excretion study (mass balance 89-102%)

	% of administered dose excreted in:								
	urine			feces			CO ₂		
¹⁴ C- label time [h]	methyl M	dodecyl M	methyl F	methyl M	dodecyl M	methyl F	methyl M	dodecyl M	methyl F
24	55	42	32	8.1	5.4	7.3	10	20	20
48	8.5	6.6	9.6	2.8	2.6	3.7	1.2	1.2	2.0
72	3.0	2.2	-	1.2	1.0	-	0.7	0.5	-
Total	71	53	54	12	9.4	12	13	23	23

- Not determined.

Tissues and carcass 6.1, 3.5 and 8.0% of methyl-¹⁴C, 1-dodecyl-¹⁴C and methyl-¹⁴C respectively

Test 2 (rats)

Tissue distribution study.

tissue/organ	% of dose		
	M [72 h]		F [48 h]
	methyl	dodecyl	
Liver	1.3	1.1	1.5
Intestines	0.3	0.4	0.5
Stomach	0.1	0.4	0.2
Gonads	0.1	0.07	0.1
Kidney	0.09	0.08	0.09
Lungs	0.05	0.04	0.06
Spleen	0.03	n.a.	0.02
Heart	0.02	n.a.	0.02
Brain and spinal cord	0.02	0.02	0.02
Pancreas	0.02	n.a.	0.02
Adrenal	-	-	0.008
Eye	-	-	0.003
Carcass	4.0	1.9	4.8

-/n.a. not analysed

Test 3 (rats)

Bile duct cannulation study, excretion data (material balance 96%)

Sample	% of dose
bile, 0-24 h	3.2
bile, 24-48 h	0.4
bile, total	3.6
urine, total	38
CO ₂ , total	18
feces, total	21
total excreted, total	80
carcass	15

Test 4 (rats)

Excretion study after dermal application

time [h]	% of administered dose excreted in:		
	urine	feces	CO ₂
24	4.5	0.5	0.6
48	4.7	0.8	0.8
72	5.1	0.4	0.9
Total	14.2	1.8	2.5

Tissues, application site and carcass 16, 48 and 16% resp.

Test 5 (rats, mice and rabbits)

Tissue distribution study after dermal application

	% of dose		
Tissue/organ	Rat	Mouse	Rabbit
Urine	14.2	11.6	42.1
Feces	1.8	1.4	2.2
CO ₂	2.5	5.0	1.4
Total excreted	18.5	18.0	45.7
Liver	0.44	0.42	0.44
Kidney	0.05	0.08	0.1
Testes	0.04	0.02	0.001
Carcass	15.6	17.1	4.6
Tissue total	16.1	17.6	5.1
Skin (application site)	48.0	48.9	39.4
Cage wash	6.1	10.6	3.9
Material balance	89	95	94
Blood (mg/g whole blood)	0.43	1.1	<0.03

Test 6 (humans)

Excretion study in humans after oral application (material balance 70-80% of applied)

	% of administered dose excreted in:					
	urine		feces		CO ₂	
time [h]	Subject 1	Subject 2	Subject 1	Subject 2	Subject 1	Subject 2
24	49.8	36.8			18.2	21.9
48	6.2	6.0			1	1
72	0.8	0.7			ND	ND
144	0.5	0.4				
Total	57.3	43.9	2.7	2.5	19.2	22.9

ND= not detected

Test 7 (humans)

Excretion study in humans after dermal application

Excretion of <0.2% of applied radioactivity.

Conclusions - Rapid and extensive absorption by rats and humans after oral administration. Excretion mainly via urine and CO₂ (less in feces).

- Dermal absorption ~40% of applied in rats and mice; rabbits ~60%. Excretion mainly via urine.

- Rate of dermal penetration in humans lower than in other species.

- Biological half-life in humans probably less than 12 h.

Rev. note: The material balance in the studies with humans was only 70-80%. This was attributed to inadequate sampling procedures.

Conclusion: DDAO was absorbed extensively and rapidly by rats. The distribution of DDAO was similar between males and females. Among all the tissues analyzed, the largest amount and the highest concentration of radioactivity was found in the liver. The fractions of dosed radioactivity appearing in the liver, kidney, and blood reached maxima within 1 hour after the oral dose. The excretion of radioactivity was rapid, with approximately 70% and greater excreted within 24 hours. Concurrent studies with two human volunteers were also conducted and showed similar results. Orally administered DDAO was rapidly and extensively absorbed by rats and humans, and excretion was similarly rapid.

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2A
Remarks: Acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Source Reference: Rice, D.P. 1977.

(b)

Test Substance

CAS Number: 1643-20-5
Identity: Dodecylamine, N,N-dimethyl-, N-oxide, ¹⁴C 1-dodecyl and ¹⁴C-methyl labeled
Purity: not stated
Carbon Chain Length Distribution: C12

Method

GLP: no
Report/Study Year: 1981
Report/Study Number: SDA195
Method/Guideline Followed: other
Vitro/Vivo: *In vivo*
Species: Sprague-Dawley rats, Albino New Zealand rabbits, and humans
Number of Animals: rats - 5 per dose; rabbits - 4 per dose; humans – 2 per dose
Doses Male: See remarks
Doses Female: See remarks
Vehicle: n/a
Route of Administration: See remarks

Exposure Time: See remarks

Remarks: The rats were fasted overnight before dosing with radiolabeled DDAO by gavage, and afterwards were housed in stainless steel metabolism cages equipped to collect CO₂ in traps containing NaOH. Feed was provided *ad libitum* approximately 6 hours post dose. Urine, feces, and CO₂ were collected at 24-hour intervals. All urine samples were frozen immediately and kept at -15°C until analysis.

The rabbits were treated as the rats, except that CO₂ was collected during the first 7 hours of each 24-hour period and estimated for the 7-24 hour interval assuming linear kinetics. Plasma for ¹⁴C determination was isolated from rat blood taken from a toe clip, and from rabbit blood drawn from the ear vein. Plasma samples for metabolite separations were isolated from blood drawn from the vena cava of rats and the heart of rabbits after ether anesthesia.

Urine was collected at 0°C from two healthy male subjects (ages 21 and 23, 70 kg) who drank 200 ml of an aqueous solution containing 50 mg of ¹⁴C-DDAO.

Dosage:

rats - 1 and 100 mg/kg

rabbits - 1 and 37-57 mg/kg

humans - 0.72-0.76 mg/kg

Results

Remarks: ¹⁴C-methyl labeled: in rats after 72 h, 96% of radioactivity was excreted
Percentage of applied radioactivity (¹⁴C 1-dodecyl labeled)

Animal	rat(72 h)		rabbit(72 h)	human(144 h)	
dose(mg/kg)	1	100	1	0.76	0.72
urine	66	54	59	57	44
feces	7	9	9	3	3
CO ₂	26	23	32	19	23
carcass	-	4	-	-	-
total	98	90	99	80	69

No unmetabolized amine oxide was excreted in urine (for cutaneous administration the metabolic pathway is comparable after absorption through the skin)

Percentage of applied radioactivity in the urine					
Species			rat	rabbit	human
metabolite	Metabolic pathway				
II	ω,B-oxidation		28	23	28

metabolite II = carboxylic acid intermediates of ω,B -oxidation, still carrying the amine oxide functional group.

Conclusion: The elimination of radioactivity by rats, rabbits, and humans dosed orally with ^{14}C -DDAO showed a similar pattern (i.e. > 70-90% within the first 24 hours). Renal clearance was the major route of elimination and accounted for more than 50% of the dose. About 20-30% of the ^{14}C -DDAO was sufficiently degraded to yield $^{14}\text{CO}_2$. Metabolite structures suggest that DDAO metabolism involves several different pathways. These pathways are proposed to be ω ,B -Oxidation of the aliphatic chain, amine oxide reduction, and aliphatic mid-chain hydroxylation. While all three species were able to degrade the alkyl chain, rabbit and human were more efficient than the rat. In contrast, rats excreted >12% of the dose as long chain compounds. Under the conditions employed, the rabbit more closely approximates the metabolism of DDAO by man than does the rat. DDAO was extensively metabolized by rats, rabbits, and humans after oral dosing. Most of the dose was eliminated in the urine or was excreted as CO_2 within 24 hours. No evidence was found to indicate that unmetabolized DDAO was excreted in the urine.

Data Quality

Reliability
(Klimisch): 2A

Remarks: Acceptable, well-documented publication/study report which meets basic scientific principles

Reference

Source Reference: Turan and Gibson, 1981.

5.1.1 ACUTE ORAL TOXICITY

(a)

Test Substance

CAS Number: 1643-20-5
Identity: Dodecylamine oxide
Purity: 30% (w/w)
Carbon Chain Length Distribution: C12

Method

GLP: n/a
Report/Study Year: 1985
Report/Study Number: Leberco50964
Method/Guideline Followed: not stated
Test type: Acute oral by gavage
Species: rat
Strain: Charles River
Sex: male and female
Vehicle: No vehicle; single dose by gavage

Number of Animals per Dose: 10 (5 male and 5 female)

Remarks: Guideline not indicated; 5 animals per dose group per sex; weight 200-250 g. Animals were fasted 18 h before dosing. Administration by oral gavage. Observations of clinical signs/mortality until day 14. Necropsy on day 14.

Results

Value:		Lower	Upper	Unit
	=	964	1210	mg a.i./kg bw

Remarks: LD50 = 1080 mg a.i./kg bw.

Results were corrected for the active level of the sample (30%). The laboratory report does not state the active level of the test sample, so even though this is not specifically stated it is assumed that the dosage levels and LD50 results were reported by the laboratory on the basis of the whole sample (i.e. not corrected for active level) and the correction was made here.

Nothing unusual was observed. No macroscopic changes up to 90% mortality level.

Necropsy findings: deep/bright red or light tan lungs sometimes with liver colored areas or petechiae, salivation, nasal and/or ocular hemorrhage, stomach irritation, stomach and/or intestines filled with gas and/or fluid, stomach and/or intestines filled with bloody fluid.

Mortalities (males and females combined, read from graph): 4/20 at low dose; 7/10 at mid dose; 9/10 at high dose.

Data Quality

Reliability (Klimisch): 3B

Remarks: Not reliable: documentation insufficient for assessment. Guideline not indicated. Uncertain whether data are expressed in terms of active ingredient or whole sample.

Reference

Source Reference: Onyx Chemical Co., 1985B.

Cited In: Pang, 1994

(b)

Test Substance

CAS Number: 1643-20-5

Identity: Lauramine oxide; dodecyldimethylamine oxide

Purity: 25.5% (w/w)

Carbon Chain Length Distribution: C12

Remarks: Ammonyx® SO

Method

GLP: not stated
Report/Study Year: 1985
Report/Study Number: Leberco50967
Method/Guideline Followed: not stated
Test type: acute oral by gavage; limit test
Species: rats
Strain: Charles River
Sex: male and female
Vehicle: no vehicle; dosed as-is
Number of Animals per Dose: 10 (5 male and 5 female)
Doses: 5 g/kg bw
Remarks: 14-day post observation period

Results

Value:		Unit
	> 5000	mg/kg bw

Remarks: There were no deaths. No macroscopic changes were observed during autopsy.

Data Quality

Reliability (Klimisch): 3B

Remarks: Not reliable: documentation insufficient for assessment.

Reference

Source Reference: Onyx Chemical Co., 1985A.

Cited In: Pang, 1994

(c)

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine oxide
Purity: 0.3%
Carbon Chain Length Distribution: C12
Remarks: Formulation containing 0.3% of the test substance was tested. No other details about composition were provided.

Method

GLP: no data
Report/Study Year: 1985
Report/Study Number: SDA128

Method/Guideline Followed: n/a
Test type: acute oral
Species: rat
Strain: Sprague-Dawley
Sex: male/female
Vehicle: water
Number of Animals per Dose: 6
Doses: not indicated
Remarks: Groups of 3 male and 3 female rats
Procedure: Up/down and limit test.

Results

Value:		Unit
	> 30	mg a.i./kg bw

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature

Reference

Source Reference: Pang, 1994.

(d)

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine oxide
Purity: 0.3% active
Carbon Chain Length C12
Distribution:
Remarks: Formulation is a hairspray containing 0.3% of the test substance. Other ingredients are: 85-95% water; 1-5% PVP/VA copolymer; 0-2% cocamide DEA; 0-2% polyquaternium-11 and <1% minors.

Method

GLP: no data
Report/Study Year: 1994
Report/Study Number: SDA128
Test type: up/down and limit test
Species: rat
Strain: Sprague-Dawley CD
Sex: female

Vehicle: water
Number of Animals per Dose: 6
Doses: 20 g/kg or greater
Remarks: One animal received 16 g/kg test material and 5 received 20 g/kg test material.

Results

Value:	Operator		Unit
	>	60	mg/kg bw

Remarks: All the animals survived; no adverse signs were observed.

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature

Reference

Source Reference: Pang, 1994.

5.1.2 ACUTE INHALATION TOXICITY

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine oxide; lauramine oxide
Purity: 0.3%
Carbon Chain Length Distribution: C12
Remarks: Formulation is a hairspray containing 0.3% of the test substance. Other ingredients are: 85-95% water; 1-5% PVP/VA copolymer; 0-2% cocamide DEA; 0-2% polyquaternium-11 and <1% minors

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: IRDC191-1447
Analytical Monitoring: no
Test Type: LC50
Species: rat
Strain: Sprague-Dawley albino
Sex: male/female

Vehicle: other
Number of Animals per Dose: 10 (5 male and 5 female)
Doses: 5.3 mg/l (corresponds to 0.016 mg AO/L)

Value	Unit
4	hour(s)

Remarks: A liquid droplet aerosol of the test substance was delivered to 54-liter glass exposure chambers via a syringe drive (Sage Instruments) and atomizer (Spraying Systems). The rats took up less than 5% of the volume in the chambers. The particle size distribution of the aerosol was determined with an Andersen® 8-stage cascade impactor. Aerosol droplets had an average equivalent aerodynamic diameter of 3.6 microns (SD 1.91 microns). The nominal exposure concentration was calculated based on the amount of test substance delivered divided by the total volume of air that flowed through the exposure chamber during the exposure period.

Results

Operator	Lower	Unit
>	0.016	mg AO/l (nominal)

Remarks: Animals were observed during exposure (4 hours) and twice daily for 14 days post-exposure. Body weights were recorded before exposure and on days 1, 3, 7 and 14 after exposure. At necropsy, the major organs in the abdominal and thoracic cavities were weighed and observed. The 4 h LD50 for the aerosol was greater than 5.3 mg/l (nominal) which corresponds to 0.016 mg AO/L. No deaths occurred during the study and no exposure-related pharmacotoxic signs were evident in any of the organs, nor were any exposure-related macroscopic changes observed in any of the animals.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; comparable to guideline study.

Reference

Source Reference: International Research and Development Corporation, 1990A.

Cited In: Pang, 1994

5.2.1 SKIN IRRITATION

(a)

Test Substance

CAS Number: 1643-20-5
Identity: Dodecyldimethylamine oxide
Purity: 30% active

**Carbon Chain Length
Distribution:**

C12

Remarks:

Commercial substance; normally produced as 30% active in water; no confirmation of active content in this report.

Method**GLP:**

yes

Report/Study Year:

1992

Report/Study Number:

C1-0024

**Method/Guideline
Followed:**

Human Cumulative Irritation 3-Patch Application Test

Analytical Monitoring:

no

Species:

human (clinical testing)

Vehicle:

water

Number of Animals:

10

Concentration:

0.45% active

Exposure:

7 days

Remarks:

Irritation screen conducted with the following concentrations: 0.3 – 0.6 – 0.9 – 1.2 – 1.5% active, a control substance, sodium dodecyl sulfate (SDS from Curtin Matheson Scientific Inc.), at 0.2 and 0.5% active, and a vehicle control of water.

Scoring system: a standardized interpretation system for 10 panelists' irritation scores for 21 days (Berger *et al.*, 1982) was converted to an interpretation system for a 1 week, 3-patch application test.

Results**Result:**

Moderately irritating

Classification:

irritating

**Primary Dermal
Irritation Index
(PDII):**

not derived from this test

Remarks:

The 0.3% concentration of the test substance, and the vehicle control, resulted in no cumulative irritation. Higher concentrations of the test substance, as well as both concentrations of the positive control, resulted in very mild cumulative irritation. Based on these results a concentration of 0.45% active was selected as appropriate for the planned human repeat insult patch testing.

Data Quality**Reliability (Klimisch):** 1B**Remarks:**

Reliable without restriction, comparable to guideline study.

Reference

Source Reference: The Stepan Company, 1992.

Other Reference: Berger and Bowman, 1982.

Cited In:

Pang, 1994

(b)

Test Substance

CAS Number: 1643-20-5
Identity: Dodecyldimethylamine oxide
Purity: 30%
Carbon Chain Length Distribution: C12
Remarks: Test substances are a mixture of amine oxide (30%), betaine (30%) and water (40%). Three such mixtures were tested, and results for all three are summarized here.

Method

GLP: yes
Report/Study Year: 1988
Report/Study Number: RICERCA88-0193
Species: New Zealand white (albino) rabbits
Concentration: 'as is'
Remarks: A dose of 0.5 ml of 'as is' test substance containing 30% AO was applied to 1 of 4 shaved (not abraded) dorsal skin sites on each of 6 rabbits, covered with gauze patch and occlusive bandage for 24 hours. The occlusive bandage consisted of hypoallergenic tape, plastic sheeting (Saran WrapTM) and elastic Vetrap^(R). After 24 hours, sites were rinsed with warm water, wiped with moistened paper towels and scored for skin irritation. Sites were scored again at 72 h following application. The scoring of test sites was done following the Draize system.

Results

Result: moderately (24 hours) to severely (72 hours) irritating
Classification: severely irritating
Primary Dermal Irritation Index (PDII): 7.0 - 7.2 - 7.6
Remarks: Erythema scores: moderate-severe at 24h, severe at 72h
Edema scores: slight to severe at 24h, severe at 72h
The average PDII was 7.3

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2A
Remarks: Comparable to guideline study.

Reference

Source Reference: Stepan Company, 1988.
Other Reference: Draize, 1965.
Cited In: Pang, 1994

(c)

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine oxide
Purity: 30%
Carbon Chain Length Distribution: C12
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1986
Report/Study Number: K-9453
Method/Guideline Followed: other
Species: rabbit
Vehicle: water
Number of Animals: 6
Concentration: 5 % active substance
Remarks: Method referred to as HSLA 16, 1500.41. Sex not indicated. Application of 0.5 ml of a 5% aqueous solution of test substance onto the skin. Observations at 24 and 72 h.

Results

Result: irritating
Classification: irritating
Remarks: Since skin effects (mild to moderate irritation) were still present at 72 h, the test should ideally have been prolonged. No information about duration of exposure. OECD 404 prescribes that test substance should be held in place with porous gauze dressing; no information on this. No information on clipping of the fur. No results on abraded skin. Edema scores: 0-2 Erythema scores: 1-2. Primary Skin Irritation Index = 2.58

Data Quality

Reliability (Klimisch): 2B
Remarks: Basic data given, comparable to guidelines/standards.

Reference

Source Reference: Onyx Chemical Company, 1986.
Cited In: Pang, 1994

(d)

Test Substance

CAS Number: 1643-20-5
Identity: lauramine oxide
Purity: 5% active
Carbon Chain Length Distribution: C12
Remarks: Ammonyx SO®. Balance of ingredients not stated.

Method

GLP: no
Report/Study Year: 1973
Report/Study Number: Leberco34700
Method/Guideline Followed: CFR 21, Part 191.1 (g), 191.11
Species: albino rabbits
Vehicle: none; delivered as-is
Number of Animals: 6
Concentration: 0.5 ml 'as is' test substance
Exposure: 24 hours
Remarks: Study was conducted prior to GLP regulations.
Intact and abraded skin was treated on each animal. Each 2x2 in. treated area was covered with a Webril® patch. The entire experimental area on the animal was sealed with Blenderm® surgical tape. Skin was evaluated at end of 24 h exposure period and again at 48 h.

Results

Result: not irritating
Classification: not irritating
Primary Dermal Irritation Index (PDII): 0

Data Quality

Reliability (Klimisch): 2B
Remarks: Reliable with restrictions. Basic data given, comparable to guidelines/standards.

Reference

Source Reference: Onyx Chemical Corporation, 1973A.
Cited In: Pang, 1994

(e)

Test Substance

CAS Number: 1643-20-5
Identity: lauramine oxide
Purity: 5% active
Carbon Chain Length Distribution: C12
Remarks: Ammonyx CDO®. Balance of ingredients not stated.

Method

GLP: not stated
Report/Study Year: 1985
Report/Study Number: Leberco50963
Method/Guideline Followed: Not stated but presumably guideline was CFR 21, Part 191.1 (g), 191.11 as in other, same tests from same laboratory
Species: albino rabbits
Vehicle: none; delivered as-is
Number of Animals: 6
Concentration: 0.5 ml 'as is' test substance
Exposure: 24 hours
Remarks: Intact and abraded skin was treated on each animal. Each 2x2 in. treated area was covered with a Webril® patch. The entire experimental area on the animal was sealed with Blenderm® surgical tape. Finally, a sheet of polyethylene is wrapped around the animal and taped to delay evaporation. Skin was evaluated at end of 24 h exposure period and again at 48 h.

Results

Result: not irritating
Classification: not irritating
Primary Dermal Irritation Index (PDII): 1.41
Remarks: Not a primary dermal irritant as defined in CFR 16:1500.41.

Data Quality

Reliability (Klimisch): 2B
Remarks: Reliable with restrictions. Basic data given, comparable to guidelines/standards. Balance of ingredients in sample is not stated. Whether or not conducted under GLP is not stated.

Reference

Source Reference: Onyx Chemical Corporation, 1973B.

Cited In: Pang, 1994

(f)

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine oxide
Purity: not given
Carbon Chain Length Distribution: C12

Method

GLP: no data
Report/Study Year: 1994
Report/Study Number: SDA128
Method/Guideline Followed: other
Species: human
Vehicle: no data
Number of Animals: 10
Concentration: 1 - 2 -3 -4 -5%
Exposure: 48 hours
Remarks: Guideline not indicated. Vehicle: no data, believed to be water. Dosage: 1 - 2 - 3 - 4 - 5%. Scores determined by totalling the 3 observation scores for each site. Max. possible score was 90.

Results

Result: slightly irritating
Classification: not irritating
Remarks: Authors classified 1% lauramine oxide as having no cumulative irritation with a score of 4.5. At conc. of 2, 3, 4 and 5%, cumulative irritation scores were 10.5, 11.5, 15.0 and 24.0 Conclusion: slight potential for very mild cumulative irritation.

Data Quality

Reliability (Klimisch): 4B
Remarks: Secondary literature.

Reference

Source Reference: Pang, 1994.

(g)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide
Purity: not given
Carbon Chain Length Distribution: C12
Remarks: 3.7% aqueous solution was tested

Method

GLP: no data
Report/Study Year: 1994
Report/Study Number: SDA128
Method/Guideline Followed: other
Species: human
Vehicle: water
Number of Animals: 10
Concentration: 3.7 %
Exposure: 48 hours
Remarks: Guideline not indicated, referred to as "patch test" indicating occlusive exposure. However, 5/10 subjects who showed mild irritation after 48 hours were re-tested in an "open" test (no patch, non-occlusive).

Results

Result: not irritating
Classification: not irritating
Remarks: 5/10 subjects: mild irritation after 48 h. These were re-tested in open patch and no irritation occurred.

Data Quality

Reliability (Klimisch): 4B
Remarks: Secondary literature.

Reference

Source Reference: Pang, 1994.

5.2.2 EYE IRRITATION

(a)

Test Substance

CAS Number: 1643-20-5
Identity: lauramine oxide
Purity: 0.3% active
Carbon Chain Length Distribution: C12

Remarks: Hair mousse containing 0.3% lauramine oxide. White foamy product.

Method

GLP: yes

Report/Study Year: 1986

Report/Study Number: 60803843

Method/Guideline Followed: Draize method; low volume procedure

Species: New Zealand albino rabbits

Vehicle: dosed as-is

Number of Animals: 6 (2 males and 4 females)

Dose:

Value	Unit
30	µg/eye

Remarks: Dose delivered as 10 µl of the formulation into the eye. Eyes were not rinsed. Eyes were examined for up to 21 days post-treatment and scored after 1, 2, 3, 4, 7, 14 and 21 days or until eyes are clear. No control substance.

Results

Result: not irritating

Classification: not irritating

Remarks: The eyes of all animals were clear of eye irritation effects after 1 day. The MAS was 0 and the median time to clear was 1 day.

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; comparable to guideline study

Reference

Source Reference: Hazleton Laboratories, 1986.

Other Reference: Draize, 1959.

Cited In: Pang, 1994

(b)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide

Purity: 30%

Carbon Chain Length Distribution: C10-16

Remarks: Balance is water

Method

<i>GLP:</i>	yes
<i>Report/Study Year:</i>	1986
<i>Report/Study Number:</i>	83.0542
<i>Method/Guideline Followed:</i>	other
<i>Species:</i>	rabbit
<i>Vehicle:</i>	water
<i>Number of Animals:</i>	6
<i>Remarks:</i>	Guideline is referred to as HSLA 16, 1500.42 Observations: 24, 48, 72 and 96 h and on day 7.

Results

Result: slightly irritating

Remarks: Corneas and irises clear, all animals. Scores for redness of conjunctivae: 0 – 1. Scores for chemosis of conjunctivae: 0 - 1

Data Quality

Reliability (Klimisch): 2B

Remarks: No information on procedures. No information on whether eye lids were held closed after application.

Reference

Source Reference: Hoechst AG, 1983A.

(c)

Test Substance

<i>CAS Number:</i>	1643-20-5
<i>Identity:</i>	lauramine oxide
<i>Purity:</i>	5% active
<i>Carbon Chain Length Distribution:</i>	C12
<i>Remarks:</i>	Ammonyx® SO; 5% lauramine oxide, tested as-is; other ingredients not stated.

Method

<i>Report/Study Year:</i>	1963
<i>Report/Study Number:</i>	IBL-4251
<i>Method/Guideline Followed:</i>	Draize method
<i>Species:</i>	rabbits
<i>Vehicle:</i>	dosed as-is
<i>Remarks:</i>	100 ul of 'as produced' sample administered to the eye

Results

Result: slightly irritating

Data Quality

Reliability (Klimisch): 4A

Remarks: Not assignable; only short abstract or summary available.

Reference

Source Reference: Onyx Chemical Corporation, 1963.

Cited In: Pang, 1994

(d)

Test Substance

CAS Number: 1643-20-5

Identity: lauramine oxide

Purity: 5% active

Carbon Chain Length
Distribution: C12

Remarks: Ammonyx CDO®. Balance of ingredients not stated.

Method

GLP: no

Report/Study Year: 1971

Report/Study Number: D-9236

Method/Guideline
Followed: U.S. Department of Agriculture, FIFRA, Section 362.3 of 7CFR part 362, paragraph (d)

Species: rabbits

Vehicle: none; delivered as-is

Number of Animals: 3

Value	Unit
0.1	ml/eye

Remarks: Treatment produced slight conjunctival irritation in all animals. This was fully reversed in 2 animals after a day and in the remaining animal after 2 days.

Results

Result: moderately irritating

Classification: not irritating

Data Quality

Reliability (Klimisch): 4A

Remarks: Not assignable; only short abstract or summary available.

Reference

Source Reference: Onyx Chemical Corporation, 1971.

Cited In: Pang, 1994

(e)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide

Purity: 0.3%

Carbon Chain Length
Distribution: C12

Remarks: Formulations containing 0.3% test substance.

Method

GLP: no data

Report/Study Year: 1994

Report/Study
Number: SDA128

Method/Guideline
Followed: Draize Test

Species: rabbit

Vehicle: other

Dose:

Value	Unit
0.01	ml

Remarks: Guideline: Draize 1959. New Zealand White rabbits, number not stated. Vehicle was the tested formulation. The eyes of some rabbits were rinsed after exposure, with distilled water.

Results

Result: slightly irritating

Remarks: Slight irritation of the conjunctivae observed in all unrinsed eyes and 2 of the 3 rinsed eyes at the 24-hour grading period. Max. av. score was 2.0 for animals with unrinsed eyes and 1.3 for those with rinsed eyes. All eyes clear after 48 hours.

Data Quality

Reliability (Klimisch): 4B

Reference

Source Reference: Pang, 1994.

5.2.3 SENSORY IRRITATION**Test Substance**

<i>CAS Number:</i>	1643-20-5
<i>Identity:</i>	lauramine oxide
<i>Purity:</i>	0.3% active
<i>Carbon Chain Length Distribution:</i>	C12
<i>Remarks:</i>	Formulation is a hairspray containing 0.3% of the test substance. Other ingredients are: 85-95% water; 1-5% PVP/VA copolymer; 0-2% cocamide DEA; 0-2% polyquaternium-11 and <1% minors

Method

<i>GLP:</i>	yes
<i>Report/Study Year:</i>	1990
<i>Report/Study Number:</i>	IRDC191-1448
<i>Method/Guideline Followed:</i>	no guideline; similar to methods described by Alarie (1966 and 1973)
<i>Analytical Monitoring:</i>	no
<i>Test Type:</i>	sensory irritation by inhalation
<i>Species:</i>	mice
<i>Strain:</i>	Swiss-Webster albinos from Charles River
<i>Sex:</i>	male
<i>Vehicle:</i>	hairspray
<i>Number of Animals per Dose:</i>	4
<i>Doses:</i>	0.2, 1.0 and 5.2 mg/l (corresponding to 0.00006, 0.003, and 0.016 mg AO/L, respectively)
<i>Exposure Period:</i>	10 min
<i>Remarks:</i>	Three groups of four male Swiss-Webster albino mice were exposed (heads only) for 10 minutes to liquid droplet aerosols of the test substance at nominal concentrations of 0.2 1.0, and 5.2 mg/l, corresponding to 0.00006, 0.003, and 0.016 mg AO/L, respectively. The group average respiratory rate was monitored by plethysmography for 5 minutes before, for 10 minutes during and for 10 minutes after exposure and the percent change in respiratory rate calculated.

Results

<i>Value:</i>	> 0.016 mg AO/L
<i>Remarks:</i>	There was no change in respiratory rate up to the highest concentration tested (5.2 mg/l product, corresponding to 0.016 mg/l AO). Note that this is not an inhalation LD50. Plethysmography for respiratory rate measurement in animals at http://www.medicine.mcgill.ca/physio/resp-web/appx1.htm

Data Quality

*Reliability
(Klimisch):* 2B

Remarks: Reliable with restrictions. Basic data given, comparable to guidelines/standards.

Reference

Source Reference: International Research and Development Corporation, 1990B.

Other References: Alarie, 1966 and 1973

Cited In: Pang, 1994

5.3 SENSITIZATION

(a)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide; lauramine oxide

Purity: 0.3%

*Carbon Chain Length
Distribution:* C12

Remarks: Hair styling mousse containing 0.3% test substance. Balance of ingredients not given.

Method

GLP: yes

Report/Study Year: 1987

Report/Study Number: HARRIS-10821

*Method/Guideline
Followed:* Human Repeat Insult Patch Test (HRIPT)

Analytical Monitoring: no

Test Type: delayed contact sensitization

Vehicle: none

Number of Animals: 101

Species: human (clinical testing)

Type	Value	Unit	Application Form
occl. patch	0.15	% active	in dist. water

Remarks: Test substance used at 50% dilution in distilled water and applied under occluded patch.
Protocol: there is no official guideline for the HRIPT; the original protocol with scoring scale was published by Stotts (1980) and the method is still widely used today. A detailed protocol is included with the study report and described as an HRIPT (human repeat insult patch test) protocol, approved by the Harris Laboratories Inc. Institutional

Review Board in 1987.

Test conditions: 2 to 2.5 inch x 7 inch Blenderm® Surgical Tape to which 7/8 inch diameter Webril® nonwoven cotton disks were centrally fixed approx. 3/4 inches apart. Induction patches were applied on Mon., Wed. and Fri. of each week for 3 consecutive weeks to lateral surface of upper arm. Patches were removed after 24 h and patch sites graded before application of the next patch. Challenge patches were applied to the original and the opposite arm of each test subject approx. 17 days after the last induction application, and worn for 24 h.

Results

Result: no evidence of sensitization

Classification: not sensitizing

Remarks: The maximum score observed in this HRIPT was 1 (= mild erythematous reaction; faint pink to definite pink). There was no evidence of sensitization.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability
(Klimisch): 1A

Remarks: Reliable without restriction; comparable to guideline study. Balance of ingredients was not stated, but since the result is negative (no sensitization), this information is less important.

Reference

Source Reference: Harris Laboratories, 1987.

Other Reference: Stotts, 1980.

Cited In: Pang, 1994

(b)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide

Purity: 10% (w/v)

Carbon Chain
Length: C12

Distribution:

Remarks: COMPOSITION: Hibiscrub® is a detergent skin cleansing solution containing 4 g/100 ml chlorhexidine gluconate as the active ingredient, 4% (w/v) isopropanol, 10% (w/w) dodecyldimethylamine oxide, Ponceau Red 4R, a mixture of 20 perfume ingredients, and D-gluconolactone
USE: Hibiscrub® is an antimicrobial preparation for pre-operative surgical hand disinfection, antiseptic handwashing and pre-operative skin antisepsis for patients undergoing surgery.

Method

GLP: no data
Report/Study Year: 1977
Report/Study Number: SDA197
Method/Guideline Followed: no guideline; in-hospital, clinical observation
Analytical Monitoring: no
Vehicle: Hibiscrub® or water
Number of Animals: 1
Species: clinical (human)
Remarks: A patient's skin was shaved and prepared with Hibiscrub® prior to surgery.
Patch testing was performed 6 weeks after the patient's dermatitis had settled and resulted in generalized eczema and facial edema after 48 hours. Ten control volunteers were also patch tested with Ammonyx LO 3.7% in water
Patch test treatments as follows:
European standard battery
Hibiscrub® 'as is' (contains 10% dodecyldimethylamine oxide)
Hibiscrub® 5% in water (contains 0.5% dodecyldimethylamine oxide)
Hibiscrub® 10% in water (contains 1.0% dodecyldimethylamine oxide)
Ammonyx LO 3.7% in water (contains 1.1% dodecyldimethylamine oxide)

Results

Result: moderately irritating

Classification: irritating

Remarks: Skin was shaved and prepared with Hibiscrub® prior to surgery. Within 6 hours, painted areas felt hot and itchy and the next morning the treated area showed papulovesicular eczema. Patch testing was performed 6 weeks after the dermatitis had settled and resulted in generalized eczema and facial edema after 48 hours. Ten control volunteers were also patch tested with Ammonyx LO 3.7% in water and five showed mild irritant responses at 48 hours. None showed the allergic reaction exhibited by the patient.

Patch test results as follows:

European standard battery: no irritation

Hibiscrub® 'as is' (contains 10% dodecyldimethylamine oxide): ++

Hibiscrub® 5% in water (contains 0.5% dodecyldimethylamine oxide): ++

Hibiscrub® 10% in water (contains 1.0% dodecyldimethylamine oxide): +++

Ammonyx LO 3.7% in water (contains 1.1% dodecyldimethylamine oxide): +++

Prior to later surgery the patient's skin was prepared with an aqueous solution of chlorhexidine digluconate; the patient did not react to this.

Data Quality

Reliability (Klimisch): 4A

Remarks: Not assignable; only short communication available; insufficient detail re. the methods that were used. Note from reviewer: the possibility that the patient's allergic reaction was caused by one of the other ingredients, such as possibly one of the perfume ingredients, was not discussed by the authors. It is, however, a real possibility.

Reference

Source Reference: Muston et al., 1977.

(c)

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine
oxide
Purity: 0.75%
Carbon Chain Length Distribution: C12
Remarks: dilution in water

Method

GLP: no data
Report/Study Year: 1994
Report/Study Number: SDA128
Method/Guideline Followed: other
Analytical Monitoring: no
Test Type: Human Repeat Insult Patch Test (HRIPT)
Vehicle: water
Number of Animals: 141
Species: human
Remarks: Guideline not stated but the method description indicates an HRIPT (human repeat insult patch test). Vehicle = 1.5% a.i. for the first 6 induction patches and 0.75% a.i. for the last 3 induction patches as well as for the challenge patches. Conc. was reduced after several subjects showed mild irritation. Induction patches of the diluted would normally be applied on Mon., Wed. and Fri. of each week for 3 consecutive weeks to lateral surface of upper arm. Patches would then be removed after 24 h and patch sites would be graded before application of the next patch. Challenge patches would normally be applied to the original and the opposite arm of each test subject approx. 2-3 weeks after the last induction application.

Results

Result: not sensitizing

Classification: not sensitizing

Remarks: At 48 h grading period, 46 subjects received scores of 0.5; 12 subjects received scores of 2. At 96 h reading, 6 individuals received scores of 0.5. Authors stated that these scores were same as those observed during induction, indicative of primary and cumulative irritation.

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature.

Reference

Source Reference: Pang, 1994.

(d)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide

Purity: not given

Carbon Chain Length
Distribution: C12

Remarks: Cosmetic formulation, diluted to 10% with dist. water.

Method

GLP: no data

Report/Study Year: 1994

Report/Study Number: SDA128

Method/Guideline
Followed: other

Test Type: Patch-Test

Vehicle: other

Number of Animals: 107

Species: human

Remarks: Guideline not stated but the method description indicates an HRIPT (human repeat insult patch test). Vehicle = formulation (product), diluted to 10% with dist. water. Induction patches with 0.3 ml of the diluted formula were applied on Mon., Wed. and Fri. of each week for 3 consecutive weeks to lateral surface of upper arm. Patches were removed after 24 h and patch sites were graded before application of the next patch. Challenge patches would normally be applied

Results

Result: not sensitizing

Classification: not sensitizing

Remarks: Four subjects showed mild erythema during challenge. Irritation disappeared by 96 hours.

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature.

Reference

Source Reference: Pang, 1994.

(e)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide

Purity: 0.15%

Carbon Chain Length C12

Distribution:

Remarks: Formulation containing 0.3% a.i. was diluted to 50% with dist. water.

Method

GLP: no data

Report/Study Year: 1994

*Report/Study
Number:* SDA128

*Method/Guideline
Followed:* other

Test Type: Patch-Test

Vehicle: other

Number of Animals: 84

Species: human

Remarks: Guideline not stated but the method description indicates an HRIPT (human repeat insult patch test). Vehicle = formulation (product) cont. 0.30% a.i., diluted to 50% with dist. water. Induction patches with 0.5 ml of the diluted formula were applied on Mon., Wed. and Fri. of each week for 3 consecutive weeks to lateral surface of upper arm. Patches were removed after 24 h and patch sites were graded before application of the next patch. Challenge patches were applied.

Results

Result: not sensitizing

Classification: not sensitizing

Remarks: Slight irritation in 9 subjects during induction phase. Four subjects showed slight erythema during challenge phase at 48 h grading period. One subject showed mild

irritation oat original site during 96 h grading period.

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature.

Reference

Source Reference: Pang, 1994.

(f)

Test Substance

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide

Purity: 0.15%

Carbon Chain Length C12

Distribution:

Remarks: Formulation containing 0.3% a.i. was diluted to 50% with dist. water.

Method

GLP: no data

Report/Study Year: 1994

Report/Study Number: SDA128

Method/Guideline Followed: other

Test Type: Patch-Test

Vehicle: other

Number of Animals: 101

Species: human

Remarks: Guideline not stated but the method description indicates an HRIPT (human repeat insult patch test). Vehicle = formulation (product) cont. 0.30% a.i., diluted to 50% with dist. water. Induction patches with 0.5 ml of the diluted formula were applied on Mon., Wed. and Fri. of each week for 3 consecutive weeks to lateral surface of upper arm. Patches were removed after 24 h and patch sites were graded before application of the next patch. Challenge patches were applied

Results

Result: not sensitizing

Classification: not sensitizing

Remarks: 24 test subjects showed single or multiple, very mild erythemathous responses during the induction phase. No sensitization responses were observed.

Data Quality*Reliability (Klimisch):* 4B*Remarks:* Secondary literature.**Reference**

Source Reference: Pang, 1994.

5.4 REPEATED DOSE TOXICITY**Test Substance***CAS Number:* 1643-20-5*Identity:* dodecyldimethylamine oxide; lauramine oxide*Purity:* 0.3% active*Carbon Chain Length
Distribution:* C12*Remarks:* Formulation is a hairspray containing 0.3% of the test substance. Other ingredients are: 85-95% water; 1-5% PVP/VA copolymer; 0-2% cocamide DEA; 0-2% polyquaternium-11 and <1% minors**Method***GLP:* yes*Report/Study Year:* 1990*Report/Study Number:* HLA297-570*Method/Guideline
Followed:* other*Analytical Monitoring:* no*Test Type:* Subchronic*Species:* albino rabbit*Strain:* New Zealand white*Sex:* 5 male/5 female*Route of
Administration:* dermal*Exposure Period:* 4 weeks*Doses:* 2 ml/kg/day*Control Group:* 5 male/5 female*Frequency of
Treatment:* 5 applications per week*Post Exposure
Observation Period:* none - necropsies were performed during week 5*Remarks:* Control treatment was 2ml/kg/day of distilled water.

Histopathology performed on: adrenals, thoracic aorta, bone marrow, brain with stem, cecum, colon, duodenum, esophagus, eyes, gross lesions,

heart, ileum, jejunum, kidneys, liver with gallbladder, lung, mesenteric lymph node, ovaries, pancreas, pituitary, prostate, rectum, salivary gland, sciatic nerve, seminal vesicle, skeletal muscle, skin of treatment site, spinal cord, spleen, stomach, submandibular lymph node, testes with epididymides, thymus, thyroid, parathyroids, tongue, trachea, urinary bladder, uterus, vagina.

Results

	Operator	Lower	Unit
NOEL	=	6	mg/kg/day

Remarks: All animals survived to termination. No significant changes in mean body weight, clinical observations, mean absolute organ weights or organ-to-body weight ratios between treated and control groups. Slight-moderate erythema in treated females, slight edema and atonia and fissuring and slight-moderate desquamation in treated group for both sexes. Both treated and control groups had high incidence of sub-acute inflammation of treated skin.

A formulation containing 0.3% lauramine oxide and other unspecified ingredients is slightly irritating to rabbit skin at 2 ml/kg/day or 6 mg/kg/day. There were no other treatment-related effects. NOEL for systemic effects = 6 mg AO/kg/day.

Data Quality

Reliability
(Klimisch): 1D

Remarks: Reliable without restriction; Hazleton laboratories protocol for 28 day subchronic dermal study.

Reference

Source Reference: The Procter & Gamble Company, 1990.

Cited In: Pang, 1994

5.5 GENETIC TOXICITY *In Vitro*

(a)

Test Substance

CAS Number: 1643-20-5
Identity: N,N-dimethyldodecylamine oxide
Purity: no data
Carbon Chain Length Distribution: C12

Method

GLP: n/a
Report/Study Year: 1984
Report/Study Number: SDA196
Method/Guideline Ames reverse mutation assay

Followed:

Test Type: *in vitro* mutagenicity
System: *Salmonella typhimurium*
Test Concentration: 250 µg/plate
Species/strain: TA1535, TA1538, TA100 and TA98
Metabolic Activation: with and without S-9
Remarks: Plate incorporation assays were performed as recommended by Ames *et al.* (1975) with the modifications of Andrews *et al.* (1978).

Results

Result: negative
Cytotoxic Concentration: 250 µg/plate was cytotoxic to TA1535 in absence of S9. Lower concentrations were not tested.
Remarks: N,N-dimethyldodecylamine oxide was not mutagenic alone, either with or without liver S9 activation. After nitrosation with nitrous acid, the N-nitroso derivative of N,N-dimethyldodecylamine oxide was mutagenic with S9 activation to *Salmonella* strain TA1535.
The authors mention obtaining similar results with S9 from hamsters and from rats. Rat S9 was used in this study.

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 1A
Remarks: Reliable without restriction; comparable to guideline study.

Reference

Source Reference: Andrews *et al.*, 1984.
Other References: Ames *et al.*, 1975

(b)

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine oxide
Purity: 29.1%
Carbon Chain Length Distribution: 0.8% C10, 97.5% C14 and 1.7% C17
Remarks: Balance is water

Method

GLP: no data
Report/Study Year: 1980
Report/Study Number: SDA111
Method/Guideline other

Followed:

Test Type: other
System: Syrian hamster embryo cells
Test Concentration: 0.1 - 0.5 - 1.0 - 5.0 - 10 and 20 µg/ml
Remarks: Positive control (3-methylcholanthrene).
Pregnant hamsters killed on days 13, 14 of gestation for preparation of target cells and feeder layer cells, respectively.
Transformation assay:
Day 0: feeder layer cells thawed and plated
Day 3: target cells thawed and plated
Day 4: feeder cells irradiated
Day 5: target cells added to irradiated feeder cells
Day 6: test substance added (7-9 dishes per dose)
Day 14: fixation and staining

Results

Result: negative
Cytotoxic Concentration: between 10 and 20 µg/ml

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2A
Remarks: Acceptable, well-documented publication/study report which meets basic scientific principles.
Positive control (3-methylcholanthrene) showed weak response and no clear dose-response relationship

Reference

Source Reference: Inoue et al, 1989.
Cited In: TSCA ITC, 1983

(c)

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine oxide
Purity: 29.1%
Carbon Chain Length Distribution: 0.8% C10, 97.5% C14 and 1.7% C17
Remarks: Balance is water

Method

GLP: no data
Report/Study Year: 1980
Report/Study SDA111

*Number:**Method/Guideline**Followed:* other

Test Type: Ames test

System: *Salmonella typhimurium* strains TA98 and TA100

Test Concentration: 10-200 µg/plate

Metabolic
Activation: with and without

Remarks: Bacterial suspension (0.1 ml) added in 0.5 ml phosphate buffer (0.1 M, pH 7.4) containing test substance.
Controls: solvent (DMSO) control, water (negative) control, positive controls (4-nitroquinoline 1-oxide, N-methyl-N'-nitro-N-nitrosoguanidine, 2-acetoaminofluorene, N-nitrosodimethylamine).

Results

Result: negative

Cytotoxic
Concentration: some cytotoxicity was observed in Ames test at 100-200 µg/plate without metabolic activation.

Remarks: Positive controls showed clear mutagenic potential. Negative and solvent controls showed no mutagenic potential.

Data Quality*Flags:* Critical study for SIDS endpoint*Reliability*
(Klimisch): 2A

Remarks: Acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Source Reference: Inoue et al, 1989.

Cited In: TSCA ITC, 1983

5.6 GENETIC TOXICITY *In Vivo***Test Substance**

CAS Number: 1643-20-5

Identity: dodecyldimethylamine oxide UDX-7577

Purity: 27.7%

Carbon Chain Length Distribution: C12

Remarks: Balance is water**Method**

GLP: no

Report/Study Year:	1975
Report/Study Number:	SDA107
Method/Guideline Followed:	EPA 84-4
Test Type:	Dominant lethal assay
Species:	mouse
Strain:	C3D2F1/J
Sex:	male/female
Route of Administration:	drinking water
Exposure Period:	5 days
Doses:	10, 100, 1000 mg/kg bw
Remarks:	Treated males (20 per treatment group), untreated females (10 per treatment group). Untreated controls. After last treatment, males were mated with untreated females for a period of 7 days. After the last treatment, each male was housed with two untreated females for one week. To study successive germ cell stages of the males, each male was then housed with two additional females for a period of seven weeks. Pregnant females were sacrificed on day 13 or 14 of pregnancy (as measured from mid-week of mating) and the number of implantations, resorptions and dead embryos was recorded. <i>Corpora lutea</i> were not counted.

Results

Result: negative

Remarks: There were no treatment related effects in any of the treatments.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability
(Klimisch): 2B

Remarks: No results of test with positive control (reference substance). According to OECD 478 *Corpora lutea* should be counted. For mice this procedure is difficult and counting of results will be inaccurate. The number of pregnant females was not indicated. No method to determine mating was described.

Reference

Source Reference: The Procter & Gamble Company, 1983.

Cited In: TSCA ITC, 1983

5.7 CARCINOGENICITY

Test Substance

CAS Number: 1643-20-5
Identity: dodecyldimethylamine oxide
Purity: not given
Carbon Chain Length Distribution: C12
Remarks: "purified" dodecylamine oxide

Method

GLP: no data
Report/Study Year: 1984
Report/Study Number: SDA106
Method/Guideline Followed: other
Species: rat
Strain: Fischer 344
Sex: male/female
Route of Administration: drinking water
Exposure Period: 93 weeks
Frequency of Treatment: 80 ml/cage/day and 5 days/week
Post Exposure Observation Period: 34-37 weeks
Doses: 1000 ppm (0.1%); corresponding to ~250 mg AO/kg bw, with or without 2000 ppm (0.2%) sodium nitrite
Remarks: Guideline not specified; no vehicle control group or not specified; treatment minus sodium nitrite serves as control for treatment with sodium nitrite.

Results

Result: negative
Remarks: No effect on tumor incidence or type was observed after exposure to DDAO or any of three other amines tested. When DDAO was given together with 0.2% sodium nitrite, an increased incidence of liver tumors occurred in males but not females.
Conclusion: Negative for DDAO alone, but positive for DDAO + sodium nitrite. Test substance together with sodium nitrite results in formation of at least 1 nitrosamine that is responsible for the increased incidence of liver neoplasms.

Data Quality

Reliability (Klimisch): 2A

Reference

Source Reference: Lijinsky, 1984.

5.8.1 TOXICITY TO FERTILITY**Test Substance**

<i>CAS Number:</i>	1643-20-5
<i>Identity:</i>	Amines, C10-16-alkyldimethyl, N-oxides; N,N-dimethyl-dodecylamine oxide; lauryl dimethylamine oxide; "Surfactant A"
<i>Purity:</i>	30.0%
<i>Carbon Chain Length</i>	Primarily C12
<i>Distribution:</i>	
<i>Remarks:</i>	Alkyl chain length distribution: 0.1% C8; 0.1% C10; 96.4% C12; 2.9% C14; 0.1% C16; 0.4% other.

Method

<i>GLP:</i>	no
<i>Report/Study Year:</i>	1979
<i>Report/Study Number:</i>	LSR 81/LIF053/472
<i>Method/Guideline Followed:</i>	other
<i>Test Type:</i>	Two generation study
<i>Species:</i>	rat
<i>Strain:</i>	Charles River CD
<i>Sex:</i>	male/female
<i>Route of Administration:</i>	oral feed
<i>Exposure Period:</i>	Test substance was administered in diet to F0 animals throughout maturation, mating, gestation and lactation.
<i>Frequency of Treatment:</i>	Rats (15 males and 30 females per group) received the test substance in their diet for 101-120 days prior to mating and throughout mating, gestation and lactation.
<i>Male Premating Exposure Period:</i>	101 days
<i>Female Premating Exposure Period:</i>	101 days
<i>Test Duration:</i>	Approximately 1 year
<i>Number of Generation Studies:</i>	2
<i>Doses:</i>	F0 animals (15 males and 30 females/group) received 0, 750, 1500, and 3000 ppm in diet for 6.5 weeks; doses were reduced to 0, 188, 375 and 750 ppm for the remainder of the study. F1 generation received 0, 188, 375, and 750 ppm in diet. Doses were converted from ppm in the diet to chemical intake based on the actual feed consumption, by reviewing recorded food consumption and animal body weights. 750 ppm corresponds to 40 mg a.i./kg / day 375 ppm corresponds to 20 mg a.i./ kg / day

	188 ppm corresponds to 11 mg a.i./ kg / day
Control Group:	yes, concurrent control group received untreated diet
Remarks:	This two-generation study on the influence of Surfactant A upon the somatic growth, development, fertility and reproductive function of rats was conducted in accordance with the Japanese Ministry of Health and Welfare Guidelines. The study was performed from November, 1979-November 1980, with a study report issued in 1983. Charles River CD rats were used. Initial doses of 0, 750, 1500, and 3000 ppm were administered in diet to males and females of the F0 generation. However, following a marked inhibition of bodyweight gain at the two highest levels, doses were reduced to 0, 188, 375, and 750 ppm. The F1 generation received 0, 188, 375, and 750 ppm in diet for 120 days prior to mating. All animals were examined daily throughout the study for any signs of reaction to the treatment. Males were weighed weekly until termination. Females were weighed weekly until mating was detected; they were then weighed on Days 1, 3, 7, 14, and 21 post coitum and on Days 1, 4, 11, 18 and 25 <i>post partum</i> . Food consumption was recorded weekly. Offspring were observed daily and weighed on Days 1, 4, 11, 18 and 25 postpartum. Animals were subjected to a complete gross necropsy and microscopic evaluation of the following tissues was done: adrenals, all tumors, brain, bone marrow, cecum, duodenum, epididymides, eye and optic nerve, heart, ileum, kidneys, liver, lungs, lymph nodes, mammary glands, esophagus, ovaries, pancreas, pituitary, prostate, seminal vesicles, spleen, stomach, testes, thymus, thyroid, urinary bladder and uterus.

Results

	Operator		Unit
NOAEL: Parental:	>	40	mg/kg day
F1 Offspring:	>	40	mg/kg day
F2 Offspring:	>	40	mg/kg day

Remarks: The 40 mg/kg day dose level corresponds with the 750 ppm dose level in feed. Administration of the test material to male and female rats for two generations at concentrations of 188, 375, and 750 ppm was associated with slight reductions in weight gain of both parents and offspring, but was without adverse effect on their mating performance and fertility. Reductions in weight gain did not exceed 10%. The general condition of the animals throughout the study was unaffected by treatment. At all treatment levels, absolute bodyweights of both sexes remained slightly below that of controls. Mating performance, fertility, and conception rate were not affected by treatment in either generation. Gestation and parturition proceeded normally. There was a slight reduction in the number of F2 offspring born at the 750 ppm level, however there were no adverse effects of treatment on litter size at birth, live birth index and birth weight in either generation. Therefore, this was not considered an adverse effect. Viability of offspring was unaffected in the first generation, but there were slight reductions in viability of the F2 offspring at 188 and 750 ppm levels. Offspring viability in the 375 ppm group was similar to the control group. This reduction was within the range of historical controls and did not appear to be dose dependent. Therefore, this was not considered an adverse effect. At all treatment levels, the rate of bodyweight gain for the F1 and F2 offspring was reduced during the lactation period, however, this reduction

was not greater than 10%. This effect appeared to be dose-related, but was not statistically significant on days 1, 4, 11 and 18 *post partum*. On day 25 *post partum*, the difference did reach significance for the two higher dosage groups in the F1 and F2 offspring. This was not considered an adverse effect since the body weight change only reached statistical significance when the rat pups were getting the majority of their calories from solid food and was not associated with any other effects. No macroscopic abnormalities or histopathological changes were attributable to treatment with the test substance.

Details for first generation (F1):

Mean number of litters in treatment groups = 25

Mean number of litters in control group = 26

Mean number of pups per litter in treatment groups = 12.8 ± 3.3

Mean number of pups per litter in control group = 11.6 ± 3.6

Mean live birth index in treatment groups = 98%

Live birth index in control group = 96%

Mean viability index in treatment groups = 93% (4 days *post partum*) to 89% (25 days *post partum*)

Viability index in control group = 93% (4 days *post partum*) to 91% (25 days *post partum*)

Data patterns are consistent with random variability (no statistically significant differences between control and treatment groups; no indication of any dose-response relationships).

Details for second generation (F2):

Mean number of litters in treatment groups = 25

Mean number of litters in control group = 21

Mean number of pups per litter in treatment groups = 11.1 ± 4.1

Mean number of pups per litter in control group = 11.5 ± 2.9

Mean live birth index in treatment groups = 96%

Live birth index in control group = 100%

Mean viability index in treatment groups = 91% (4 days *post partum*) to 93% (25 days *post partum*)

Viability index in control group = 99% (4 days *post partum*) to 99% (25 days *post partum*)

Data patterns are consistent with random variability (no statistically significant differences between control and treatment groups; no indication of any dose-response relationships). The only exception to this is that the viability index at 25 days *post partum* in the treatment groups is significantly different from the controls but well within historical control data from this laboratory (based on 39 prior studies).

Data Quality

Flags: Critical study for SIDS endpoint

Reliability
(*Klimisch*): 1B

Remarks: This study was conducted prior to the adoption of GLP compliance standards. However, it was conducted in accordance with the Japanese Ministry of Health and Welfare Guidelines, and was reviewed and found to be acceptable by the

laboratory's Quality Assurance Unit. The following statistical methods were used: Multiple t-test; Mann-Whitney U-test; x2-test; or Fisher's Exact Probability test.

Reference

Source Reference: Lion Corporation, 1979B.

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

(a)

Test Substance

<i>CAS Number:</i>	1643-20-5
<i>Identity:</i>	Amines, C10-16-alkyldimethyl, N-oxides; N,N-dimethyl-dodecylamine oxide; lauryl dimethylamine oxide
<i>Purity:</i>	30.0%
<i>Carbon Chain Length Distribution:</i>	Primarily C12
<i>Remarks:</i>	Alkyl chain length distribution: 0.1% C8; 0.1% C10; 96.4% C12; 2.9% C14; 0.1% C16; 0.4% other.

Method

<i>GLP:</i>	no
<i>Report/Study Year:</i>	1979
<i>Report/Study Number:</i>	LSR 80/LIF047/147
<i>Method/Guideline Followed:</i>	other
<i>Species:</i>	rat
<i>Strain:</i>	Charles River CD
<i>Sex:</i>	female
<i>Route of Administration:</i>	gavage
<i>Exposure Period:</i>	Test substance was administered via gavage to groups of female rats during days 7 to 17 (inclusive) of gestation.
<i>Frequency of Treatment:</i>	Rats (32 females per group) received the test substance via gavage daily during days 7 to 17 (inclusive) of gestation.
<i>Test Duration:</i>	Approximately 4 months
<i>Doses:</i>	F0 animals received 0, 50, 100 or 200 mg/kg/day of the test substance via gavage.
<i>Control Group:</i>	yes, concurrent vehicle
<i>Remarks:</i>	This study was conducted in accordance with the Japanese Ministry of Health and Welfare Guidelines. The study was performed from July, 1979 through November, 1979. Charles River CD rats were used. Animals were examined daily throughout the study for any treatment-related adverse signs. Maternal bodyweights were recorded on Days 0, 2, 7-17 inclusive, and Day 20 <i>post</i>

coitum. Food consumption was measured twice weekly during gestation. Approximately two-thirds of the animals in each group were killed on Day 20 of gestation for examination of their uterine contents, including number of *corpora lutea* in each ovary, number of implantation sites, number of resorption sites (early or late), number of live and dead fetuses in each uterine horn, including an estimation of time of death of non-viable fetuses, weight and sex of fetuses, individual placental weights, and external abnormalities. Extensive skeletal examinations were also performed on approximately half of each litter, and visceral examinations were performed on the remainder of the fetuses.

The remaining one-third of the females in each treatment group was permitted to deliver their young naturally and rear their own offspring until weaning on Day 25 *post partum*. The following were recorded: gestation length, parturition, litter size at birth, birth-weight of offspring, viability of neonates, growth of offspring, incidence of abnormal offspring, sex ratio, and post-natal development (including physical development, auditory and visual function, activity, behaviour, learning and locomotor function).

F1 animals (22 males and 22 females) were paired at 10 weeks of age. Males were weighed weekly until termination. Females were weighed weekly until mating was detected and during gestation Days 0, 2, 7, 9, 11, 13, 15, 17 and 20 *post coitum*. On Day 20 of gestation, the females were killed and uterine contents were examined macroscopically and for the following: number of *corpora lutea* in each ovary, number of implantation sites, number of resorption sites (early or late), number and distribution of live and dead fetuses in each uterine horn, weight and sex of individual fetuses, individual placental weights and external abnormalities.

For skeletal examinations, a modification of Dawson's staining technique was used (Tesh, 1968).

For visceral examinations, Wilson's technique was used (Teratology, 1965).

Results

NOAEL
Maternal: 100 mg AO/kg bw/day

NOAEL
Teratogenicity: 100 mg AO/kg bw/day

Remarks: Administration of the test material to pregnant rats, from day 7 to day 17 of gestation, at dose levels of 50, 100 and 200 mg/kg/day was associated, at the highest dose level, with a slight reduction of maternal bodyweight gain and food intake, with elevated water consumption. However, reductions in bodyweight gain and food intake were less than 10%. In females killed on day 20 of gestation, mean fetal weight was depressed at the highest dose level, and this was associated with a slight retardation of fetal ossification. However, in females allowed to litter, parturition, survival, and growth and development of F1 offspring were unaffected by previous treatment with the test substance. The subsequent growth, mating performance and fertility of F1 animals was similar in all groups, but in F1 females derived from F0 females that received 200 mg/kg/day, fetal and placental weights were slightly elevated compared with concurrent controls. Dosages of 50 and 100 mg/kg/day were tolerated without discernible influence upon the dam or upon the course and outcome of pregnancy. At terminal necropsy of F1 animals, no macroscopic changes were

observed that could be related to treatment of F0 females.

**Data
Quality**

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 1B

Remarks: This study was conducted prior to the adoption of GLP compliance standards. However, it was conducted in accordance with the Japanese Ministry of Health and Welfare Guidelines, and was reviewed and found to be acceptable by the laboratory's Quality Assurance Unit. The following statistical tests were used: Multiple 't'-test, Mann-Whitney U-test, Chi-squared test and Fisher's Exact Probability test (Armitage modification).

Reference

Source Reference: Lion Corporation, 1979A.

Other References: Tesh, 1968.
Teratology, 1965.

(b)

Test Substance

CAS Number: 1643-20-5

Identity: Amines, C10-16-alkyldimethyl, N-oxides; N,N,-dimethyl-dodecylamine oxide, lauryl dimethylamine oxide; "Surfactant A"

Purity: 30.0%

*Carbon Chain Length
Distribution:* Primarily C12

Remarks: Alkyl chain length distribution: 0.1% C8; 0.1% C10; 96.4% C12; 2.9% C14; 0.1% C16; 0.4% other.

Method

GLP: no

Report/Study Year: 1980

*Report/Study
Number:* LSR 81/LIF051/007

*Method/Guideline
Followed:* other

Species: rabbit

Strain: New Zealand white

Sex: female

*Route of
Administration:* gavage

Exposure Period: Test substance was administered via gavage to groups of female rabbits during days 6 to 18 (inclusive) of gestation.

Frequency of Treatment:	Rabbits (14 females per group) received the test substance via gavage daily during days 6 to 18 (inclusive) of gestation.
Test Duration:	Approximately 5 months
Doses:	Animals (14 per group) received 0, 40, 80 or 160 mg/kg/day of the test substance via gavage.
Control Group:	yes, concurrent vehicle
Remarks:	This study was conducted in accordance with the Japanese Ministry of Health and Welfare Guidelines. The study was conducted from May, 1980 through October, 1980. Animals were artificially inseminated using pooled semen from New Zealand White bucks. Females (14 per group) received 0, 40, 80 or 160 mg/kg/day of the test substance via oral gavage during gestation days 6-18 inclusive. Animals were examined daily throughout the study for any treatment-related adverse signs. Animals were weighed daily and reported on Days 0, 6, 8, 10, 12, 14, 16, 18, 23, and 28 after insemination. Food consumption was measured over five phases during gestation (Days 1-5; 6-11; 12-17; 18-23; and 24-28). On Day 29 after insemination, animals were sacrificed and examined macroscopically for evidence of disease or adverse reaction to treatment. The following was recorded: number of <i>corpora lutea</i> in each ovary, number of implantation sites, number of resorption sites (early or late), number of live and dead fetuses in each uterine horn, including an estimation of time of death of non-viable fetuses, weight and sex of fetuses, individual placental weights, and external abnormalities. Extensive skeletal examinations were also performed on all fetuses from each litter.

Results

NOAEL
Maternal: >160 mg AO/kg bw/day

NOAEL
Teratogenicity: >160 mg AO/kg bw/day

Remarks: It was concluded that oral administration of the test material to pregnant rabbits, from Day 6 to Day 18 of gestation, at dose levels of 40, 80 and 160 mg/kg/day had no adverse effects upon survival and development *in utero*. Maternal condition was generally unaffected by treatment with the test material; however, maternal bodyweight gain was depressed in all treated groups, although at 40 mg/kg/day terminal bodyweights similar to those of controls were achieved. Three females receiving 80 mg/kg/day and three females receiving 160 mg/kg/day died or were killed *in extremis*, but no direct involvement of the test substance was apparent. Food intake, when compared with pre-treatment values, was reduced during the second half of the treatment period in groups receiving 40 and 80 mg/kg/day, and from the commencement of treatment in animals receiving 160 mg/kg/day. Water intake was also decreased in all treated groups. Reductions in body weight gain, food intake and water intake did not exceed 10%. Litter response was unaffected by any treatment with the test material. No adverse effects upon litter responses and development were recorded. No teratogenic responses were observed.

Data Quality

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 1B

Remarks: This study was conducted prior to the adoption of GLP compliance standards. However, it was conducted in accordance with the Japanese Ministry of Health and Welfare Guidelines, and was reviewed and found to be acceptable by the laboratory's Quality Assurance Unit. The following statistical tests were used: Multiple 't'-test, 't'-test, Mann-Whitney U-test, Chi-squared test and Fisher's Exact Probability test (Armitage modification).

Reference

Source Reference: Lion Corporation, 1980.

Other Reference: Tesh, 1968.

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SIDS DOSSIER

CAS NO. 3332-27-2

1-Tetradecanamine, N,N-dimethyl-, N-oxide

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2571-88-2
2530-44-1
2605-79-0
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

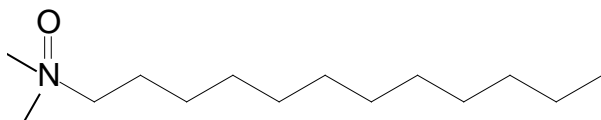
Sponsor Country: United States
Date: July, 2006

1. GENERAL INFORMATION**1.01 SUBSTANCE INFORMATION**

- A. CAS number** 3332-27-2
- B. Name (IUPAC name)**
- C. Name (OECD name)** 1-Tetradecanamine, N,N-dimethyl-, N-oxide
- D. CAS Descriptor**
- E. EINECS-Number** 2220593
- F. Molecular Formula** C₁₆H₃₅NO
- G. Structural Formula**

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

Representative C₁₂ dimethyl amine oxide



- H. Substance Group** Amine Oxides category
- I. Substance Remark** None
- J. Molecular Weight** 258 grams/mole

1.02 OECD INFORMATION

- A. Sponsor Country:** United States
- B. Lead Organization:** Environmental Protection Agency (EPA)

Contact person: Oscar Hernandez
Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460
U.S.A.
Tel: (202) 564-7641

Fax: (202) 564-7450**C. Name of responder**

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the

nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

Myristamine oxide,
Myristyldimethylamine oxide,
N,N-Dimethyl 1-tetradecanamine N-oxide,
N,N-Dimethylmyristylamine oxide,
Tetradecyldimethylamine oxide

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

- (a) United States
26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)
Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.
- (b) Europe
(i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tones (AISE, 2002)
- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in industrial, institutional and commercial applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%

Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA 2002.

1.10 ADDITIONAL REMARKS**A. Options for Disposal**

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

2. PHYSICAL-CHEMICAL DATA

2.0.1 EPISuite™ ESTIMATION OF PHYSICAL/CHEMICAL PROPERTIES

Test Substance

CAS Number: 3332-27-2
Identity: N,N-dimethyltetradecylamine N-oxide
Purity: not relevant
Carbon Chain Length Distribution: C14

Method

Report/Study Number: SDA122
Method/Guideline Followed: EPIWIN
Remarks: All estimates apply to the pure, dry substance and not their solutions in water.

Results

	Estimate
Molecular Weight (grams/mole):	257.46
Water Solubility (mg/l):	0.32
Octanol Water Partition Coefficient (Log Kow):	5.66
Bioconcentration Factor (Log BCF):	2.655
Boiling Point (°C):	449.82
Melting Point (°C):	183.30
Vapor Pressure(Pa):	1.48E-6
Henry's Law Constant (atm/(mole/m ³)):	1.818E-8
Atmospheric Oxidation Half-Life (hours):	4.27
Soil Adsorption Coefficient (Log Koc):	4.803

Remarks: Trends analysis, based on the N,N-Dimethyl Amine Oxides:
For every extension of two –CH₂– units to the alkyl chain

- Water solubility decreases by 1 order of magnitude.
- The Log Kow increases by ~ 1 unit [or the octanol/water partition coefficient increases by 1 order of magnitude].
- The Log BCF increases by ~ 0.25 units [or the BCF nearly doubles; it increases by a factor of 1.8].
- The boiling point increases by ~ 23°C, although these are theoretical values, as most surfactants decompose before they boil.
- The melting point increases by ~ 15°C.
- The Log Koc increases by ~ 0.5 unit [or the soil adsorption coefficient increases by a factor of 3].

Trends are similar for the N,N-Dihydroxyethyl Amine Oxides - The substitution of the nitrogen with two hydroxyethyl groups (vs. the two methyl groups of the N,N-Dimethyl Amine Oxides) increases the hydrophilicity of the hydrophilic head group of the surfactant. This results in a higher water solubility, a lower Log Kow and a lower Koc.

CAS #	Chain Length	MW (g/mole)	Water Sol. (mg/l)	Log Kow	Log BCF	BP (°C)	MP (°C)	VP (Pa)	Log Koc	Atm Oxidation half-life (hours)
N,N-Dimethyl Amine Oxides										
2605-79-0	C10	201.36	30.35	3.69	2.142	403.41	152.60	4.57E-5	3.739	5.26
1643-20-5	C12	229.41	3.13	4.67	⁽¹⁾ 2.392	426.62	167.95	2.09E-5	4.271	4.71
3332-27-2	C14	257.46	0.32	5.66	2.655	449.82	183.30	1.48E-6	4.803	4.27
7128-91-8	C16	285.52	0.032	6.64	2.911	473.03	198.65	2.59E-7	5.334	3.90
N,N-Dihydroxyethyl Amine Oxides										
2530-44-1	C12	289.46	29.89	3.13	1.712	536.73	229.76	3.39E-12	2.360	2.36
14048-77-2	C18	373.63	0.029	6.08	2.481	606.35	262.28	7.45E-15	3.955	2.04
93962-62-0	C18:1	371.61	0.045	5.86	2.815	609.93	263.95	5.43E-15	3.955	2.95

⁽¹⁾The value obtained by KOWWIN is 1.989, which is an outlier. The expected value, based on linear extrapolation between C10, C14 and C16 amine oxide, is 2.392.

Data Quality

Reliability
(Klimisch): 2D

Remarks: Reliable with restrictions. Predictive modeling of the physical/chemical properties of the C10-18 even numbered, single chainlength amine oxides has been carried out using EPIWIN V. 3.0. When compared with measured data obtained for CAS# 70592-80-2, EPIWIN results were found to be of limited accuracy for these endpoints: partition coefficient, BCF and water solubility. This is attributed to the inherent limitations of the algorithms with surface-active materials, which have a tendency to partition to interphases between oils/fats and water and whose phase behavior is a function of temperature and concentration, characterized by a phase diagram. EPIWIN outputs for the melting point, boiling point and vapor pressure can be considered as useful predictors for pure, dry state amine oxides, although it must be remembered that the commercial grade amine oxides are always produced, marketed and used in water solutions of approximately 25-35% active substance.

Reference

Source Reference: EPIWIN, Version 3.0.

2.1 MELTING POINT

Test Substance

CAS Number: 3332-27-2
Identity: C14 amine oxide; tetradecylamine oxide
Carbon Chain Length Distribution: C14

Method

Report/Study Year: 1985
Report/Study Number: SDA628

Results

Value:	Operator	Lower (°C)	Upper (°C)
	=	125	129

Data Quality

Reliability
(Klimisch): 2A

Remarks: Reliable with restrictions. Acceptable, well-documented publication/study report, meets basic scientific principles.

Reference

Source Reference: Devinsky F *et al*, 1985.

2.2 BOILING POINT**Test Substance**

CAS Number: 3332-27-2
Identity: N,N-dimethyltetradecylamine N-oxide
Carbon Chain Length Distribution: C14

Method

GLP: no
Report/Study Year: 2001

Results

Decomposition: yes
Remarks: Amine oxides undergo thermal decomposition between 90 and 200°C.

Data Quality

Reliability (Klimisch): 2D
Remarks: Reliable with restrictions ; Secondary literature source

Reference

Source Reference: Kirk Othmer Encyclopedia of Chemical Technology, 2001

4. ECOTOXICITY

4.1.1 TOXICITY TO FISH (ACUTE)

Test Substance

CAS Number: 3332-27-2
Identity: N,N-dimethyltetradecylamine N-oxide
Purity: 23.7%
Carbon Chain Length Distribution: C14
Remarks: Balance is water

Method

GLP: No
Report/Study Year: 1992
Report/Study Number: CRL F92042
Method/Guideline Followed: Directive 92/69/EEC, C.1; OECD Guideline 203
Test Type: acute, semi-static, renewal at 48 hrs
Analytical Monitoring: No
Species: *Brachydanio rerio*

Value	Unit
96	hour(s)

Remarks: 7 fish per vessel; 1 vessel per conc. Nominal test conc. 0 - 0.47 - 0.95 - 1.9 - 3.79 mg/l (active ingredient). Aerated. Hardness 209 mg/l as CaCO₃. pH 7.4-8.2. O₂ >93% saturation. Temp. 21-22 °C. Statistics by Spearman Karber binomial test method.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
LC50:	c	=	2.4	n/a
LC50	c	=	2.0	2.9

Remarks: No analyses. Test substance is expected to be stable for the duration of this test, however some decrease in test concentration is possible. 96 hour LC50 (calc.) = 2.4 (2.0-2.9)mg/l (active ingredient).

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2B
Remarks: No information about frequency of physical measurements (pH, Oxygen and temperature). No analyses to confirm test concentrations.

Reference

Source Reference: Akzo Nobel, 1992B.

4.2.1 AQUATIC INVERTEBRATES TOXICITY(ACUTE)**Test Substance**

CAS Number: 3332-27-2
 Identity: N,N-dimethyltetradecylamine N-oxide
 Purity: 24%
 Carbon Chain Length: C14
 Distribution:
 Remarks: Balance is water

Method

GLP: no
 Report/Study Year: 1994
 Report/Study Number: CRL F94176
 Method/Guideline Followed: OECD Guideline 202
 Test Type: acute, static
 Analytical Monitoring: no
 Limit Test: no
 Species: *Daphnia magna*

Exposure Period:

Value	Unit
48	hour(s)

Remarks: Nominal test conc. 0.0 - 1.2 - 2.16 - 3.9 - 7.0 - 12.6 mg/l; 20 daphnids per concentration; hardness approx. 12°dH (200 mg/l CaCl₂·2H₂O + 180 mg/l MgSO₄·7H₂O); no vehicle. pH and dissolved oxygen were measured at initiation and at the end of the test.

Results

Unit: mg/l

	Measured/ Computed	Operator	Lower	Upper
EC50:	c	=	2.4	2.9
48h EC50	c	=	2.6	n/a

Remarks: No analyses. Results based on nominal conc. Test conc. may have decreased during test. No information about feeding. The pH ranged from 8.0 to 8.1 and the dissolved oxygen concentrations were in the 8.6 - 9.1 range.

Data Quality

Flags: Critical study for SIDS endpoint
 Reliability (Klimisch): 2B
 Remarks: No analyses.

Reference

Source Reference: Akzo Nobel Chemicals, 1994.

4.3 TOXICITY TO AQUATIC PLANTS e.g. ALGAE

Test Substance

CAS Number: 3332-27-2
Identity: N,N-dimethyltetradecylamine N-oxide
 1-Tetradecanamine, N,N-dimethyl-, N-oxide
Purity: 23.7%
Carbon Chain Length Distribution: C14
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1992
Report/Study Number: CRL F92120
Method/Guideline Followed: OECD Guideline 201
Analytical Monitoring: no
Species: *Selenastrum capricornutum*
Endpoint: other

Exposure Period:

Value	Unit
72	hour(s)

Remarks: 3 reps./conc. and 6 controls. Initial cell density 25000 cells/ml. Standard OECD algal growth medium (OECD Guideline 201); hardness (Ca + Mg) 0.6 mmol/l. Nominal concentrations 0.0 - 0.024 - 0.047 - 0.095 - 0.19 - 0.38 mg/l (active ingredient). Temp. 20-22°C. Continuous illumination. Shaken. Cell densities observed at 0, 24, 48 and 72h (spectrophotometrically).

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC10:	c	=	0.017	n/a
EC50:	c	=	0.082	n/a
EC20	c	=	0.029	n/a

Remarks: Concentrations were probably stable during the test, but some degradation may have occurred. Individual cell counts not reported. Growth in controls not reported. pH not reported.

Results calculated according to Bruce & Versteeg (1992) in mg/l:

EbC10 = 0.017

EbC20 = 0.029

EbC50 = 0.082

ErC10 = 0.032

ErC20 = 0.058

ErC50 = 0.18

Data Quality

<i>Flags:</i>	Critical study for SIDS endpoint
<i>Reliability (Klimisch):</i>	2B
<i>Remarks:</i>	No analyses, some degradation possible. Individual cell counts, growth in controls, pH not reported.

Reference

Source Reference: Akzo Nobel Chemicals, 1992.

5. TOXICITY

5.5 GENETIC TOXICITY *in vitro*

(a)

Test Substance

CAS Number: 3332-27-2
Identity: N,N-dimethyltetradecylamine N-oxide
Purity: 26.7%
Carbon Chain Length Distribution: 2.6% C12, 96.2% C14 and 1.2% C16
Remarks: Balance is water

Method

GLP: no data
Report/Study Year: 1980
Report/Study Number: SDA111
Method/Guideline Followed: other
Test Type: other
System: Syrian golden hamster embryo cells
Test Concentration: 0.1 - 0.5 - 1.0 - 5.0 - and 10 µg/ml
Remarks: Positive control (3-methylcholanthrene).
Pregnant hamsters killed on days 13, 14 of gestation for preparation of target cells and feeder layer cells, respectively.
Transformation assay:
Day 0: feeder layer cells thawed and plated
Day 3: target cells thawed and plated
Day 4: feeder cells irradiated
Day 5: target cells added to irradiated feeder cells
Day 6: test substance added (7-9 dishes per dose)
Day 14: fixation and staining

Results

Result: negative
Cytotoxic Concentration: between 5 and 10 µg/ml

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2A
Remarks: Acceptable, well-documented publication/study report which meets basic scientific principles. Positive control (3-Methylcholanthrene) showed weak response and no clear dose-response relationship.

Reference

Source Reference: Inoue et al, 1989.

(b)

Test Substance

CAS Number: 3332-27-2
Identity: N,N-dimethyltetradecylamine N-oxide
Purity: 26.7%
Carbon Chain Length Distribution: 2.6% C12, 96.2% C14 and 1.2% C16
Remarks: Balance is water

Method

GLP: no data
Report/Study Year: 1980
Report/Study Number: SDA111
Method/Guideline Followed: other
System: *Salmonella typhimurium strains TA98 and TA100*
Test Concentration: 10-200 µg/plate
Metabolic Activation: with and without
Remarks: Bacterial suspension (0.1 ml) added in 0.5 ml sodium phosphate buffer (0.1M, pH 7.4) containing the test substance. Solvent DMSO.
Controls: solvent (DMSO) control, water (negative) control, positive controls (4-nitroquinoline 1-oxide, N-methyl-N'-nitro-N-nitrosoguanidine, 2-acetoaminofluorene, N-nitrosodimethylamine).

Results

Result: negative
Cytotoxic Concentration: cytotoxicity was observed in Ames test at 100-200 µg/plate without metabolic activation
Remarks: Positive controls showed clear mutagenic responses. Water and solvent controls showed no mutagenic responses.

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2A
Remarks: Acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Source Reference: Inoue et al, 1989.

6. REFERENCES

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Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey

SIDS DOSSIER

CAS NO. 70592-80-2

Amines, C10-16-alkyldimethyl, N-oxides

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
3332-27-2
68955-55-5
2605-79-0
7128-91-8
2571-88-2
61788-90-7
85408-48-6
85408-49-7
61791-47-7
2530-44-1
14048-77-2
61791-46-6
93962-62-0

Sponsor Country: United States
Date: January, 2006

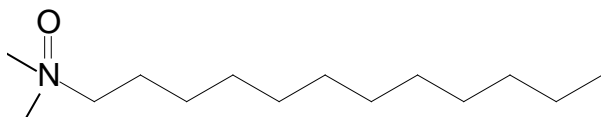
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number** 70592-80-2
- B. Name (IUPAC name)**
- C. Name (OECD name)** Amines, C10-16-alkyldimethyl, N-oxides
- D. CAS Descriptor**
- E. EINECS-Number** 2746872
- F. Molecular Formula** Unspecified
- G. Structural Formula**

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

Representative C₁₂ dimethyl amine oxide



- H. Substance Group** Amine Oxides category
- I. Substance Remark** None
- J. Molecular Weight** Unspecified

1.02 OECD INFORMATION

- A. Sponsor Country:** United States
- B. Lead Organization:** Environmental Protection Agency (EPA)

Contact person: Oscar Hernandez

Address	U.S. Environmental Protection Agency 1200 Pennsylvania Ave. Mail Code 7403M Washington, DC 20460 U.S.A. Tel: (202) 564-7641 Fax: (202) 564-7450
---------	-------------------------------------------------------------------------------------------------------------------------------------------------------------------

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The other eleven amine oxide substances are structural analogues to the four sponsored substances. These compounds provide supporting data and all fifteen substances are included in this category. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound. It should be noted that the nomenclature and CAS identifications for these amine oxides are based on historical and geographical considerations, not on significant differences in the structure and composition of the commercial substances.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyl oxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

Alkyl (C₁₀₋₁₆) dimethyl amine oxide,
N,N-dimethyl alkyl amine oxide (C₁₀₋₁₆)

1.3 IMPURITIES

Remarks: Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

Value: None
Remarks: No additives

1.5 QUANTITY

(a)
Value: 26,000 metric tonnes in the U.S. This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.
Source: Soap and Detergent Association, 2002A. Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.

(b)
Value: (i) Annual production in Europe is approximately 16,000 (2000 data).
(ii) A figure of 21,570 metric tonnes has been surveyed for all amine oxides formulated in laundry & cleaning products in the EU during 2002.
Values for individual CAS numbers and substances are not available.
Source: (i) Modler and Inoguchi, 2004
(ii) AISE/HERA, 2002

(c)
Value: 6,800 metric tonnes/year in Japan. This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.
Source: Japanese Soap and Detergent Association, 2002

1.6 LABELLING AND CLASSIFICATION

Labelling
Remarks: dangerous for the environment ; irritating
following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification
Remarks: Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN**7.2.1 A.General****Type of Use:**main
industrial
use**Category:**Wide dispersive use
Personal and domestic use
Cleaning/Washing agent**Remarks:**

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in industrial, institutional and commercial applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources:

Soap and Detergent Association, 2002B; CTFA, 2003; AISE, 2002; Human & Environmental Risk Assessment on ingredients of European household cleaning products (HERA): Amine Oxides, 2005; and Japanese Soap and Detergent Association, 2002.

See also "Use and Exposure Information on Amine oxides", available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

Remarks:

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources:

Soap and Detergent Association, 2002A and 2002B; AISE/HERA 2002.

1.10 ADDITIONAL REMARKS**A. Options for Disposal**

Remarks: Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

Reference:

B. Last Literature Search

Remarks: 2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

2. PHYSICAL CHEMICAL PROPERTIES

2.0.1 EPISuite™ ESTIMATION OF PHYSICAL/CHEMICAL PROPERTIES

Test**Substance***CAS Number:* 70592-80-2*Identity:* Amines, C10-16-alkyldimethyl, N-oxides*Remarks:* SMILES : CCCCCCCCCCN(=O)(C)C
MOL FOR: C12 H27 N1 O1**Method***Report/Study Number:* SDA122**Results**

	Estimate	Exp. Database Match
Molecular Weight (grams/mole):	201.36	
Water Solubility (mg/l):	30.35	n/a
Octanol Water Partition Coefficient (Log Kow):	3.69	n/a
Bioconcentration Factor (Log BCF):	2.142	
Boiling Point (°C):	403.41	n/a
Melting Point (°C):	152.60	n/a
Vapor Pressure(mmHg):	3.43E-007	n/a
Henry's Law Constant (atm/(mole/m ³)):	2.994E-009	n/a
Atmospheric Oxidation Half-Life (hours):	5.5	n/a
Soil Adsorption Coefficient (Log Koc):	3.739	

Data Quality*Reliability
(Klimisch):* 2D

Remarks: Reliable with restrictions. Predictive modeling of the physical/chemical properties of the C10-18 even numbered, single chainlength amine oxides has been carried out using EPIWIN V. 3.0. When compared with measured data obtained for CAS# 70592-80-2, EPIWIN results were found to be of limited accuracy for these endpoints: partition coefficient, BCF and water solubility. This is attributed to the inherent limitations of the algorithms with surface-active materials, which have a tendency to partition to interphases between oils/fats and water and whose phase behavior is a function of temperature and concentration, characterized by a phase diagram. EPIWIN outputs for the melting point, boiling point and vapor pressure can be considered as useful predictors for pure, dry state amine oxides, although it must be remembered that the commercial grade amine oxides are always produced, marketed and used in water solutions of approximately 25-35% active substance.

Reference

Source Reference: EPIWIN, Version 3.0.

2.12 DISSOCIATION CONSTANT

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: 32%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

Report/Study Year: 2002
Report/Study Number: 4033020301
Method/Guideline Followed: OECD Guideline 112

Results

Acid Based Constant: 4.1 ± 0.1 (n=3)
Remarks: Temp. was 25-26.9°C.
Triplicates.
Positive control imidazole, result OK.

Data Quality

Reliability (Klimisch): 1A

Reference

Source Reference: The Procter & Gamble Company, 2002B.

2.2 BOILING POINT

(a)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: unknown
Carbon Chain Length Distribution: C10-16

Method

GLP: no
Report/Study Year: 2001
Method/Guideline Followed: other

Results

Decomposition: yes

Remarks: Amine oxides undergo thermal decomposition between 90 and 200°C.

Data Quality

Reliability (Klimisch): 2D

Remarks: Reliable with restrictions ; Secondary literature source

Reference

Source Reference: Kirk Othmer Encyclopedia of Chemical Technology, 2001

(b)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: 32%

Carbon Chain Length Distribution: C10-16

Remarks: Balance is water

Method

GLP: no

Report/Study Year: 1983

Report/Study Number: SDA101

Method/Guideline Followed: other

Remarks: Guideline not stated; pressure = atmospheric.

Results

Decomposition: yes

Remarks: Test substance decomposes before reaching boiling point.

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature source

Reference

Source Reference: TSCA ITC, 1983.

2.4 VAPOUR PRESSURE**Test Substance**

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: 32%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1983
Report/Study Number: SDA101
Temperature (°C): 20

Results

Value:	Operator	Lower	Upper	Unit
	=	12	23	hPa

Remarks: 12-23 hPa is equivalent to 9-17mmHg. The material in this study was tested "as is", i.e. as a 32% aqueous solution. Thus, the measured value is most likely related to the vapour pressure of the water and not the amine oxide.

Data Quality

Reliability (Klimisch): 4B
Remarks: Documentation is limited, and the vapour pressure that was reported is likely that of the water and not the amine oxide.

Reference

Source Reference: TSCA ITC, 1983. Interagency Testing Committee.
Other References: The Procter & Gamble Company, Physical chemical studies available within Procter & Gamble files for Alkyl (C10-16) Dimethyl Amine Oxide.

2.5 PARTITION COEFFICIENT**Test Substance**

CAS Number: 70592-80-2
Identity: Amines, C10-16 alkyldimethyl, N-oxides; C12/14 alkyl dimethyl amine oxide; TSIN GTS02902
Purity: 32%
Carbon Chain Length Distribution: C10-16 (average 12.7)
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 2002
Report/Study Number: 4033020302
Method/Guideline Followed: other (calculated)
Partition Coefficient: octanol-water
Temperature °C: room temp.
Remarks: An attempt was first made to measure the log Kow using the HPLC method as in OECD Guideline 117. However, no peaks were detected that could be attributed unequivocally to the test substance, even though the reference substance peaks indicated that the procedure was working well. The Log Pow was then estimated as the quotient of the measured solubilities of the test substance in n-octanol and in water. Water solubility determined as follows: 10 g test substance/15 ml deionized water, stirred 24 h at room temp., centrifuged at 2,500 rpm to separate undissolved material from the solution. Analyze solution by Disulfine Blue Active Substances method (ref.). Two replicates (n=2). Solubility in n-Octanol determined as follows: 1 g test substance/20 ml n-octanol, stirred 24 h at room temp., centrifuged at 2,500 rpm, evaporated octanol, redissolved residue in deionized water. Analyze solution by DBAS and by N determination (ref.). No replicates (n=1). Log Pow was estimated as the quotient of the solubilities of the test substance in n-octanol (33.9 g/l) and in water (409.5 g/l). No pH adjustments were made.

Results

Log P _{ow} :	Operator	Lower	Upper
	=	-1.08	n/a

Remarks: This Kow is of limited use from a risk assessment perspective. Whereas the Kow provides reasonably good predictions of fish bioconcentration factors for hydrophobic, nonionic substances that undergo minimal metabolism or biotransformation, for other categories of substances such as surfactants, these Kow-based QSARs are not appropriate (Cowan *et al.*, 1995).

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2A
Remarks: Acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Source Reference: The Procter & Gamble Company, 2002C.

Other References: Osburn Q. W. (1982).

Penz O, Schaab A, Brunn K (2002).

Cowan, C.E., D.J. Versteeg, R.J. Larson and P.J. Kloepper-Sams (1995).

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

(a)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: 32%
Carbon Chain Length Distribution: C10-16 (average 12.7)
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 2002
Report/Study Number: 4033020302
Method/Guideline Followed: other
Solubility Media: Water
Remarks: Water solubility determined as follows: 10 g test substance/15 ml deionized water, stirred 24 h at room temp., centrifuged at 2,500 rpm to separate undissolved material from the solution. Analyze solution by Disulfine Blue Active Substances method (Osburn, 1982). Two replicates (n=2). No pH adjustments were made.

Results

Value:	Operator	Lower	Upper	Unit	Temp. (°C)
=		409.5	n/a	g/l	n/a

Examine Different Polarities: No data

pKa (at 25 °C): Not applicable

Stable: yes

Data Quality

Reliability (Klimisch): 2A

Remarks: Reliable with restrictions. Acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Source Reference: The Procter & Gamble Company, 2002C.

Other References: Osburn Q. W. (1982). Penz O, Schaab A, Brunn K (2002).

(b)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: 32%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1999
Report/Study Number: SDA101
Method/Guideline Followed: other
Solubility Media: Water

pH:

Operator	Lower	Upper
=	7.2	n/a

Remarks: Guideline not stated.

Results

Temperature Effects: Stable up to 38 °C.
Examine Different Polarities: No data
pKa (at 25 °C): No data
Description: very soluble ($> 10^4$ mg/L)
Stable: yes
Remarks: Other than excessive heat, which can lead to discoloration, no physical factors are known to affect its stability.

Data Quality

Reliability (Klimisch): 4B
Remarks: Secondary literature sources.

Reference

Source Reference: TSCA ITC, 1983.

3. ENVIRONMENTAL FATE AND PATHWAYS

3.0.1 EQC MODEL

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: not relevant
Carbon Chain Length Distribution: C10-16

Method

Report/Study Year: 2003

Report/Study Number: EQC-001

Method/Guideline Followed: EQC model Level III version 2.8

Remarks: EQC Model, Level III, Version 2.7 (2002). Input parameters generated with EPISuite™ unless otherwise indicated:
MW = 237.83
Temp. = 22°C
Solubility in water = 409500 g/m³.
Vapor Pressure = 3.43E-007 mmHg
Log Kow = 2.69. Basis: Water solubility data in this dataset.
Melting Point = 132°C
Half-life in water = 96 hours. Basis: River-water die-away study with effluent from CAS study with amine oxide. Vandepitte V. and De Baere G. (1997). Biodegradation (aerobic/anaerobic) of Dimethyl Dodecyl Amine Oxide (DDAO), presented at annual meeting of the Society for Environmental Toxicology and Chemistry, San Francisco.
Half-life in soil = 720 hours. Basis: Surfactants that biodegrade rapidly in screening tests (OECD 301A through F), generally biodegrade quickly in soils. A structurally analogous category to amine oxides, for which soil biodegradation data are available, are the QAC surfactants (quaternary ammonium compounds). The half-lives for C₁₈-TMAC (C₁₈ trimethyl ammonium chloride) ranged from 3.2 to 8.7 days in various soils. The half-life for C₁₂-TMAC in sludge-amended soil was 1 month; the latter half-life was used as a conservative estimate for the half-life of amine oxides in soils. From: Boethling R. S. and Lynch D. G. (1992) "Quaternary Ammonium Surfactants" In: The Handbook of Environmental Chemistry. Volume 3 Part F, Anthropogenic Compounds. O. Hutzinger (chief ed.); N. T. de Oude (vol. ed.). Springer-Verlag Publishers, New York.
Half-life in sediment = 720 hours. Basis: Measured rates in sediment are not available for amine oxides; soil biodegradation rate was used as a surrogate.
Half-life in suspended particles = 720 hours. Basis: Assumed same rate as for soil and sediment.
Half-lives in air, fish, aerosol assumed negligible.
EQC standard environment.

Influx via water compartment only; absolute amount of influx is irrelevant since we are estimating the relative distribution.

Results

Fugacity Model Level III v2.7

Air (%)	Water (%)	Soil (%)	Sediment (%)
0.00	99.5	0.00	0.5

Data Quality

Reliability (*Klimisch*): 2D

Remarks: Reliable with restrictions. Model output, not measured data.

Reference

Source: Trent University Canadian Environmental Modeling Centre at
Reference: www.trentu.ca/cemc/welcome.html. Fugacity model level III, Version 2.8.
Other: Mackay D., A. DiGuardo, S. Paterson and C. Cowan, 1996.
References: Mukerjee P & Mysels KJ, 1971.

3.1.2 STABILITY IN WATER

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: 32%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

Report/Study Year: 2002
Report/Study Number: 4033020303
Method/Guideline Followed: Directive 92/69/EEC, C.7
Test Type: abiotic
Remarks: OECD Guideline for the Testing of Chemicals 111. Experiment conducted at 50 °C. Solutions were extracted with chloroform/methanol/formic acid (80:20:1) and analyzed by Flow Injection/Mass Spectrometry FI/MS) using a mobile phase of chloroform/acetonitrile (1:1) with 1 mmol ammonium acetate.

Results

Degradation Products: no

Remarks: Results are only reported for the C12 homologue, because the analytical method did not produce consistent results for the C14 homologue. There was no significant

decrease in concentration of the C12 homologue after 45 days at 50 °C, at any of the pH levels tested. Both the C12 and C14 homologues were tested for hydrolytic stability at pH 4, 7 and 9. The test substance is hydrolytically stable.

Data Quality

Reliability (Klimisch): 1A

Reference

Source Reference: The Procter & Gamble Company, 2002D.

3.2.1 MONITORING DATA (ENVIRONMENT)

(a)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: not applicable
Carbon Chain Length Distribution: C10-16
Remarks: "Sample purity" is not relevant for field monitoring; background concentrations are measured in the environment.

Method

GLP: no data
Report/Study Year: 2002
Report/Study Number: SDA999
Method/Guideline Followed: see below
Type of Measurement: amine oxide concentrations
Media: river water
Remarks: Grab river water samples (200 ml) were collected at 7 locations in 4 urban rivers that receive sewage treatment effluent and untreated household wastewater (Tamagawa, Edogawa, Arakaw, Yodogawa). Three of the sites are near drinking water intake sites; two are just below municipal wastewater effluent discharge points.
Sampling was done 4 times during the year at 3-month intervals at each location (June 2002, October 2002, December 2003 and March 2003). Water samples were characterized by BOD, TOC, suspended solids, pH, Cl, NH₄, Methylene Blue Active Substance.
Samples were preserved with sodium azide.
River water was extracted by solid phase extraction column.
Analyses of C₁₀, C₁₂, C₁₄ and C₁₆ amine oxide by Liquid Chromatography-Electron Spray Ionization -Mass Spectrometry (detection limit 0.01 µg/l).

General analytical items:	methods used
pH (Hydrogen ion):	JIS K 0102 12.1
BOD (Biochemical Oxygen Demand), (mg/L):	JIS K 0102 21 and 32.1
SS (Suspended Solids), (mg/L):	Japanese EA Method No.59 App.6, 1971
Cl ⁻ (Chloride ion), (mg/L):	Tio-cyanide mercury (II) absorptiometry
NH ₄ -N (Ammonium ion nitrogen), (mg/L):	JIS K 0102 42.1 and 42.5
TOC (Total Organic Carbon), (mg/L):	JIS K 0102 22.1
MBAS (Methylene Blue Activated Substance), (mg/L):	JIS K 0102 30.1.1

Results

Concentration:	Operator	Lower	Upper	Unit
	=	<0.01	0.34	µg/l

Remarks: Recoveries of samples spiked with 0.2 µg/l AO ranged from 81.1 - 105%. Concentrations in all locations ranged from < 0.01 µg/l to 0.34 µg/l. Median concentration = 0.04 µg/l. 95th percentile high concentration = 0.25 µg/l (95% of samples are at or below the 95th percentile high value). Mostly, C₁₂ amine oxide was detected, and some low levels of C₁₀ amine oxide. AO concentrations in nearly half of the samples taken (13/28) were below detection limit (< 0.01µg/L). The maximum concentration of AO detected was 0.34µg/L in Hirakata-oohashi of Yodogawa in March. In the Tamagawa River, total AO concentrations ranged from < 0.01 to 0.10 µg/L. - at Hamura-zeki, AO concentrations were below detection limit (< 0.01µg/L). - at Tamagawara-bashi, AO concentrations ranged from 0.02 to 0.10 µg/L. - at Den-en-chofu-zeki-ue AO concentrations ranged from 0.04 to 0.09µg/L. In the Arakawa River, total AO concentrations ranged from < 0.01 to 0.26 µg/L. - at Chisui-bashi, AO concentrations were between < 0.01µg/L and 0.16µg/L. - at Sasame-bashi, AO concentrations were between < 0.01µg/L and 0.26µg/L. In the Edogawa River at Kanamachi-josuijo-shusuiko, AO concentrations were between < 0.01µg/L and 0.17µg/L. In the Yodogawa River at Hirakata-oohashi, AO concentrations were between < 0.01µg/L and 0.34µg/L.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2A

Remarks: Reliable with restrictions. Acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Source: The Japanese Soap and Detergent Association, Human Safety and Environment
Reference: Task Force. 2003.
Other
References: Nishiyama A., Yamamoto A. and Takei T. (2003).

(b)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: not relevant for field monitoring
Carbon Chain Length: C10-16
Distribution:

Method

Report/Study Year: 1996
Report/Study Number: SDA121
Type of Measurement: background concentration
Media: surface water
Remarks: Twenty-four hour flow-proportional samples of raw and treated sewage collected on 3 consecutive days at 6 sewage treatment plants [May - July 1996]. Samples for analysis of surfactant were preserved with 1% formaldehyde, frozen and lyophilized. Analyses for: COD, BOD, pH, N, P and amine oxide. Quality control samples of raw and treated sewage were spiked with 5 and 250 ppb amine oxide. Lyophilized samples were extracted with solvent (chloroform/methanol/formic acid/water in 80:20:1:3 ratio). Duplicate analyses by Flame Ionization/tandem Mass Spectrometry (FI/MS/MS). Raw sewage concentrations of amine oxide were corrected, using the recovery of field spikes ($39.5 \pm 73\%$ on average) for each particular plant. Treated sewage concentrations were not corrected (below detection limit of 0.3 ppb).

Results

Remarks: Influent conc. varied from 9 - 130 $\mu\text{g/l}$.
Effluent conc. varied from
Average removal of amine oxide varied from $> 94.9 - > 99.5\%$.
Removal of amine oxide was consistent between plants and similar to BOD removal.

Average removals by treatment plant:

De Meern: $>96.9 \pm 0.2\%$
Kralingseveer: $96.4 \pm 3.6\%$
Horstermeer: $96.8 \pm 1.7\%$
Eindhoven: $>98.3 \pm 0.3\%$
Steenwijk: $96.3 \pm 4.0\%$
Bennekom: $> 96.9 \pm 1.8\%$

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2A

Remarks: Acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Source Reference: The Procter & Gamble Company, 1996A.

(c)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: not relevant

Carbon Chain Length Distribution: all chainlengths

Method

GLP: no

Report/Study Year: 2003

Report/Study Number: SDA121bis

Type of Measurement: calculation

Media: sewers

Remarks: This is an estimation of the % loss of amine oxide in the sewers, en route to the sewage treatment plants, based on actual, measured influent concentrations and calculated, predicted influent concentrations in the Netherlands.

Treatment plant locations and types:

De Meern: carrousel

Kralingseveer: carrousel

Horstermeer: aeration tank

Eindhoven: aeration tank

Steenwijk: aeration tank

Bennekom: carrousel

Results

Concentration:	Operator	Lower	Upper	Unit
=		78	98.5	%

Remarks: Theoretical losses of amine oxide (AO) in sewers (also "pipe loss") were calculated, as follows:

Assumptions:

100% of AO used is disposed of down-the-drain after use, and its consumption is distributed uniformly across The Netherlands.

AO consumption data from the year 2000 are representative for the consumption at the time of the monitoring study (Summer of 1996).

The influent concentrations at the six locations that were monitored are representative for the country.

Input values:

Population of The Netherlands: 16105000 (from: www.lonelyplanet.com - 2003).

Annual consumption of AO in The Netherlands: 688000 kg (Chemical Economics Handbook, 2000 Edition; AO consumption data pro-rated based on population; EU consumption is 16×10^6 kg and the population of The Netherlands is 4.3% of the EU population.

Average daily water consumption = 200 liters/person.day

Formulas:

Predicted influent conc. = {av. AO usage/av. water usage}/person.day = 589 ppb

Predicted pipe loss (%) = $100 - [(C_i/C_u) \times 100]$ where C_i = measured influent conc. and C_u = predicted influent conc. (589 ppb)

Influent concentrations by treatment plant, and average (ppb):

De Meern: 9

Kralingseveer: 130

Horstermeer: 14

Eindhoven: 22

Steenwijk: 68

Bennekom: 44

Average influent concentration = 32 ppb (S.D. 32.8 ppb)

Predicted pipe loss by treatment plant, and average (%)

De Meern: 98.5

Kralingseveer: 78

Horstermeer: 97.5

Eindhoven: 96

Steenwijk: 88.5

Bennekom: 92.5

Average, predicted pipe loss = 92% (S.D. 11.4%)

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2A

Remarks: These calculations were given the same Klimisch score as the field monitoring study upon which they were based (report # SDA 121).

Reference

Source Reference: Soap and Detergent Association Report, 2005.

Other References: The Procter & Gamble Company (1996A).
Matthijs *et al.* 1995.

(d)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: not relevant for monitoring study
Carbon Chain Length Distribution: C10-16

Method

GLP: no
Report/Study Year: 2004
Report/Study Number: MVL368
Method/Guideline Followed: no guidelines available for monitoring studies
Type of Measurement: analysis of concentrations in aqueous samples by HPLC-MS
Media: municipal wastewater and final effluent
Remarks: P&G's Kansas City manufacturing site is a major producer of C10-16 dimethylamine oxide. The wastewater from the plant is directed to the Kaw Point municipal wastewater treatment plant (NPDES permit KS-0038563), which treats wastewater by grit removal, primary clarification, activated sludge treatment and final clarification. Sampling was done in March of 2004 to determine the concentrations of the predominantly C12/14 dodecylamine oxide in raw wastewater and final effluent. Daily flow-based composite concentrations from 3 consecutive days are reported. Analytical: solid phase extraction followed by detection by LC-MS; quantitation calibrated with single point addition addition of deuterated dodecylamine oxide as internal standard; detection limit for each homolog = 0.5 µg/l in raw wastewater and 0.015 µg/l in final effluent. Samples preserved with 8% formalin. Spike recoveries for the C10, C12, C14, and C16 dimethyl amine oxides (triplicate samples) were 91%, 110%, 129% and 60% respectively indicating acceptable recoveries for the dominant alkyl chainlength materials. LAS was measured as a reference compound. The total concentration of LAS (C10, C11, C12, C13 and C14 homologs combined) in final effluent ranged from 80 to 144 µg/l. This is within the range reported in the literature for LAS.

Results

Concentration:	Operator	Lower	Upper	Unit
	=	0.02	0.11	µg/l

Remarks: The reported concentrations bracket the range of C12 dimethylamine oxide concentrations found in final effluent. C12 dimethylamine oxide was found to be the dominant alkyl dimethyl amine oxide in both raw wastewater and final effluent, representing >80% of all amine oxide species present. The corresponding concentrations of C12 dimethyl amine oxide in raw wastewater were 24-51 µg/l and the corresponding removal is >99.5%. Lower levels of C10, C14 and C16 analogs were found in raw wastewater (< 5 µg/l) and the corresponding effluent

samples contained no detectable quantities (< 0.05 µg/l).

Data Quality

Flags: confidential

*Reliability
(Klimisch):* 2A

Remarks: Reliable with restrictions. Acceptable, well-documented publication/study report, meets basic scientific principles.

Reference

Source Reference: The Procter & Gamble Company, 2005.

(e)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: not relevant for field monitoring study

Carbon Chain Length Distribution: C10-16

Method

GLP: No

Report/Study Year: 1999

*Report/Study
Number:* E98-053

*Type of
Measurement:* background concentrations

Media: other

Remarks: Sewage treatment plants of these types: oxidation ditch (OD); activated sludge (AS); trickling filter (TF); lagoon (L); rotating biological contactor (RBC). Twenty-four hour composite samples of influent and effluent collected during each of 3 days. Daily samples composited based on treatment plant flow to form 3-day, flow-based composite of each sample type. Influent, primary and final effluent analyzed by flow injection/mass spectrometry. Raw sewage samples were corrected for average recovery obtained with quality control samples; effluent samples were not corrected (concentrations in effluent were usually below analytical detection limit).

Results

Remarks: Influent concentrations (avg. of C12 and C14); amine oxide removals and BOD removals for each treatment plant(type):

Carmel, IN (AS): 12.5 µg/l; 96.8% (AO) and 98.1% (BOD)

Durham, OR (AS): 11.9 µg/l; 96.0% (AO) and 98.5% (BOD)

Lodi, CA (AS): 2.9 µg/l; 74.6% (AO) and 98.8% (BOD)

Opelika, AL (OD): 2.31 µg/l; 63.0% (AO) and 99.0% (BOD)

Rockaway Val., NJ (OD): 7.97 µg/l; 63.5% (AO) and 96.6% (BOD)
San Benito, TX (L): 6.28 µg/l; 94.9% (AO) and 87.5% (BOD)
Rose Hill, KS (L): 10.5 µg/l; 94.9% (AO) and 90.0% (BOD)
St Clairsville, OH (RBC): 27.8 µg/l; 93.8% (AO) and 93.8% (BOD)
Oskaloosa, IA (TF): 18.5 µg/l; 90.6% (AO) and 93.8% (BOD)
Sedalia, MO (TF): 12.2 µg/l; 82.3% (AO) and 88.7% (BOD)
Effluent concentrations of amine oxide (avg. of C12 and C14);
AS type plants: 0.40 - 0.74 µg/l
Trickling Filters: 1.75 - 2.16 µg/l
Oxidation Ditches: 0.86 - 2.91 µg/l
Lagoons: 0.54 - 0.85 µg/l
RBC: 1.73 µg/l
The unexpectedly low removals (

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2B

Remarks: Summary report. Raw data and analyses not available.

Reference

Source Reference: The Procter & Gamble Company, 2001.

Other References: The Procter & Gamble Company, 2000.

(f)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: not relevant

Carbon Chain Length Distribution: all

Method

GLP: no

Report/Study Year: 2003

*Report/Study
Number:* E98-053bis

*Type of
Measurement:* calculation

Media: sewers

Remarks: This is an estimation of the % loss of amine oxide in the sewers, en route to the sewage treatment plants, based on actual, measured influent concentrations and calculated, predicted influent concentrations in the United States.
Treatment plant locations and types:
Carmel, Indiana: activated sludge
Durham, Oregon: activated sludge

Lodi, California: activated sludge
 Rockaway Valley, New Jersey: oxidation ditch
 Opelika, Alabama: oxidation ditch
 San Benito, Texas: lagoon
 Rose Hill, Kansas: lagoon
 St. Clairsville, Ohio: rotating biological contactor
 Oskaloosa, Iowa: trickling filter
 Sedalia, Missouri: trickling filter

Results

Concentration:	Operator	Lower	Upper	Unit
	=	96.3	98.5	%

Remarks: Theoretical losses of amine oxide (AO) in sewers (also "pipe loss") were calculated, as follows:

Assumptions:
 100% of AO used is disposed of down-the-drain after use.
 Consumption of AO is uniformly distributed across the U.S.
 AO consumption data from the year 2000 are representative for the consumption at the time of the monitoring study (done in 1998-99).
 The sub-set of ten locations that were monitored is representative for the situation across the country.

Input values:
 (1) Annual consumption of AO in the U.S.: 20411 Tons (Chemical Economics Handbook, 2000 Edition). Note: 1 Ton = 2000 lbs = 909.09 kg.
 (2) Population of the U.S.: 240 million
 Divide (1) by (2) to obtain the average per-person AO usage in the U.S. = 212.0 mg/person.day

Formulas:
 Predicted influent conc. = {av. AO usage/av. local water usage}/person.day
 Predicted pipe loss (%) = $100 - [(C_i/C_u) \times 100]$ where C_i = measured influent conc. and C_u = predicted influent conc. based on local population and water usage.
 Treatment plant; measured influent conc. and local water consumption

City: $\mu\text{g/L} - (\text{L/person.day})$
 Carmel: 12.5 - (318.5)
 Durham: 11.9 - (455.0)
 Lodi: 2.9 - (518.9)
 Rockaway Valley: 8.0 - (645.6)
 Opelika: 2.3 - (471.9)
 San Benito: 6.3 - (227.5)
 Rose Hill: 10.5 - (481.8)
 St. Clairsville: 27.8 - (500.5)
 Oskaloosa: 18.5 - (682.5)
 Sedalia: 12.2 - (413.6)

Average calculated pipe losses, by treatment plant(%)
 Carmel: 98.12
 Durham: 97.45
 Lodi: 99.29
 Rockaway Valley: 97.57
 Opelika: 99.49

San Benito: 99.33
Rose Hill: 97.61
St. Clairsville: 93.44
Oskaloosa: 94.04
Sedalia: 97.62
Average, predicted pipe loss = 97.4% (SD 1.1%)

Data Quality

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 2B

Remarks: Reliable with restrictions. These calculations were given the same Klimisch score as the field monitoring study upon which they were based (study # E98-053).

Reference

Source Reference: The Procter & Gamble Company, 2003B.

Other References: The Procter & Gamble Company, 2001.
Matthijs *et al.* (1995).

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS**Test Substance**

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides C12/14 alkyl dimethyl amine oxide

Purity: 32%

*Carbon Chain Length
Distribution:* C12-14 (av. C12.7)

Remarks: Balance is water

Method

Report/Study Year: 2002

Report/Study Number: 4033020304

*Method/Guideline
Followed:* OECD Guideline 106

Test Type: adsorption

Media: water - soil

Remarks: Test temp. 24 °C. Test substance measured by Flow Injection/Mass Spectrometry.
Three soil types were tested:
Soil type 1: pH 6.1; 2.7% organic matter; 3.2% clay
Soil type 2: pH 4.6; 0.8% organic matter; 11% clay
Soil type 3: pH 7.9; 2.6% organic matter; 24% clay

Results

Remarks: Kd = 8, 56 and 18 l/kg for C12 homologue in 3 soil types.
Kd = 24, 17 and 33 l/kg for C14 homologue in 3 soil types.

Data Quality

Reliability (Klimisch): 1A

Reference

Source Reference: The Procter & Gamble Company, 2002A.

3.5 BIODEGRADATION

(a)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides C12/14 amine oxide C12/14 [N-methyl ¹⁴C-labeled] amine oxide C12/14 [alpha-carbon ¹⁴C-labeled] amine oxide

Purity: 30.61% (unlabeled material, in water) 100% radio-pure (¹⁴C-labeled materials, in 90:10 EtOH)

Carbon Chain Length Distribution: C10-16

Remarks: Specific activities of radiochemicals: 8.7 µCi/mg [N-methyl ¹⁴C-labeled] 6.8 µCi/mg [alpha-carbon ¹⁴C-labeled].

Method

GLP: yes

Report/Study Year: 1996

Report/Study Number: WESTON 96-003

Test Type: anaerobic

Method/Guideline Followed: other

Inoculum: anaerobic sludge

Inoculum Acclimated: yes

Acclimated to what Concentration: 1-5 mg/l

Acclimated for what Duration: 15 weeks

Control Substance: other

Test Substance Initial Concentration:	Value	Unit	Expressed as
	1	mg/l	Test substance

n/a	n/a	n/a
-----	-----	-----

Remarks: WESTON's standard protocol, "Die-away of Radiolabeled Substrates in Anaerobic Sludge", designed to meet US EPA regulation 40 CFR Part 792. Acclimation in anaerobic reactor to gradually increasing conc. from 1 mg/l to 5 mg/l in weekly increments of 1 mg/l for first five weeks, then constant at 5 mg/l. Total solids level in biodegradation test = 20.730 mg/l. Radiochemical conc. ~ 10 µCi/l. Duplicate treatments. Abiotic control. Analysis for metabolites by RAD-TLC.

Results

Kinetics
Measured as: other

Half Life: *Mineralization:* 43 hrs.
Primary Biodegradation: n/a

Result: inherently biodegradable

Degradation Products: no

Remarks: Kinetics measured as ^{14}C -gases $\{^{14}\text{CO}_2 + ^{14}\text{CH}_4\}$.
Biotic treatments: Mineralization and primary biodegradation most closely described by 3/2 order functions without growth, as follows:
 $Y = [a(1 - \exp^{-bX})] + cX$
a = deflection point at which rate changes from 1st to zero order(%)
b = first order rate constant(h^{-1})
c = zero order rate constant ($\% \cdot \text{h}^{-1}$)
Abiotic control for N-methyl ^{14}C -labeled test subst.: 68.7% of radioactivity was extractable (parent compound); 23.3% was non-extractable and associated with solids.
Abiotic control for alpha-carbon ^{14}C -labeled test subst.: 97.9% of radioactivity was extractable (parent compound); 2.2% was non-extractable and remained with solids.

Test substance I: N-methyl ^{14}C -labeled amine oxide

Test substance II: alpha-carbon ^{14}C -labeled amine oxide

Mineralization and primary biodegradation of I.				
	$R^2(\%)$	a(%)	b(h^{-1})	c(% per day)
Mineralization	0.95	35.4 +/- 2.82	3.84 +/- 1.65	0.386 +/- 0.034
Primary biodegradation	0.96	19.9 +/- 2.27	20.7 +/- 18.0	0.636 +/- 0.046
Mineralization and primary biodegradation of II.				
Mineralization	0.99	18.9 +/- 0.9	79.5 +/- 152	0.428 +/- 0.012
Primary biodegradation	0.98	10.0 +/- 1.8	22.1 +/- 32.2	0.542 +/- 0.024

Loss of parent (%)	Time (hrs)	Mineralization (%)	Time (hrs)
I.			
II.		I.	II.

50	47.4	73.8	50	37.8	72.7
75	86.7	120.0	75	103.0	131.0
90	110.0	148.0	90	142.0	166.0
95	118.0	157.0	95	154.0	178.0
99	124.0	164.0	99	165.0	187.0

The ^{14}C mass balances { % evolved as ^{14}C -gases + % recovered as parent substance + % non-extractable ranged from 110% to 125.6% for both test substances (I and II) and at various time intervals throughout the experiment. This indicates that the relatively small fraction of radioactivity that was not associated with ^{14}C gases or with amine oxide parent substance, was associated with the solids (incorporated in microbial biomass).

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Reference

Source Reference: The Procter & Gamble Company, 1996B.

(b)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides C12/14 amine oxide C12/14 [N-methyl ^{14}C -labeled] amine oxide C12/14 [alpha-carbon ^{14}C -labeled] amine oxide

Purity: 30.61% (unlabeled material, in water) 100% radio-pure (^{14}C -labeled materials, in 90:10 EtOH)

Carbon Chain Length Distribution: C10-16

Remarks: Specific activities of radiochemicals: 8.7 $\mu\text{Ci}/\text{mg}$ [N-methyl ^{14}C -labeled] 6.8 $\mu\text{Ci}/\text{mg}$ [alpha-carbon ^{14}C -labeled].

Method

GLP: yes

Report/Study Year: 1996

Report/Study Number: WESTON 95-090

Test Type: anaerobic

Method/Guideline Followed: other

Inoculum: Mixture of anaerobic sludge from bench-scale anaerobic acclimation reactor from Weston study 95-070 + unacclimated anaerobic feed sludge

Inoculum
Acclimated: yes
Acclimated to what
Concentration: 1-5 mg/l
Acclimated for what
Duration: 15 weeks
Control Substance: other

Value	Unit	Expressed as
1	mg/l	Test substance

Remarks: WESTON's standard protocol, "Mineralization of Radiolabeled Test Substance in Anaerobic Sludge", designed to meet US EPA regulation 40 CFR Part 792. Acclimation in anaerobic reactor to gradually increasing conc. from 1 mg/l to 5 mg/l in weekly increments of 1 mg/l for first five weeks, then constant at 5 mg/l. Total solids level in biodegradation test = 31.013 mg/l. Radiochemical conc. ~ 4.67 µCi/l. Duplicate treatments. Abiotic control. Analysis for metabolites by RAD-TLC.

Results

Kinetics
Measured other
as:

Half Life: *Mineralization:* 4.5 days (N-methyl ¹⁴C-labeled Amine Oxide) 14.3 days (alpha-carbon ¹⁴C-labeled Amine Oxide)
Primary Biodegradation: n/a

Result: inherently biodegradable

Degradation
Products: no

Remarks: Kinetics measured as ¹⁴C-gases {¹⁴CO₂ + ¹⁴CH₄}. Mineralization of N-methyl ¹⁴C-labeled Amine Oxide most closely described by 3/2 order function without growth, as follows:

$$Y = [a(1 - \exp^{-bX})] + cX$$

a = deflection point at which rate changes from first to zero order, a%

b = first order rate constant (days⁻¹)

c = zero order rate constant (%.days⁻¹)

Mineralization of alpha-carbon ¹⁴C-labeled Amine Oxide most closely described by 3/2 order function with growth, as follows:

$$Y = [a(1 - \exp^{-bX - cX.X})] + dX$$

a = deflection point at which rate changes from first to zero order, a%

b = first order rate constant (days⁻¹)

c = linear growth term (days⁻²)

d = zero order rate constant (%.days⁻¹)

Test substance I: N-methyl ^{14}C -labeled amine oxide
 Test substance II: alpha-carbon ^{14}C -labeled amine oxide

Kinetic parameters:

	function	r^2	a(%)	b	c	d
I.	3/2 no growth	0.987	67.3±2.75	0.286±0.0295	0.318±0.0623	---
II.	3/2 with growth	0.999	55.6±1.61	0.0559±0.00557	0.307±0.0324	0.00894±0.00168

Based on these models, the predicted times necessary to reach various levels of mineralization are listed below.

Mineralization (%)	Time (hrs)	
	I.	II.
50	4.5	14.3
75	24.5	63.2
90	71.4	112.1
95	87.1	128.4
99	99.7	141.5

The total amount of ^{14}C evolved as ^{14}C -gases was 85.7 (±1.9)% for test substance I and 75.5 (±0.5)% for test substance II. The remainder of the ^{14}C would be expected to be incorporated in the biomass, but that fraction was not measured in this experiment.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Reference

Source Reference: The Procter & Gamble Company, 1996F.

(c)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides Dodecyl Dimethyl Amine Oxide

Carbon Chain Length Distribution: 72% C12; 22.1% C14; 3.5% C16

Remarks: Test substance contained 70% H₂O, 26.8% DDAO, 1.0% Petroleum Ether Extract, 1.0% Na₂SO₄, 0.31% unreacted amine and 0.09% H₂O₂. pH = 7.1.

Method*GLP:* no data*Report/Study Year:* 1976*Report/Study Number:* TDR-77008*Test Type:* aerobic*Method/Guideline Followed:* other*Inoculum:* predominantly domestic sewage, adapted*Inoculum Acclimated:* no*Acclimated to what Concentration:* no details given*Acclimated for what Duration:* no details given*Control Substance:* other

Test Substance Initial Concentration:	Value	Unit	Expressed as
	20	mg/l	Test substance

Remarks: Method: As described in Sturm (ref.). Biodeg. measured by CO₂ evolution. Six replicates, 1 blank, 1 pos. control (dextrose). Analyses: Total N, organic (Kjeldahl) N, nitrate (Brucine method) and DDAO (Disulfine Blue Active Substance method or DBAS, ref.). TLC on chloroform extracts of selected samples and blank treatment.

Results

Kinetics Measured as: CO₂ (Carbon Dioxide Evolution)

<i>Kinetics of Test Substance:</i>	Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
	2	day(s)	=	23.3	n/a
	26	day(s)	=	63.1	n/a
<i>Kinetics of Control Substance:</i>	Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
	26	day(s)	=	91.3	n/a

Half Life: Mineralization: not determined*Primary Biodegradation:* n/a*Result:* inherently biodegradable*Degradation Products:* yes

Remarks: Primary biodegradation, as DDAO, was approx. 97.5% in 2 days, at which time approx. 23.3% of the theoretical carbon had evolved as CO₂. These results

indicate that intermediates were present after primary degradation.

Data Quality

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 2A

Remarks: Acceptable, well-documented publication/study report which meets basic scientific principles.

Reference

Source Reference: The Procter & Gamble Company, 1977.

Other References: Osburn, Q. W. (1975).

Sturm, R.N. (1973)

4. ENVIRONMENTAL TOXICITY

4.1.1 TOXICITY TO FISH (ACUTE)

Test Substance

CAS Number: 70592-80-2
 Identity: Amines, C10-16-alkyldimethyl, N-oxides
 Purity: 27.4% active
 Carbon Chain Length Distribution: C10-16
 Remarks: Balance (72.6%) is water

Method

GLP: no
 Report/Study Year: 1972
 Report/Study Number: NPS-72.004
 Method/Guideline Followed: EPA OPP 72-1
 Test Type: acute, static
 Analytical Monitoring: yes
 Limit Test: no
 Species: *Lepomis macrochirus*

Value	Unit
96	hour(s)

Remarks: Fish mean length 43 mm. Nominal test conc. 0.0 - 0.21 - 0.46 - 1.0 - 2.1 - 4.6 mg/l; No aeration; Temp. 18.05 °C; pH 7.1; Hardness 35 mg/l as CaCO₃; O₂ 57-103% sat. Analyses: report mentions that 100 ml samples were taken, preserved with 1 ml of 37% formaldehyde and sent to the sponsor (P&G) for analyses. The analytical results are not included with the report.

Results

Unit: mg/l

	Measured/ Computed	Operator	Lower	Upper
LC50:	c	=	3.13	n/a
LC50	c	=	2.02	4.84

Remarks: No report made on number of fish, light/dark cycle, feeding, pH, whether or not dosing vehicle was used. Temperature of test water was slightly too low and O₂ at study termination was low (57% sat.). Recalculation of results by the reviewer using the 45% trimmed Spearman-Kärber method gave LC50 of 1.38 [1.32-1.44] mg/l.

Data Quality

*Reliability
(Klimisch):* 3A

Remarks: Identity of the test substance not reported, but believed to be CAS # 70592-80-2 because this material was used in several tests around the same time (1972).
Exposure concentrations uncertain; no analyses.

Reference

Source Reference: The Procter & Gamble Company. 1972.

4.1.2 TOXICITY TO FISH (PROLONGED)

(a)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl; N-oxides C12/14 alkyl dimethyl amine oxide
Purity: 25.43% active
Carbon Chain Length Distribution: C10-16; average 12.7
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1976
Report/Study Number: TDR-76008
Method/Guideline Followed: "Recommended Bioassay Procedures for Fathead Minnow (*Pimephales promelas*), Chronic Test"; U.S. EPA National Water Quality Laboratory; Duluth, MN; April 1971 (Revised January 1972).
Test Type: chronic, flow-through
Analytical Monitoring: yes
Limit Test: no
Species: *Pimephales promelas*
Exposure Period:

Value	Unit
302	day(s)

Remarks: Analyses: MBAS (Methylene Blue Active Substance) analytical method. Unless otherwise indicated, the results are expressed on the basis of active ingredient.

Statistical Methods: Moving averages method for acute toxicity; appropriate analyses (e.g., Bartlett's test, Student T test, one-way ANOVA) at the 95% CL were performed for the chronic toxicity test.

Test System: 96-hour static acute test: 40-60 day old (~34 mm and 0.3 g) fathead minnow fry (*Pimephales promelas*); 10 per concentration; varying water hardness (48 - 230 mg/l) and pH (6.0 - 9.0); results based upon m concentrations of active ingredient; LC50 determined by moving averages method.

15-Day flow-through chronic test: Started with 12-day old fathead minnow larvae (30 larvae in each duplicate test tank, or 60 larvae per concentration). Fish were fed twice daily *ad libitum* with 48-hr old brine shrimp (*Artemia salina*). Exposure concentrations were 0.5, 1.0 and 2.0 mg/l (nominal, active ingredient). This corresponded with 0.52, 1.03 and 1.85 mg/l (m, active ingredient). After 15 days of exposure, fish were removed, counted and measured for length. Weights were not determined.

302-Day flow-through chronic test: Started with 18-hour old embryos (eggs) of fathead minnows (40 eggs in each duplicate test tank, or 80 eggs per concentration). Exposure concentrations were 0, 0.06, 0.13, 0.25, 0.5 and 1.0 mg/L (nominal, active ingredient). A Mount and Brungs Proportional Diluter was used and set for 12 volume replacements in 24 hours. Weekly analysis of all concentrations. On day 5, the replicates (spawning tanks) were thinned to 25 fish in each, with an additional 25 fish in a third replicate for survival, length and weight measurements. Fish were fed 2x/day *ad libitum* with 48-h old brine shrimp. Fish were counted and lengths m via photographs on days 30 and 60. On day 120, fish in the spawning tanks were thinned to 15 per replicate, another 5 fish per replicate were removed for histopathology analysis; spawning substrates were added to the tanks. Following egg laying, percent hatchability was recorded. Twenty-five fry (larvae) per test concentration continued to be exposed for another 60 days, during which survival and growth were m. The same feeding regime continued. The test was terminated after one week passed during which there were no further spawns in any of the tanks. All adult fish in the spawning tanks were sacrificed at 302 days of exposure. Their lengths, weights, sex and condition were recorded. Photos were taken of individuals showing abnormal morphology. The number of males per tank differed from the ratio specified by EPA but this was not modified to assess the possibility of sex-specific mortality. This may have influenced the production of eggs in the test.

Results

Unit: mg/l

	Measured/ Computed	Operator	Lower	Upper
NOEC:	m	=	0.42	n/a
LOEC	m	=	0.88	n/a
LC50	m	n/a	2.61	3.46

Remarks: LC50 [96-hour, m] 2.61 - 3.46 mg/l
 NOEC [15-day, survival, m] 0.52 mg/l
 NOEC [15-day, growth, m] >1.03 mg/l

NOEC [302-day, hatchability, m] 0.42 mg/l
LOEC [302-day, egg production, m] >0.88 mg/l

Exposure concentrations: During the 302-day chronic study, approximately 40 MBAS analyses were conducted at each test concentration. Mean m values were: 0.02, 0.06, 0.11, 0.21, 0.42 and 0.88 mg/L (vs. nominals of 0, 0.06, 0.13, 0.25, 0.5 and 1.0). MBAS analysis of the dilution water indicated 0.02 mg/L on average. m conc. were 80-90% of nominal. Static acute test: The 96-hr LC50 ranged from 2.7 and 3.5 mg/L (nom.) under various water quality conditions. Acute toxicity was not significantly affected by changes in pH or water hardness.

15-Day flow-through chronic test: There were no adverse effects on survival at conc. ranging from 0.13 to 0.5 mg/l (active ingredient, nominal). Survival at these concentrations ranged from 85 to 95%. Survival at 1.0 mg/l (nom.) was 47% and at 2.0 mg/l (nom.) was zero % on day 15. The NOEC for survival was 0.42 mg/l (m). Mean length ranged from 17.2 at 1.0 mg/l (nom.) to 19.1 (control). Growth at conc. up to and including 1.0 mg/l (nom.) did not differ significantly from controls. The NOEC for growth was 0.88 mg/l (m).

302-Day flow-through chronic test: F0 survival was significantly reduced at the high concentration (1.0 mg/L, nom.) at 30, 60 and 120 days of exposure. Mean survival in the controls and all concentrations below 1.0 mg/L (nom.) were comparable. The NOEC for F0 survival was 0.42 mg/l. F0 length was unaffected at the end of the test although length appeared to be affected at 30 and 60 days in the 1.0 and 0.5 mg/L (nom.) exposures. The condition factor was comparable for controls and all exposures at the end of the test. The NOEC for F0 growth was 0.88 mg/l. During spawning, the number of spawns, total egg production, number of eggs per spawn and number of eggs per female were recorded. There was considerable tank-to-tank variability in these parameters, which is attributed to the different male/female ratios in the spawning tanks, due to a conscious decision to keep males in the exposure tanks to evaluate the possibility of sex-specific mortality. The number of eggs per spawn was the least variable parameter, ranging from 66.5 at 0.13 mg/l (nom.) to 164.5 at 1.0 mg/l (nom.), compared to 126.0 eggs per spawn in the controls. The data suggests that amine oxide up to a concentration of 1.0 mg/l (nom.) does not adversely affect egg production. The NOEC for F0 egg production was 0.88 mg/l. F1 egg hatchability was not significantly affected at 0.5 mg/l (nom.) and significantly reduced at 1.0 mg/L (nom.). The NOEC for F1 egg hatchability was 0.42 mg/l. F1 fry survival at 30 and 60 days post hatch was significantly reduced at 1.0 mg/l (nom.). No differences were seen in fry growth (as measured by length) at any of the concentration levels. Histological examinations indicated a particular occluding abnormality of the eyes in about half the surviving fish at 1.0 mg/L. Histological analysis of livers showed no toxicant related effects. No other test substance-related adverse effects were observed.

Data Quality

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 2A

Remarks: Accepted, well documented study report which meets basic scientific principles. The level of study documentation, analytical confirmation of exposures and

statistical analyses make up for the lack of formal GLP practices in 1975-76.

Reference

Source Reference: The Procter and Gamble Company, 1976.

Other References: Maki, A. W. (1979).

Versteeg, D. J. and J. M. Rawlings (2003).

(b)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Carbon Chain Length Distribution: C10-16

Method

GLP: no

Report/Study Year: 1983

Report/Study Number: SDA101

Method/Guideline Followed: other

Test Type: acute and chronic

Species: bluegill, fathead minnow, golden orfe

Result

s

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	0.42	n/a
LC50:	m	=	2.4	6.4

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature. Insufficient information to assess data quality.

Reference

Source Reference: TSCA ITC, 1983.

4.2.1 AQUATIC INVERTEBRATES TOXICITY (ACUTE)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: not given
Carbon Chain Length Distribution: C10-16
Remarks: Test substance identified in summary report as "C13 amine oxide".
 Probably a C10-16 amine oxide with average chain length between C12 and C13.

Method

GLP: no
Report/Study Number: SDA108
Test Type: acute, flow-through
Species: *Daphnia magna*

Value	Unit
96	hour(s)

Remarks: No experimental details. Brief summary only.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC50:	c	=	1	n/a
EC50	c	=	0.8	1.2

Remarks: Statistics by Probit analysis.

Data Quality

Reliability (Klimisch): 4B

Reference

Source: The Procter & Gamble Company, (no date). Data summary for two Amine
Reference: Oxides.

4.2.2 AQUATIC INVERTEBRATES TOXICITY (PROLONGED)**Test Substance**

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: not provided
Carbon Chain Length Distribution: C10-16; average 12.7
Remarks: Balance is water

Method

GLP: no

Report/Study Year: 1979
 Report/Study Number: SDA110
 Method/Guideline Followed: other
 Test Type: chronic, flow-through
 Analytical Monitoring: yes
 Limit Test: no
 Species: *Daphnia magna*

Exposure Period:

Value	Unit
21	day(s)

Remarks: Test Method: Modified 0.5 L proportional diluter delivers test material to mixing cells at predefined concentrations; food is added via a 6-channel peristaltic pump and cell contents drained through siphon tube to the flow-splitter box. Flow-splitter box is drained through four 2.5 cm sections of 1 mm outer diam. capillary tubing to restrict flow to test chambers, which are 1-L beakers with a 2.5 x 5 cm notch covered with 60-mesh stainless steel screen to prevent escape of newly produced young. Feed is a 1000 mg/L suspension of ground trout chow and alfalfa, renewed daily. Dilution water is carbon- and reverse osmosis-filtered well water, hardness 120 mg/L CaCO₃, pH 7.2-7.4, O₂ 8.5-9.5 mg/L, temp. 20-22 °C. Physical measurements (pH, oxygen, temp.) taken initially. Temp. is monitored continuously. pH and oxygen are measured every 3-5 days throughout the test period. Daphnids are < 12h old. Young are randomly assigned to test chambers, 5 per replicate, 4 replicates, thus 20 F0 animals per concentration. F0 mortality is recorded at 24h, 96h, 7d and daily thereafter. Production of F1 animals starts on day 7 or 8.

Records are kept of the following endpoints:

- 1) Survival of F0 animals, each observation day
- 2) Total number of F1 animals produced by F0 animals
- 3) Mean brood size (F1/F0)
- 4) Percentage of days that young were produced in each replicate, for all conc. and controls

Analyses: At time of inoculation, sample of test medium is taken and preserved with H₂SO₄ at pH 2 and 5 °C for analysis with MBAS (Methylene Blue Active Substance) analytical method. Unless otherwise indicated, the results are expressed on the basis of measured concentrations of active ingredient.

Statistical Methods: Probit analysis. All calculations based on mean measured concentrations.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	0.7	n/a

EC50:	c	=	1.01	n/a
EC50	c	=	0.88	n/a
EC50	c	=	0.77	1.04

Remarks: Exposure concentrations: Not specified.

21-day test: Among the 4 endpoints measured, reproduction was the most sensitive indicator of chronic toxicity.

21-day EC50 (av. brood size) = 1.10 (0.95-1.07) mg/l

21-day EC50 (total young production) = 0.88 (0.77-1.04) mg/l

21-day EC50 (% of days that reproduction occurred) = 1.04 (0.98-1.11) mg/l

21-day LC50 = 0.96 (0.90-1.03) mg/l 96-h LC50 = 1.01 (0.85-1.21)

The NOEC for reproduction of *Daphnia magna* was 0.7 mg/L.

Daphnia magna is a reasonably good indicator of chronic toxicity of amine oxide to fish.

Fish (fathead minnows) were somewhat more sensitive, with a NOEC of 0.42 mg/L (see report # TDR-76008).

Data Quality

Flags: Critical study for SIDS endpoint

Reliability
(Klimisch): 2A

Remarks: Reliable with restrictions. Acceptable, well-documented publication/study report, meets basic scientific principles

Reference

Source Reference: Maki AW., 1979.

4.3 TOXICITY TO AQUATIC PLANTS e.g. ALGAE

(a)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides C12/14 alkyl dimethyl amine oxide

Purity: 31%

Carbon Chain Length
Distribution: C12-14 (av. C12.7)

Remarks: Balance is water

Method

GLP: yes

Report/Study Year: 1997

Report/Study
Number: IMW-95-0060-05

Method/Guideline
Followed: OECD Guideline 201

Analytical Monitoring: yes
Species: *Diatoma elongatum*
Endpoint: other

Exposure Period:	Value	Unit
	239	hour(s)

Remarks: Endpoints are biomass and growth rate.
Initial cell conc. 4400 cells/ml Nominal test conc. 0 - 0.003 - 0.010 - 0.032 - 0.056 - 0.10 - 1.0 - 3.2 mg/l (active ingredient).
Conditions: 50 ml test substance + 50 ml algal suspension; 2 reps. per treatment; 4 controls; Temp. 21-25 °C; continuous illumination 60-120 uE/m²/sec; shaken at 100 rpm.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	0.056	n/a
EC10:	c	=	0.084	n/a
EC50:	c	=	0.83	n/a
EC20:	c	=	0.18	n/a

Remarks: Results based on initial, nominal test conc. Morphology of algae normal at all conc. except at 3.2 mg/l. Reference substance results comparable to historical controls. Of several parametric models, the model that assumes effect on growth rate and exponential growth appeared to best fit the data; this model was applied. Test substance had significant effect on growth rate but not biomass, as supported by minor changes in algal size and a ErC50/EbC50 ratio of 2, similar to ratio that would be expected based on balanced growth.

Results calculated according to Bruce and Versteeg (1992), in mg/l:

	EC50	EC20	EC10
Growth Rate	2.16 [1.73-2.69]	0.55 [0.35-0.86]	0.27 [0.14-0.50]
Biomass	0.83 [0.59-1.18]	0.18 [0.10-0.35]	0.084 [0.036-0.194]

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Remarks: Reliable; guideline study.

Reference

Source Reference: Procter & Gamble Eurocor, 1997B.

Other References: Bruce and Versteeg (1992).

(b)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides C12/14 alkyl dimethyl amine oxide

Purity: 31%

Carbon Chain Length Distribution: C12-14 (av. C12.7)

Remarks: Balance is water

Method

GLP: yes

Report/Study Year: 1997

Report/Study Number: IMW-95-0060-03

Method/Guideline Followed: OECD Guideline 201

Analytical Monitoring: yes

Species: *Scenedesmus subspicatus*

Endpoint: other

Exposure Period:

Value	Unit
72	hour(s)

Remarks: Initial cell conc. 104 cells/ml. Nominal test conc. 0 - 0.003 - 0.011 - 0.034 - 0.06 - 0.11 - 0.34 - 1.1 - 3.4 mg/l (active ingredient). Conditions: 50 ml test substance + 50 ml algal suspension; 2 reps. per treatment; 4 controls; Temp. 21-25 °C; pH 7.9-8.3; continuous illumination 60-120 uE/m²/sec; shaken at 100 rpm. Additional flasks for analysis with 0, 0.003, 0.11 and 3.4 mg/l.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	0.034	n/a
EC10:	c	=	0.0043	n/a
EC50:	c	=	0.059	n/a
EC20	c	=	0.011	n/a

Remarks: Results based on initial nominal test conc. Of several parametric models, the model that assumes effect on growth rate and exponential growth appeared to best fit the data; this model was applied. Morphology of algae was abnormal at conc. of 0.06 mg/l and higher. Reference substance results comparable to historical controls. Results of test strongly influenced by test substance-dependent increase in cell size (e.g. 3x size of controls, at

0.34 mg/l). Morphology observations support this. This also explains the unusually high ErC50/EbC50 ratio of 3.0 compared to the normal ratio of 1.8 for balanced growth. Test substance had significant effect on cell division, which was not reflected in total cell volume. The ECx values based on cell counts therefore provide the best description of the effect on algal growth.

Results calculated according to Bruce and Versteeg (1992), in mg/l:

	EC50	EC20	EC10
Growth Rate	0.28 [0.20-0.38]	0.039 [0.022-0.068]	0.014 [0.007-0.028]
Biomass	0.059 [0.030-0.116]	0.011 [0.004-0.030]	0.0043 [0.0012-0.0154]

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Reference

Source Reference: Procter & Gamble Eurocor, 1997C.

Other References: Bruce and Versteeg (1992).

(c)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides C12/14 alkyl dimethyl amine oxide

Purity: 31%

Carbon Chain Length Distribution: C12-14 (av. C12.7)

Remarks: Balance is water and something else

Method

GLP: yes

Report/Study Year: 1996

Report/Study Number: IMW-95-0060-02

Method/Guideline Followed: OECD Guideline 201

Analytical Monitoring: yes

Species: *Selenastrum capricornutum*

Endpoint: other

Exposure Period:

Value	Unit
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72 hour(s)

Remarks: Initial cell conc. 10000 cells/ml Nominal test conc. 0 - 0.01 - 0.03 - 0.06 - 0.11 - 0.20 - 0.35 - 0.61 - 1.09 mg/l (active ingredient). Conditions: 50 ml test substance + 50 ml algal suspension; 2 reps. per treatment; 4 controls; Temp. 21-25 °C; pH 8.0-8.6; continuous illumination 60-120 $\mu\text{E}/\text{m}^2/\text{sec}$; shaken at 100 rpm. Analytical measurements in extra flasks of 0, 0.001, 0.11 and 1.09 mg/l.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	0.01	n/a
EC10:	c	=	0.0058	n/a
EC50:	c	=	0.079	n/a
EC20	c	=	0.014	n/a

Remarks: Results based on initial nominal test conc. Of several parametric models, the model that assumes effect on growth rate an exponential growth appeared to best fit the data; this model was applied.

The morphology of algae was abnormal at conc. of 0.03 mg/l and higher.

Reference substance results comparable to historical controls. Results of test strongly influenced by test substance-dependent increase in cell size (up to 3x size of controls, at highest conc.). Morphology observations support this. Test substance apparently interferes with cell division, which explains the unusually high ErC50/EbC50 ratio of 4.4 compared to the normal ratio of 1.8 for balanced growth. Therefore, the ECx calculations were based on the effect of the test substance on cell counts (as opposed to total cell volume).

Results calculated according to Bruce and Versteeg (1992), mg/l:

	EC50	EC20	EC10
Growth Rate	0.40 [0.30-0.52]	0.067 [0.038-0.118]	0.025 [0.012-0.057]
Biomass	0.079 [0.049-0.128]	0.014 [0.006-0.032]	0.0058 [0.0021-0.0161]

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; comparable to guideline study

Reference

Source Reference: The Procter & Gamble Company, 1997.

Other References: Bruce and Versteeg (1992).

(d)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides C12/14 alkyl dimethyl amine oxide

Purity: 31%

Carbon Chain Length Distribution: C12-14 (av. C12.7)

Remarks: Balance is water

Method

GLP: yes

Report/Study Year: 1996

Report/Study Number: IMW-95-0060-01

Method/Guideline Followed: OECD Guideline 201

Analytical Monitoring: no

Species: *Selenastrum capricornutum*

Endpoint: other

Exposure Period:

Value	Unit
72	hour(s)

Remarks: Initial cell conc. 9000 cells/ml 2 replicates/treatment and 4 replicates/control. Nominal test conc. 0 - 0.0032 - 0.010 - 0.018 - 0.032 - 0.058 - 0.10 - 0.18 - 0.32 mg/l (active ingredient). Conditions: 50 ml test subst. + 50 ml algal suspension; Temp. 21-25 °C; pH 7.9-8.9; continuous illumination 60-120 $\mu\text{E}/\text{m}^2/\text{sec}$; shaken at 100 rpm. Reference substance used to check viability.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	0.032	n/a
EC10:	c	=	0.0015	n/a
EC50:	c	=	0.014	n/a
EC20	c	=	0.0031	n/a

Remarks: NOEC and EC50 values are for growth rate. ErC50, 95% confidence interval is also given. NOEC is based on initial nominal test conc. Of several parametric models, the model that assumes effect on growth rate and exponential growth appeared to best fit the data. This model was applied. Morphology of algae was abnormal at conc. of 0.01 mg/l and higher. Reference substance results comparable to historical controls. Effect conc. based on biomass (EbC50) not computed. The EbC50 may be lower than the ErC50, based on experience.

Results calculated by Bruce and Versteeg (1992) in mg/l:

	EC50	EC20	EC10
Growth Rate	0.079 [0.060-0.103]	0.012 [0.007-0.020]	0.0044 [0.0022-0.0089]
Biomass	0.014 [0.009-0.020]	0.0031 [0.0016-0.0060]	0.0015[0.0007-0.0032]

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; comparable to guideline study

Reference

Source Reference: The Procter & Gamble Company, 1996C.

Other References: Bruce and Versteeg, 1992.

(e)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: 31.2%

Carbon Chain Length Distribution: C10-16

Method

GLP: yes

Report/Study Year: 2003

Report/Study Number: WE-06-396

Method/Guideline
Followed: OECD Guideline 201

Analytical Monitoring: no

Species: *Chlorella vulgaris*

Endpoint: n/a

Value	Unit
72	hours

Remarks: Test concentrations 0 - 0.05 - 0.11 - 0.23 - 0.52 - 1.14 - 2.49 - 5.48 - 12.06 mg/l (nominal, active ingredient).
Temp. 22.8 - 23.4 °C
pH 7.74 - 8.38
NOEC (biomass) calculated using Dunnett's T-test.
NOEC (growth rate) calculated using Welch's T-test.
ECxx calculated using method of Bruce and Versteeg (1992).

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC10:	c	=	0.63	n/a
EC50:	c	=	1.14	n/a
EC20:	c	=	0.77	n/a

Remarks: Results are in terms of initial, nominal concentrations of active substance.
Results were obtained for growth rate and biomass. Biomass was the more sensitive endpoint.
Results calculated according to Bruce and Versteeg (1992), in mg/l:
NOECb = 0.016 (0.000 - 0.019)
ECb10 = 0.63 (0.56 - 0.71)
ECb20 = 0.77 (0.71 - 0.85)
ECb50 = 1.14 (1.06 - 1.22)
Results for growth rate(average and 95% confidence interval):
NOECr = 0.16 (conf. int. n/a)
ECr10 = 1.47 (1.47 - 1.47)
ECr20 = 1.55 (1.51 - 1.59)
ECr50 = 1.70 (1.69 - 1.72)

Data Quality*Flags:* Critical study for SIDS endpoint*Reliability (Klimisch):* 1A*Remarks:* Reliable without restriction, guideline study.**Reference**

Source Reference: The Procter & Gamble Company, 2003A.

Other References: Bruce and Versteeg (1992).

(f)

Test Substance*CAS Number:* 70592-80-2*Identity:* Amines, C10-16-alkyldimethyl, N-oxides C12/14
amine oxide*Purity:* 30.2%*Carbon Chain Length* C10-16*Distribution:**Remarks:* Balance is water**Method***GLP:* no*Report/Study Year:* 1999

Report/Study Number: E96-018

Analytical Monitoring: yes

Species: river periphyton

Endpoint: population density and diversity

Exposure Period:

Value	Unit
28	days

Remarks:

Microcosm study. Species: river periphyton community. Natural colonization of river periphyton on unglazed clay tiles (2415 mm²) and on cobble stones, accomplished by placing these substrates in high water quality areas of the Little Miami river and Big Darby Creek in Ohio for 36 days during early summer. Colonized substrates were transported to the laboratory and placed in exposure chambers connected to a proportional diluter delivering 6 exposure conc. and 15 volume turnovers per day. 3 reps. per conc. and 5 substrates per rep. Periphyton, test substance and water quality sampled at 1 or 2-week intervals.

Statistical method: Population and community metric data by one-way ANOVA for each sampling day and substrate/river group to determine NOEC. Two-way ANOVAs to determine location vs. substrate-type effect relationships.

Conditions:

flow-through; light cycle 15h on 9h off; light intensity 530 µE/m²/sec; temp. 22-23°C. Concentrations 0; 6.25; 12.5; 25; 50 and 100 µg/l.

Results

Unit: mg/l

	Measured/ Computed	Operator	Lower	Upper
NOEC:	c	=	0.067	n/a

Remarks: Av. measured conc. ranged from 67-137% of nominal. Analytical method and results not reported. 110 taxa identified (87 diatom, 12 green, 7 blue-green, 2 euglenoid, 1 chrysophyte and 1 red); 18 dominant taxa; considerable variation by river type and substrate type; NOECs were estimated for each unique test group (i.e. Little Miami River tile, Little Miami River cobble and Big Darby tile). Thus, amine oxide effects on 3 periphyton communities could be evaluated. One way ANOVA followed by Dunnett's multiple comparison was performed. Of the 280 results (unique test group + sample time + population or community metric) obtained for each exposure concentration, there were relatively few significant differences (reductions or increases) from the controls, as seen below:

Concentration	Reduction	Increase
6.25 (n=280)	6 (2.1%)	10 (3.6%)
12.5 (n=280)	5 (1.8%)	6 (2.1%)
25 (n=280)	6 (2.1%)	1 (0.4%)
50 (n=280)	4 (1.4%)	14 (5.0%)
100(n=280)	5 (1.8%)	19 (6.8%)

Combined (n=1680)	26 (1.5%)	50 (3.0%)
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No significant, dose-dependent adverse effects were observed on the population density and diversity of the periphyton. Using the low end of the average % of nominal concentration (67%) to set a measured value in the high exposure chambers, the NOEC for each of the three periphyton communities is 67 µg/l.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2A

Remarks: While not a "guideline" test, the study was conducted under GLP-comparable conditions; microcosm studies are a recognized and generally accepted test system for evaluating ecotoxicity effects of chemical substances.

Reference

Source Reference: The Procter & Gamble Company, 1999B.

(g)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides C12/14 alkyl dimethyl amine oxide

Purity: 31%

Carbon Chain Length Distribution: C12-14 (average 12.7)

Remarks: Balance is water

Method

GLP: yes

Report/Study Year: 1996

Report/Study Number: IMW-95-0060-04

Method/Guideline Followed: OECD Guideline 201

Analytical Monitoring: yes

Species: *Anabaena flos-aquae*

Endpoint: other

Value	Unit
238.5	hour(s)

Remarks: Initial cell conc. 30 cells/ml, 2 replicates/treatment and 4 replicates/control. Nominal test conc. 0 - 0.004 - 0.011 - 0.035 - 0.061 - 0.11 - 0.35 - 1.1 - 3.5

mg/l (active ingredient). Conditions: 50 ml test subst. + 50 ml algal suspension; 2 reps. per treatment; 4 controls; Temp. 21-25 °C; pH 7.9-8.2; continuous illumination 60-120 uE/m²/sec; shaken at 100 rpm; reference substance used to check test system viability. Analytical monitoring in extra flasks of 0, 0.004, 0.11 and 3.5 mg/l.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	1.1	n/a
EC10:	c	=	1.9	n/a
EC50:	c	=	3.0	n/a

Remarks: Results based on initial, nominal test conc. Of several parametric models, the model that assumes effect on growth rate and exponential growth appeared to best fit the data; this model was applied.

Morphology of algae was normal at all conc.

Reference substance results comparable to historical controls.

No parametric models appeared to fit the data well; growth rate in most treatments surpassed the controls. Although considerable variability in size, algal cell density appeared to be best expression of algal growth. Results are based on this measurement.

ErC50 = 5.3 mg/l

ErC10 = 1.9 mg/l

EbC50 = 3.0 mg/l

EbC10 = 2.3 mg/l

NOEC = 1.1 mg/l

Due to the poor dose-response in this test, none of the concentrations yielded 100% effect. The confidence intervals were very large, therefore the EC50, EC20 or EC10 values could not reliably be estimated using the method of Bruce and Versteeg (1992).

Data Quality

Flags: Critical study for SIDS endpoint

Reliability
(*Klimisch*): 2C

Remarks: Reliable with restrictions; guideline study. Poor dose-response relationship resulted in very large confidence intervals for the results.

Reference

Source Reference: Procter & Gamble Eurocor, 1997A.

Other References: Bruce and Versteeg (1992).

(h)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: not given

Carbon Chain Length Distribution: C10-16

Method

GLP: no

Report/Study Year: 1974

Report/Study
Number: MEM-74017

Method/Guideline
Followed: not a guideline method

Analytical
Monitoring: no

Species: *Navicula* and *Selenastrum*

Endpoint: biomass

Exposure Period:

Value	Unit
5	days

Remarks: Algae are exposed for 5 days, then harvested by centrifugation. Algal cultures that showed no growth are re-inoculated into fresh medium. The Minimum Algistatic Concentration (MAC) is the concentration that inhibited growth completely during the exposure period and allowed recovery during the 10-day post-exposure period in fresh medium.
Test concentrations: 0 - 1 - 5 - 10 - 50 mg/l (nominal, test substance).

Results

Unit: mg/l

Measured/ Computed	Operator	Lower	Upper
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Remarks: For both algal species tested, the MAC was between 1 and 5 mg/l (nominal, test substance).

Data Quality

Reliability
(Klimisch): 4A

Remarks: Not assignable because of insufficient information. Brief summary of results + graphs showing algal growth curves for the different treatments; insufficient information about experimental method, no information about test substance purity; statistical endpoints (ECxx and NOEC) normally generated by current guideline studies were not reported.

Reference

Source Reference: The Procter & Gamble Company, 1974.

(i)

Test Substance*CAS Number:* 70592-80-2*Identity:* Amines, C10-16-alkyldimethyl,
N-oxides*Purity:* not given*Remarks:* Literature review**Method***GLP:* yes*Report/Study Year:* 1983*Report/Study Number:* SDA101

Analytical Monitoring: yes

Species: other algae*Remarks:* Algal species not given.**Result****s**

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC50:	c	=	1	5

Data Quality*Reliability (Klimisch):* 4B**Reference**

Source Reference: TSCA ITC, 1983.

5. TOXICITY

5.1.1 ACUTE ORAL TOXICITY

(a)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: 30%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: yes
Report/Study Year: 1987
Report/Study Number: 87.0797
Method/Guideline Followed: EEC Guideline B.1. and OECD Guideline 401
Test type: Acute oral toxicity; limit test
Species: Wistar rats
Strain: SPF71
Sex: male/female
Vehicle: deionized water
Number of Animals per Dose: 10 (5 male and 5 female)
Doses: 600 mg/kg bw (active ingredient)
Remarks: Rats weighed 169.2 g (males) and 166.2 g (females) and were 6-10 weeks old at the start of the study. Rats were fasted from about 16 h prior to dosing until 3-4 h after dosing. Dosing by gavage of 10 ml/kg bw of a 20% solution of the test material in deionized water. Feed and water *ad libitum* after dosing. Observations once (weekends) or twice (weekdays) daily for 14 days after dosing.

Results

Value:	Operator	Lower	Upper	Unit
	>	600	n/a	mg/kg bw

Remarks: LD50 result was same for males as for females. No deaths or clinical symptoms were noted.

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 1A

Reference

Source Reference: Hoechst AG. 1987A.

(b)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides;
Cocodimethylamine oxide
Purity: 27.72%
Carbon Chain Length Distribution: C10-16
Remarks: Balance (72.28%) is water

Method

GLP: no
Report/Study Year: 1978
Report/Study Number: 3029.234
Method/Guideline Followed: EPA OPP 81-1
Test type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
Vehicle: distilled water
Number of Animals per Dose: 10 (5 male and 5 female)
Doses: 2.0, 2.8, 3.9, 5.4, 7.6 g test substance = 554, 776, 1080, 1497, 2107 mg AO/kg bw
Remarks: Five animals per dose group per sex; weight 190-268 g.; vehicle-treated controls; feeding *ad libitum*; food was withheld 18-20 h prior to dosing. Observations: mortality/clinical signs several times on day 1 and daily until day 14. Body weights on days 0 and 14. Necropsy on day 14.

Results

Value:	Operator	Lower	Upper	Unit
	=	1330	n/a	mg a.i./kg bw

Remarks: Average LD50 = 1330 mg a.i./kg bw

Clinical symptoms: decreased motor activity, diarrhea, blanching. Rattling in high dose for up to 1 hour after dosing. Necropsy findings: deep/bright red or light tan lungs sometimes with liver colored areas or petechiae, salivation, nasal and/or ocular haemorrhage, stomach irritation, stomach and/or intestines filled with gas and/or fluid,

stomach and/or intestines filled with bloody fluid.

Mortalities: 554 mg/kg and 776 mg/kg (no deaths); 1080 mg/kg (4/10); 1497 mg/kg (5/10); 2107 mg/kg (10/10)

Data Quality

Reliability (Klimisch): 1A

Reference

Source Reference: The Procter & Gamble Company, 1978A.

(c)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: not indicated

Carbon Chain Length Distribution: C10-16

Method

GLP: no

Report/Study Year: 1983

Report/Study Number: SDA101

Method/Guideline Followed: other

Test type: LD50

Species: unspecified

Strain: no data

Sex: no data

Vehicle: no data

Doses: no data

Remarks: Method not specified

Results

Value:	Operator	Lower	Upper	Unit
	=	1610	1850	mg/kg bw

Remarks: No single value is given, only the range of LD50 values is provided.

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature

Reference

Source Reference: TSCA ITC, 1983.

5.1.3 ACUTE DERMAL TOXICITY

(a)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides;
P0434
Purity: 27.72%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1978
Report/Study Number: 3029.232
Method/Guideline Followed: EPA OPP 81-2
Analytical Monitoring: no
Test Type: LD50
Species: rabbit
Strain: New Zealand white
Sex: male/female
Vehicle: no data
Number of Animals per Dose: 6 (3 intact skin; 3 abraded skin)
Doses: Single dose of 2 ml/kg = 520 mg/kg bw (active ingredient)
Remarks: Dose calculated based on density of 0.94 and active ingredient level of 27.72%. No controls; feeding *ad libitum*; rabbits weighed 2.1-2.4 kg; observations: mortality/clinical signs after removal of the dressing and daily until day 14; body weights on days 0 and 14; necropsies on day 14.

Results

Value:	Operator	Lower	Upper	Unit
	>	520	n/a	mg/kg bw

Remarks: Clinical: erythema, desquamation, fissuring, eschar formation, exfoliation of skin in all animals Necropsy results: stomach irritation, red spots or petechiae on lungs and tan colored lungs.

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2A

Remarks: Number of animals too small (6 total).
Minor comments: Specific gravity of test substance was not reported; it was determined to be 0.94 from another source. No data on body weights on day 14.
Time of clipping of fur not indicated.

Reference

Source Reference: The Procter & Gamble Company, 1978D.

(b)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: 27.5%
Carbon Chain Length Distribution:
Remarks: Balance is water.

Method

GLP: no data
Report/Study Year: 1978
Report/Study Number: IRDC 191-200
Method/Guideline Followed: Other
Analytical Monitoring: no
Test Type: LD50
Species: Rabbit
Strain: New Zealand white
Sex: male/female
Vehicle: other
Number of Animals per Dose: 6
Doses: Single dose of 2 ml/kg = 520 mg/kg bw (active ingredient)
Remarks: Guideline not specified. Dose calculated from density of 0.94 and active ingredient level of 27.5%. Test substance applied 'as produced' to shaved areas (~25% of body surface) on backs of animals; occluded, 24 hours. Observations at 24 h and daily thereafter for 14 days for pharmacotoxic signs, dermal irritation and mortality. Gross necropsy for all animals at end of 14 day observation period.

Results

Value:	Operator	Lower	Upper	Unit
	>	520	n/a	mg AO/kg bw

Remarks: Result expressed in terms of active ingredient. No deaths occurred. All animals appeared normal throughout 14 day observation period, except 1 female with impaired use of hind

leg days 2-14 and 1 male with diarrhea on day 13. Observations: erythema - moderate to marked but predominantly marked; edema - slight to moderate but predominantly moderate; atonia - none to marked but predominantly moderate; desquamation none to moderate but predominantly moderate as of day 10; coriaceousness - none to marked but predominantly moderate to marked after day 10; fissuring - none to moderate but predominantly slight to moderate. Varying degrees of subcutaneous hemorrhaging, blanching and exfoliation (0 to 5 animals, depending on observation day) and eschar formation in 4 to 6 animals after day 2.

Data Quality

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 2A

Remarks: Insufficient information to determine whether this is a guideline study. Minor comment: Specific gravity of test substance was not reported; it was determined to be 0.94 from another source.

Reference

Source Reference: The Procter & Gamble Company, 1978C.

(c)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: 28%

*Carbon Chain Length
Distribution:* 0.85% C10 and lower; 81.19% C12; 15.76% C14; 2.20% C16

Remarks: Balance is water.

Method

GLP: no data

Report/Study Year: 1978

Report/Study Number: IRDC 191-188

*Method/Guideline
Followed:* other

Analytical Monitoring: no

Test Type: LD50

Species: rabbit

Strain: New Zealand white

Sex: male/female

Vehicle: other

Number of Animals
per Dose: 6

Doses: Single dose of 2 ml/kg = 530 mg/kg bw (active ingredient)

Remarks: Guideline not specified. Dose calculated based on density of 0.94 and active ingredient level of 28%. Test substance applied 'as produced' to shaved areas (~25% of body surface) on backs of animals; occluded, 24 hours. Observations at 24 h and daily thereafter for 14 days for pharmacotoxic signs, dermal irritation and mortality. Gross necropsy for all animals at end of 14 day observation period.

Results

Value:	Operator	Lower	Upper	Unit
	>	530	n/a	mg AO/kg bw

Remarks: Result expressed in terms of active ingredient. One death due to pneumonia. Observations: erythema - moderate to marked but predominantly marked after day 7; edema - slight to moderate; atonia - none to marked but predominantly slight to moderate after day 2; desquamation none to moderate but predominantly slight to moderate as of day 8; coriaceousness - none to marked but predominantly slight to moderate after day 3; fissuring - none to moderate but predominantly slight to moderate after day 8. Progressive subcutaneous hemorrhaging and eschar formation (3 out of 5 animals on day 14), exfoliation in 1 animal.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2A

Remarks: Insufficient information to determine whether this is a guideline study. Minor comment: Specific gravity of test substance was not reported; it was determined to be 0.94 from another source.

Reference

Source Reference: The Procter & Gamble Company, 1978B.

5.2.1 SKIN IRRITATION

(a)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Carbon Chain Length Distribution: C10-16

Method

GLP: no

Report/Study Year: 1983

Report/Study Number: SDA101

Method/Guideline Followed: other

Species: human
Concentration: 0.2%
Remarks: Guideline not indicated. No experimental detail provided. Dose was 0.2%. Vehicle not reported.

Results

Result: not irritating
Classification: not irritating

Data Quality

Reliability (Klimisch): 4B
Remarks: Secondary literature.

Reference

Source Reference: TSCA ITC, 1983.

(b)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: not indicated
Carbon Chain Length Distribution: C10-16

Method

GLP: no
Report/Study Year: 1983
Report/Study Number: SDA101
Method/Guideline Followed: other
n/a
Species: rabbit
Vehicle: no data
Remarks: Secondary literature. No specifics reported.

Results

Result: irritating
Classification: irritating

Data Quality

Reliability (Klimisch): 4B

Reference

Source Reference: TSCA ITC, 1983.

5.2.2 EYE IRRITATION

(a)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: 28%
Carbon Chain Length Distribution: 81.3% C12; 16.1% C14; 2.6% C16
Remarks: Balance is water.

Method

GLP: no data
Report/Study Year: 1978
Report/Study Number: IRDC 191-189
Method/Guideline Followed: Draize Test
Species: rabbit
Vehicle: water
Number of Animals: 9

Dose:

Value	Unit
0.1	ml

Remarks: New Zealand White rabbits; 4 males and 5 females in 3 groups of 3.
Right eye was treated and held closed for about 1 second. Left eye served as untreated control for each animal. Group II was washed with 20 ml lukewarm water about 4 seconds after dosing.
Group I - 'as produced'; unwashed eye
Group II - 'as produced'; washed eye
Group III - 10% (w/w) solution in distilled water; unwashed eye
Follow up examinations after 1 hour and 1, 2, 3, 4, 7, 14, 21, 28, 35 days after dosing except for Group III where last observation was 21 days after dosing.

Results*Result:* irritating*Classification:* irritating

Remarks: Group I MAS = 61.0, calculated from day 21 results. Extremely irritating.
Group II MAS = 38.8, calculated from day 3 results. Extremely irritating.
Group III MAS = 23.7, calculated from 1 hour results. Moderately irritating.
MAS = Maximum Average Score out of maximum possible score of 110.
'As produced' test substance and 10% (w/v) solution are primary eye irritants.

Data Quality*Flags:* Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Remarks: Guideline study

Reference

Source Reference: The Procter & Gamble Company, 1978G.

Other References: Draize, J.H. (1959)

(b)

Test

Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: 27.84%

Remarks: Balance is water.

Method

GLP: no data

Report/Study Year: 1978

Report/Study
Number: Springborn 3029.235

Method/Guideline
Followed: Draize Test

Species: rabbit

Vehicle: water

Number of Animals: 6

Dose:	Value	Unit
	0.1	ml

Remarks: New Zealand White rabbits; 2 males and 4 females in 2 groups of 3.
Right eye was treated and held closed for about 1 second. Left eye served as untreated control. Group I was not rinsed. Group II was rinsed with about 20 ml lukewarm tap water approx. 4 seconds after dosing.
Follow up examinations after 1 hour and 1, 2, 3, 4, 7, 14, 21, 28 and 35 days after dosing.
'As produced' test substance.

Results

Result: irritating

Classification: irritating

Remarks: Group I MAS = 30.0, calculated from day 1 results.
Group II MAS = 13, calculated from day 1 results.
Vascularization (=invasion of cornea by blood vessels) of the eyes in 4 out of 6 animals.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Remarks: Guideline study

Reference

Source Reference: The Procter & Gamble Company, 1978H. Rabbit Eye Irritation Study of P0434.

Other References: Draize, J.H. (1959)

(c)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: 27.5%

Carbon Chain Length Distribution: 81.2% C12; 17.3% C14

Remarks: Balance is water.

Method

GLP: no data

Report/Study Year: 1978

Report/Study Number: IRDC 191-187

Method/Guideline Followed: Draize Test

Species: rabbit

Vehicle: water

Number of Animals: 9

Dose:

Value	Unit
0.1	ml

Remarks: New Zealand White rabbits; 5 males and 4 females in 3 groups of 3.
Right eye was treated and held closed for about 1 second. Left eye served as untreated control for each animal. Group II was washed with 20 ml lukewarm water about 4 seconds after dosing.
Group I - 'as produced'; unwashed eye
Group II - 'as produced'; washed eye
Group III - 10% (w/w) solution in distilled water; unwashed eye
Follow up examinations after 1 hour and 1, 2, 3, 4, 7, 14, 21, 28, 35 days after dosing except for Group III where last observation was 14 days after dosing.

Results

Result: irritating

Classification: irritating

Remarks: Group I MAS = 60.0, calculated from day 7 results. Extremely irritating.
Group II MAS = 45.7, calculated from day 3 results. Severely irritating.
Group III MAS = 18.3, calculated from day 1 results. Moderately irritating.
MAS = Maximum Average Score out of maximum possible score of 110.
'As produced' test substance is primary eye irritant; 10% (w/w) solution is probable primary eye irritant.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Reference

Source Reference: The Procter & Gamble Company, 1978F.

Other References: Draize, J.H. (1959)

(d)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: not relevant

Carbon Chain Length Distribution: C10-16

Method

GLP: no

Report/Study Year: 1983

Report/Study Number: SDA101

**Method/Guideline
Followed:** other

Species: rabbit

Vehicle: no data

Remarks: No experimental details given. Substance tested 'as produced' and at 1.4%.

Results

Result: moderately irritating

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature.

Reference

Source Reference: TSCA ITC, 1983.

5.3 SENSITIZATION

(a)

Test Substance

CAS Number: 70592-80-2
Identity: dodecyldimethylamine oxide
Purity: 27.72%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: No
Report/Study Year: 1978
Report/Study Number: 78-837-21
Method/Guideline Followed: Buehler method
Analytical Monitoring: no
Test Type: delayed contact hypersensitization
Vehicle: none
Number of Animals: 30; Test = 20 (10 male, 10 female); Control = 10 (5 male, 5 female)
Species: Guinea Pig, Hartley albino strain
Remarks: Study conducted prior to effective date of GLP regulations.
Protocol modified from the procedure of Buehler (1965).
Induction: The upper left quadrant of the back was clipped with electric clippers. The following day, a 20 x 20 mm Webril patch moistened with 0.4 ml of 'as produced' test substance was placed on the clipped areas of 20 test animals, for 6 hours. Patches were reapplied weekly to the same, freshly clipped areas, for 3 consecutive weeks.
Irritation screen: a screening study was conducted during the induction phase with 4 additional animals and 1, 2, 5 and 10%(v/v) of test substance, to determine the highest non-irritating concentration that could be used at induction. Depilated animals were scored for erythema severity using a 0-3 scale, 24 and 48 h post-challenge.
Challenge: After a two-week rest period, test and control animals were challenged with a 10% (v/v) solution on a fresh application site for 6 hours.

Results

Result: no evidence of sensitization
Classification: not sensitizing

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2A

Reference

Source Reference: The Procter & Gamble Company, 1978E.

Other References: Buehler EV, 1965.

(b)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Carbon Chain Length Distribution: C10-16

Method

GLP: no

*Report/Study
Year:* 1983

*Report/Study
Number:* SDA101

Test Type: no data

Vehicle: no data

Species: human

Remarks: Dose is 0.2%; no distinction made between challenge and induction. No information about the vehicle or the guideline followed.

Results

Result: not sensitizing

Classification: not sensitizing

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature. Insufficient detail provided.

Reference

Source Reference: TSCA ITC, 1983.

(c)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: not given

Carbon Chain Length Distribution: C10-16

Method

GLP: no
Report/Study Year: 1983
Report/Study Number: SDA101
Vehicle: no data
Species: guinea pig
Remarks: No details are provided in this review. The dose is stated as 2.8%, vehicle not specified. No distinction between challenge and induction dose.

Results

Result: not sensitizing
Classification: not sensitizing

Data Quality

Reliability (Klimisch): 4B
Remarks: Secondary literature. Insufficient information given.

Reference

Source Reference: TSCA ITC, 1983.

(d)

Test Substance

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: not given
Carbon Chain Length Distribution: C10-16

Method

GLP: no
Report/Study Year: 1983
Report/Study Number: SDA101
Method/Guideline Followed: other
Test Type: no data
Vehicle: no data
Species: human
Remarks: Dose was 0.25%. No distinction made between induction and challenge. No further details were provided in the report.

Results

Result: not sensitizing

Classification: not sensitizing

Data Quality

Reliability (Klimisch): 4B

Remarks: Secondary literature.

Reference

Source Reference: TSCA ITC, 1983.

5.4 REPEATED DOSE TOXICITY

(a)

Test Substance

CAS Number: 70592-80-2

Identity: C12-14 amine oxide; C10-16 dimethyl amine oxide

Purity: The test substance is a liquid hand dishwashing product containing 3% C12-14 amine oxide, 23% C12-14 alkylethoxylate sulphate, 5% ethanol, 5% alkyl sulfate. Balance is water.

Carbon Chain Length Distribution: C10-16, predominantly C12 and C14

Method

GLP: Yes

Report/Study Year: 1987

Report/Study Number: Springborn 3029.1381

Method/Guideline Followed: Not stated. Similar to OECD 411.

Test Type: Subchronic (91-day) dermal toxicity

Species: Rabbit

Strain: New Zealand White

Sex: Male/female

Route of Administration: Dermal

Exposure Period: 6-hours per day 5 days per week; for 91-days

Doses: 0.5, 1.0 and 2.5% (w/v) of the formula containing 3% AO; this corresponds to 0.30, 0.60 and 1.5 mg a.i./kg bw of the C12-14 amine oxide.

Control Group: Treated with vehicle (deionized water)

Remarks: Each dosage group contained 5 males and 5 females. Young adult animals (2-3 kg body weight) were used in the study. All dosing solutions were prepared in deionized water. All animals were dosed with 2ml/kg bw of dosing solutions. Solutions were distributed over shaved backs of the test animals using a glass rod. Study was conducted to assess the overall dermal profile of a formulation that happened to contain amine oxide, rather than toxicity of

amine oxide specifically. Doses were selected to provide a substantial exaggeration from the consumer dishwashing concentration (i.e., approximately 0.12% dishwashing detergent in a sink of water).

Dermal scoring was conducted prior to each application of test material. Animals were observed once daily for general appearance, behavior and pharmacotoxic signs. Body weights were recorded weekly. Blood samples were taken prior to the first dose and at necropsy. Hematologic evaluations included: total leukocyte count, erythrocyte count, hemoglobin, hematocrit, platelet count, differential leukocyte count, mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration. Animals were sacrificed at the completion of the 91-day dosing period. At necropsy, any gross pathologic changes were noted, liver, kidney and total body weights were obtained, and organs were preserved for microscopic examination. The following organs were examined: lung, heart, aorta, tongue, trachea, esophagus, thyroid/parathyroid, submandibular and ileocolic lymph nodes, stomach, liver, gall bladder, duodenum, jejunum, ileum, caecum, colon, rectum, urinary bladder, kidney, adrenal, psoas muscle, thymus, spleen, pancreas, bone with marrow, skin at the test material application site, brain, spinal cord, sciatic nerve, submandibular salivary gland, pituitary, eye and reproductive organs.

Statistical methods: Appropriate data were analyzed using one-way analysis of variance. The data were then subjected to Bartlett's test for homogeneity of variances. A least significant difference criterion was used if Bartlett's test was not significant. Wilcoxon's rank sum test was used if Bartlett's test was significant.

Results

Remarks: NOEL > 2.5% or > 1.50 mg a.i./kg bw, for systemic effects. However, the 2.5% dosage level produced slight, transient skin irritation at the site of test material application on days 6-28 and day 73 of the study.

There were no treatment-related deaths throughout the course of the study. There were no signs of systemic toxicity or compound-related microscopic or macroscopic lesions in any dosage group. Mean body weights and organ weights at study termination did not differ significantly among various groups in either study. A slight but statistically significant increase in the mean corpuscular hemoglobin was noted in male animals in the 0.5% dosage group, and slight increases in platelet, eosinophil and basophil counts were noted in females in the 1% treatment group. Since there were no dose response relationships, these findings were considered incidental. There were no other hematologic changes in treated animals. Males in the 1% dosage group showed a slight increase in absolute and relative liver weights. However, since this was not dose dependent, and since there were no microscopic changes in the livers of these animals, this was not considered biologically significant.

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restriction

Reference

Source Reference: The Procter & Gamble Company, 1987.

Other References: Petersen, D.W. 1988.

(b)

Test Substance

CAS Number: 70592-80-2

Identity: C12-14 amine oxide; C10-16 dimethyl amine oxide

Purity: The test substance is a liquid hand dishwashing product containing 5% C12-14 amine oxide, 27% C12-14 alkylethoxylate sulphate, 5% ethanol. Balance is water.

Carbon Chain Length Distribution: C10-16, predominantly C12 and C14

Method

GLP: Yes

Report/Study Year: 1986

Report/Study Number: IRDC 191-1064

Method/Guideline Followed: Not stated. 28-Day similar to OECD 410, except animals dosed on abraded skin. 91-Day similar to OECD 411.

Test Type: Repeated dose (28-day) dermal toxicity and Subchronic (91-day) dermal toxicity

Species: Rabbit

Strain: New Zealand White

Sex: Male/female

Route of Administration: Dermal

Exposure Period: 6-hours per day 5 days per week; for 28- or 91-days

Doses: 28-day study: 0.1, 0.5 and 1.0% (w/v) of the formula containing 5% AO corresponding to 0.1, 0.5 and 1.0 mg a.i./kg bw of C12-14 amine oxide

91-day study: 0.5, 1.0 and 2.5% (w/v) of the formula containing 5% AO corresponding to 0.5, 1.0 and 2.5 a.i. mg/kg bw of C12-14 amine oxide

Control Group: One for each study treated with vehicle (deionized water)

Remarks: Each dosage group contained 5 males and 5 females. Studies were conducted to assess the overall dermal profile of formulations that happened to contain amine oxide, rather than toxicity of amine oxide specifically. Doses were selected to provide a substantial exaggeration from the consumer dishwashing concentration (i.e., approximately 0.12% dishwashing detergent in a sink of water).

Animals were 3 1/2 months old at the start of the study. All dosing solutions were prepared in deionized water. For the 28-day study, animals were dosed on shaved skin that had been abraded with the blunt end of a scalpel blade. For the 91-day study, animals were dosed on intact, shaved skin. All animals were dosed with 2ml/kg bw of dosing solutions. On each animal the test site was an area approximately 15 cm wide from the shoulder to the rump. Solutions were distributed over the entire test site area using a glass rod.

Dermal scoring was conducted prior to each application of test material. Animals were observed once daily for general appearance, behavior and pharmacotoxic signs, and twice daily for mortality. Body weights were recorded weekly.

Blood samples were taken prior to the first dose and at necropsy. Hematologic evaluations included: total leukocyte count, erythrocyte count, hemoglobin, hematocrit, platelet count, differential leukocyte count, mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration.

Animals were sacrificed at the completion of the 28- or 91-day dosing period. At necropsy, any gross pathologic changes were noted, liver, kidney and total body weights were obtained, and organs were preserved for microscopic examination. The following organs were examined: lung, heart, thoracic aorta, tongue, trachea, esophagus, thyroid/parathyroid, submandibular and ileocolic lymph nodes, stomach, liver with gall bladder, duodenum, jejunum, ileum, caecum, colon, rectum, urinary bladder, kidney, adrenal, psoas muscle, thymus, spleen, pancreas, femur with marrow, skin at the test material application site, brain, thoracolumbar spinal cord, sciatic nerve, pituitary, eye and reproductive organs.

Statistical methods: Differences in body weights, organ:body weight ratios, and hematological data were analyzed. Bartlett's test for homogeneity of variances was performed to determine the appropriate statistical test to use for treatment-control comparisons. A least significant difference criterion was used if Bartlett's test was not significant. Wilcoxon's rank sum test was used if Bartlett's test was significant.

Results

Remarks: 28-day (abraded skin) study: NOEL = 1% or 1 mg a.i./kg bw of C12-14 amine oxide, for systemic effects. However, the 1% dosage level produced local dermal effects, i.e., slight to moderate erythema and edema at the test application site. There were no localized dermal effects at dosage levels of 0.5% or 0.1%.

91-day (intact skin) study: NOEL = 2.5% or 2.5 mg a.i./kg bw of C12-14 amine oxide, for systemic effects. However, the 2.5% dosage level produced slight to moderate erythema, edema, atonia and desquamation at the test application site. Slight and slight to moderate erythema were also noted at the application sites in the 0.5% and 1.0% groups, respectively.

There were no treatment-related deaths throughout the course of the study. There were no signs of systemic toxicity, hematologic changes or compound-related microscopic or macroscopic lesions in any dosage group. Mean body weights and organ weights at study termination did not differ significantly among various groups in either study. The low dosage group in the 91-day study (0.5%) showed a slight but significant increase in liver:body weight ratio. However, since this was not dose dependent, and since there were no microscopic changes in the livers of these animals, this was not considered biologically significant.

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restriction.

Reference

Source Reference: The Procter & Gamble Company, 1986.

Other References: Petersen, D.W. 1988.

(c)

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides

Purity: 27.72%

Carbon Chain Length Distribution: C10-16

Remarks: Balance is water

Method

GLP: no

Report/Study Year: 1980

*Report/Study
Number:* P0434

*Method/Guideline
Followed:* EPA OPP 82-1

Test Type: Sub-chronic

Species: rat

Strain: Sprague-Dawley

Sex: male/female

*Route of
Administration:* oral feed

Exposure Period: 91 days

Doses: 0.0 - 0.1 - 0.2 - 0.4% a.i. in diet
0.1% in diet = 63 mg a.i./kg/day (males) and 80 mg a.i./kg/day(females)
0.2% in diet = 112 mg a.i./kg/day (males) and 150 mg a.i./kg/day(females)
0.4% in diet = 236 mg a.i./kg/day (males) and 301 mg a.i./kg/day(females)

Accuracy of dose preparation was 93-110% of nominal (control samples contained 0.07% a.i.); homogeneity: CV: 7-20%.

Control Group: yes

Remarks: Rats, 6 weeks old, males 168-231 g.; females 124-174 g.
20 animals per sex per dose level.
Diets prepared weekly; homogeneity determined in batches from weeks 1, 2 and 5.
Observations: Mainly as required by OECD 408 with the exception of: clinical signs were recorded weekly, functional observations, haematology (no platelets and blood clotting potential), clinical chemistry (no protein, sodium, potassium, and cholesterol), organ weights (not for adrenals, epididymides, uterus, thymus and spleen) and histopathological observations in control and animals treated at 0.2% (of the high dosed animals only 10/sex were examined).

Results

	Operator	Lower	Upper	Unit
NOAEL	=	80	n/a	mg a.i./kg
LOAEL	=	150	n/a	mg a.i./kg

Remarks: Statistically significant decreases in mean body weight were noted in group 4 males and group 3 and 4 females.

Overall body weight gain during the study:

0.0 %– 288 g (males)	272 g (females)
0.1 %– 273 g (males) / 95% ctrl	276 g (females) / 98% ctrl
0.2 % – 266 g (males) / 92% ctrl	249 g (females) / 82% ctrl
0.4% - 218 g (males) / 76% ctrl	242 g (females) / 74% ctrl

Ophthalmoscopic examination revealed lenticular opacities pertaining to the posterior cortex of the lens in males at the mid and high dose, but these effects have not been observed in chronic feeding studies. No compound-related changes were noted in hematology and blood chemistry parameters with the exception of alkaline phosphatase. No compound-related changes were noted in the urinalysis performed. No compound-related gross pathological findings were noted in the treated animals compared to controls. No consistent differences were noted in organ weights and organ to body weight ratios when compared to controls. No compound-related histopathological changes were observed in test animals compared to controls.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2A

Remarks: No analysis for stability and contaminated control diet (notes 2, 3).
1. The ALP level of control animals was rather low for rats of this strain and age. Since the increased level of ALP in males was not related with dose and at the 0.1% dose level in males, no concomitant other adverse effects were reported, no toxicological relevance is attributed to this increased level of ALP.
2. Diet was prepared once weekly. No analyses for stability under storage conditions (4°C) were provided.

3. Contamination of the control diet with the test substance was seen, due to the fact that the test substance was mixed with the powdery diet. No measures were taken to prevent contamination. This renders the values found with control animals less reliable.

4. The study was reported to be a range finding study for a long term study.

Reference

Source Reference: The Procter & Gamble Company, 1980.

5.7 CARCINOGENICITY

(a)

Test Substance

<i>CAS Number:</i>	70592-80-2
<i>Identity:</i>	Amines, C10-16-alkyldimethyl, N-oxides; alkyldimethylamine Oxide (ADAO)
<i>Purity:</i>	27%
<i>Carbon Chain Length Distribution:</i>	C10-16 (majority C12)

Method

<i>GLP:</i>	yes
<i>Report/Study Year:</i>	1979
<i>Report/Study Number:</i>	297-320
<i>Method/Guideline Followed:</i>	other
<i>Species:</i>	mouse
<i>Strain:</i>	CD-1
<i>Sex:</i>	male/female
<i>Route of Administration:</i>	dermal
<i>Exposure Period:</i>	two years
<i>Frequency of Treatment:</i>	Applied to clipped skin once daily for three days per week, for 104 weeks
<i>Doses:</i>	Group 1: 0.1 ml distilled water; Group 2: 0.1 ml of 0.05% ADAO; Group 3: 0.1 ml of 0.13% ADAO; Group 4: 0.1 ml of 0.26% ADAO on a 100% (w/v) active basis
<i>Remarks:</i>	Doses were selected based on a 13 week study in which the high dose caused epidermal proliferative changes. ADAO (0.1 ml) was administered to the clipped dorsal skin of 75 males and 75 females per group. Mortality checks were made twice daily and the mice were observed for gross signs at each treatment period. Individual body weights were recorded weekly

during the first 13 weeks of the study and monthly thereafter. At the end of the study, all survivors were killed and microscopic evaluations of tissues were performed.

Study was conducted in conformance with "Good Laboratory Regulations in non-clinical laboratory studies" - Federal Register V43, No. 247, 12/22/78, Docket No. 76 N-0400. Tissues examined microscopically included skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction, thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder, pancreas, spleen, kidneys, adrenals, bladder, seminal vesicles, prostate, testes or ovaries and uterus, eyes, brain, pituitary, and spinal cord.

Results

Result: negative

Remarks: Males in the high dose group had decreased overall survival. In contrast, females at the mid-dose group had increased survival rates compared to controls. These random values were within historical variability of controls and were not considered treatment related. There were no statistical differences in group average body weights, organ weights, and organ to body weight ratios among treated animals compared to controls. Compound related skin irritation (diffuse acanthosis and hyperkeratosis) was observed microscopically in the high dose group of mice. No skin tumors were observed in any group. There were no compound-related skin or systemic neoplasms in the study. There was no evidence of a carcinogenic response after chronic percutaneous administration of ADAO.

Data Quality

*Reliability
(Klimisch):* 1A

Remarks: This study was conducted prior to the adoption of GLP compliance standards. However, it was conducted in conformance with "Good Laboratory Regulations in non-clinical laboratory studies" - Federal Register V43, No. 247, 12/22/78, Docket No. 76 N-0400.

Reference

Source Reference: The Procter & Gamble Company, 1979A.

Other References: Published in:

Cardin CW, Domeyer BE and Bjorkquist L, 1985.

Statistical methods used:

(1) Snedecor, GW and WG Cochran (1980) ;

(2) Miller R.G. Jr. (1966) ;

(3) Bartlett, M.S. (1937)

(4) Hollander, M. and D.A. Wolfe (1973);

(5) Draper, N.R. and W. Smith (1966);

(6) Siegel, S. (1956).

(b)

Test Substance

<i>CAS Number:</i>	70592-80-2
<i>Identity:</i>	Amines, C10-16-alkyldimethyl, N-oxides; alkyldimethylamine oxide (ADAO)
<i>Purity:</i>	27%
<i>Carbon Chain Length Distribution:</i>	C10-16 (majority C12)

Method

<i>GLP:</i>	no
<i>Report/Study Year:</i>	1979
<i>Report/Study Number:</i>	P0571
<i>Method/Guideline Followed:</i>	other
<i>Species:</i>	rat
<i>Strain:</i>	Charles River
<i>Sex:</i>	male/female
<i>Route of Administration:</i>	oral feed
<i>Exposure Period:</i>	two years
<i>Frequency of Treatment:</i>	Rats received feed containing the test substance daily for 104 weeks.
<i>Doses:</i>	Rats (60 males and 60 females per group) received 0, 0.01, 0.1 and 0.2 % of the test compound (100% (w/v) active basis) in the diet daily for two years.
<i>Remarks:</i>	<p>This study was conducted from 1979-1981, with the study report issued in 1983. The study was reviewed for quality assurance in accordance with the US FDA's GLP Regulations of June 20, 1979. Charles River CD rats were used for this study. The rats were observed twice daily for signs of overt toxicity and for mortality. Detailed observations were recorded weekly. At approximately 15 weeks, a random selection of rats was inspected for dacryoadenitis at weekly intervals. Individual body weights were recorded weekly for the first 14 weeks of study, biweekly for the next 12 weeks and monthly thereafter. Individual food (with test material) consumption measurements were recorded weekly. Ophthalmoscopic examinations were conducted for all rats once during the pretest period and at 3, 6, 12, 16, 19, 22 and 24 months of the study. Hematological, biochemical, and urinalysis tests were conducted on all rats to be sacrificed at 52 weeks of the study.</p> <p>Hematological and biochemical tests were conducted for all rats at study termination. Tissues examined microscopically included skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, costochondral junction, thymus, larynx, trachea, lungs and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, adrenals, bladder, seminal vesicles, prostate, testes or ovaries and uterus, eyes, brain, pituitary, and spinal cord.</p>

Results

Result: negative

Remarks: There were no significant differences in survival at 104 weeks. There were no significant, compound-related differences in mean feed consumption, clinical chemistry or ophthalmology. Body weights were lower in treated males compared to controls at several time points during the study. Mean body weights were significantly lower at the 0.2% dose in both males and females. Increases in kidney, heart, ovary and brain weights (females) and brain weight (males) occurred in the high dose animals due to decreases in mean body weight. Mean absolute liver weight was decreased statistically in males at 0.1%, but was within the range of normal biologic variability and therefore was not considered related to test substance administration. There were no compound-related effects on histopathic examination. There was no evidence of a carcinogenic response after chronic dietary administration of the test substance.

Data Quality

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 1B

Remarks: This study was conducted prior to the adoption of GLP compliance standards. However, it was reviewed and found acceptable by the laboratory's Quality Assurance Department in accordance with the US FDA's Good Laboratory Practice Regulations of June 20, 1979.

Reference

Source Reference: The Procter & Gamble Company, 1979B.

Other References: Published in
Cardin CW, Domeyer BE and Bjorkquist L, 1985.
Statistical methods used: Snedecor, GW and WG Cochran (1967).

5.8.1 TOXICITY TO FERTILITY

Test Substance

CAS Number: 70592-80-2

Identity: Amines, C10-16-alkyldimethyl, N-oxides, dodecyl dimethyl amine oxide (DDAO)

Purity: 25%

*Carbon Chain Length
Distribution:* C10-16 (majority C12)

Method

GLP: no

Report/Study Year: 1966

*Report/Study
Number:* SDA103

*Method/Guideline
Followed:* other

Test Type:	other
Species:	rat
Strain:	other
Sex:	male/female
Route of Administration:	oral feed
Exposure Period:	two years
Frequency of Treatment:	Rats received feed containing the test substance daily for 104 weeks.
Male Premating Exposure Period:	100 days
Female Premating Exposure Period:	100 days
Test Duration:	Two year feeding study; reproduction study extended into the second litter of the third generation.
Number of Generation Studies:	3
Doses:	Rats (20 males and 20 females per group) received 0, 0.005, 0.02 and 0.1% of the test substance in the diet daily for two years total.
Control Group:	yes, concurrent no treatment
Remarks:	<p>This study was initiated in 1966, with the study report issued in 1970. Charles River CD rats were used in this study. This reproduction study was conducted as part of a larger, two-year chronic feeding study. Twenty males and twenty females from each test group and control group were mated for the reproduction study, which extended into the second litter of the third generation. F1a litters were examined, weighed, and sacrificed at weaning and the parents (F0) were remated 10 days after the last litter was weaned.</p> <p>Twenty males and twenty females from the second litter (F1b) of each group were selected at weaning to continue on their respective diets. F0 animals were continued on their diets for the remainder of the two years. Body weights and food consumption for the weanlings were recorded at weekly intervals for eight weeks.</p> <p>When F1b animals were 100 days old, they were mated, and 10 days after weaning, their first litters (F2a) were remated as in the parental generation. The same procedure was repeated to produce two additional litters of the third generation (F3a, F3b). Parents from the F1b and F2b generation were sacrificed and autopsied after the second litters were destroyed. The F3b animals were necropsied at 21 weeks and their tissues were studied histologically.</p> <p>Gross autopsies were performed and organ to body weight comparisons were made on liver and kidneys. Histological examination was performed on liver, heart, spleen, pancreas, adrenal, stomach, small intestine, urinary bladder, gonads and mesenteric lymph nodes. Blood was analyzed for total red blood cell count, total white blood cell count, differential white blood cell count, hemoglobin, and hematocrit.</p>

Results

NOEL:		Operator	Lower	Upper	Unit
	Parental:	=	0.1	n/a	%
	F1 Offspring:	=	0.1	n/a	%
	F2 Offspring:	=	0.1	n/a	%

Remarks: Average body weight gain, food consumption and feed efficiency of the test and control groups of each parental generation (F1, F1b, F2b) were not significantly different from each other during the initial 8-week feeding periods. Organ weights, body weights, organ/body weight ratios and averages of hematologic values obtained from the parents at necropsy were within normal ranges for animals of that age. Histologic examinations of selected tissues were non-remarkable.

None of the pups produced by any of the matings showed evidence of gross abnormalities. There was no indication at any point in the study that the test material had any effect with regard to fertility, reproduction, gestation, partition, lactation, or growth of the resulting offspring.

Data Quality

*Reliability
(Klimisch):* 3B

Remarks: This study was initiated prior to the adoption of GLP compliance standards. Only a summary describing the study methods and results was available. No raw data were available.

Reference

Source Reference: The Procter & Gamble Company, 1966.

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY**Test Substance**

CAS Number: 70592-80-2
Identity: Amines, C10-16-alkyldimethyl, N-oxides
Purity: 32%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: yes
Report/Study Year: 1999
*Report/Study
Number:* ARGUS 916-025

<i>Method/Guideline Followed:</i>	EPA OTS 798.4900
Species:	rat
Strain:	Sprague-Dawley
Sex:	female
Route of Administration:	gavage
Exposure Period:	14 days
Frequency of Treatment:	daily from day 6 to 19 of gestation
Test Duration:	until day 20 of gestation
Doses:	25, 100 and 200 mg a.i./kg bw
Control Group:	yes, concurrent vehicle
<i>Remarks:</i>	<p>Rats weighed 218-262 g. and were 72 days old.</p> <p>Dosing solutions prepared weekly.</p> <p>Statistical methods: Bartlett's test, ANOVA, Dunnett's, Kruskal-Wallis, Dunn.</p> <p>Procedures: Female rats were mated with untreated males (1/1) from the same strain. The day of detection sperm was defined as day 0 of gestation. Females were treated daily from day 6 to 19 of gestation inclusive. Mortality was checked twice daily. Clinical symptoms of dams were noted on day 0 and twice daily (pre-dose and 1 hour post-dosing) from day 6 to 20. Body weights were recorded on day 0 and daily from day 6 to 20. Food consumption was determined on day 0, 6, 9, 12, 15, 18 and 20. All females were subjected to macroscopic examination on day 20 or on day of death. The uteri were removed, weighed and examined for no. of <i>corpora lutea</i>, no. of implantation sites and no. and location of fetuses and resorptions. Fetuses were inspected on total number, sex, weight and external, visceral (1/2 of fetuses) and skeletal (1/2 of fetuses).</p>

Results

NOAEL	Operator	Lower	Upper	Unit
Maternal:	=	25	n/a	mg a.i./kg bw

NOAEL	Operator	Lower	Upper	Unit
Teratogenicity:	=	25	n/a	mg a.i./kg bw

<i>Remarks:</i>	Dose (mg a.i./kg bw)	0	25	100	200	D R
Maternal data						
Mortality	0/25	0/25	0/25	2/25*		
Clinical signs (A)			+	+		x
Body weight - day 11-20				dc		
Body weight gain - day 6-20			dc	dc		x
Corrected body weight				dc		

(corrected for uterus weight)					
Relative food intake - day 0-20			dc	dc	x
Uterus weight				dc	
Necropsy	No treatment related effects				
No. of pregnant females	24/25	25/25	24/25	24/25	
No. of <i>corpora lutea</i> and implantation sites /dam	No treatment related effects				
Pre-implantation loss	No treatment related effects				
Post-implantation loss/resorptions				i	
Embryonic / fetal resorptions				i/-	
No. live fetuses/ dam				d	
Fetal data					
No. of litters included in evaluations	24	25	24	22	
Fetal weight				dc	
External examination / sex	No treatment related effects				
Anomalies -visceral	No treatment related effects				
- skeletal (B)		+**	+	x	

* One animal died on day 18 of gestation due to an intubation error, the other female died spontaneously on day 19 of gestation.

Local alopecia was observed in all dose groups. Other clinical signs included excessive salivation, rales, urine-stained abdominal fur, brown or red peri-oral substance, laboured breathing, gasping, brown peri-nasal substance and soft liquid faeces. In the animals that died additionally emaciation, brown or red peri-vaginal substance, chromorhinorrhea, brown peri-anal substance, dehydration and ungroomed coat was seen. One animal of the high dose group had a mass in the left axilla.

A dose-dependent increase in the litter incidence of fetuses showing bifid thoracic vertebrae centra. Delayed ossification became apparent at the 200 mg a.i/kg group.

** The apparent skeletal effects observed at 25 mg/k/day were attributed to non-adverse, normal developmental variations.

dc = decrease

"+" = present

DR = dose-response

"x" = dose-response relationship present

"i" = inconclusive

Data Quality

Reliability
(Klimisch): 2A

Remarks: No analyses for stability (note 1).

1. No information on stability of the test substance in aqueous solution was provided. Since solutions were stored for about one week, it can not be excluded that the actual amount administered was less than the reported doses.
2. In females dosed at 100 mg a.i./kg the incidence of bifid thoracic was significantly increased compared with control females, but it remained within historical control ranges. Incomplete ossification was seen in all treatments groups and controls. However, at 200 mg a.i./kg the incidence was increased compared to controls and historical controls.
3. Minor remark During the first two weeks of the study temperature incidentally was outside the ranges of the protocol.

Reference

Source Reference: The Procter & Gamble Company, 1999C.

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SIDS DOSSIER

CAS NO. 68955-55-5

Amines, C12-18-alkyldimethyl, N-oxides

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2571-88-2
2530-44-1
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
70592-80-2
85408-49-7
85408-48-6
93962-62-0

Sponsor Country: United States

Date: July, 2006

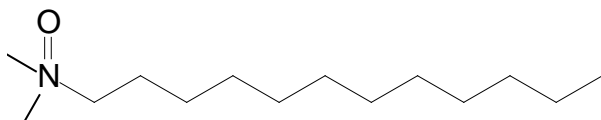
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number** 68955-55-5
- B. Name (IUPAC name)**
- C. Name (OECD name)** Amines, C12-18-alkyldimethyl, N-oxides
- D. CAS Descriptor**
- E. EINECS-Number** 2732812
- F. Molecular Formula Unspecified**
- G. Structural Formula**

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

Representative C₁₂ dimethyl amine oxide



- H. Substance Group** Amine Oxides category
- I. Substance Remark** None
- J. Molecular Weight** Unspecified

1.02 OECD INFORMATION

- A. Sponsor Country:** United States
- B. Lead Organization:** Environmental Protection Agency (EPA)

Contact person: Oscar Hernandez
Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
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C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
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USA
Tel: (202) 662-2523
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Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of

these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyl-oxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

Alkyl (C₁₀₋₁₈) dimethyl amine oxide,
N,N-dimethyl alkyl amine oxide (C₁₂₋₁₈)

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

- (a) United States
26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)
Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.
- (b) Europe
(i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tonnes (AISE, 2002)
- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

<u>Labelling</u>	dangerous for the environment ; irritating
Remarks:	following CESIO recommendations (CESIO, 2000; CESIO, 2003)
<u>Classification</u>	Very toxic to aquatic organisms (R50); Irritating to skin (R38); Risk of serious damage to eyes (R41)
Remarks:	following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or other applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%

Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS**A. Options for Disposal**

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

2. PHYSICAL/CHEMICAL PROPERTIES

2.2 BOILING POINT

Test Substance

CAS Number: 68955-55-5
Identity: Amines, C12-18-alkyldimethyl, N-oxides
Chain Length Distribution: C12-18

Method

GLP: no
Report/Study Year: 2001
Method/Guideline Followed: other

Results

Decomposition: yes
Remarks: Amine oxides undergo thermal decomposition between 90 and 200°C.

Data Quality 2D (Klimisch) – Reliable with restrictions.

Reference Kirk Othmer Encyclopedia of Chemical Technology, 2001

3. ENVIRONMENTAL FATE AND PATHWAYS**3.5 BIODEGRADATION****Test Substance**

CAS Number: 68955-55-5
Identity: Amines, C12-18-alkyldimethyl, N-oxides
Purity: 29.8%
Chain Length Distribution: C12-18
Remarks: Balance (70.2%) is water

Method

GLP: no
Report/Study Year: 1990
Report/Study Number: CRL F90054
Test Type: aerobic
Method/Guideline Followed: OECD Guideline 301 D
Inoculum: activated sludge, domestic, non-adapted
Inoculum Acclimated: no
Control Substance: Acetic acid, sodium salt
Test Substance Initial Concentration: 2 mg/l as test substance
Remarks: Test duration 28 days. Biodegradation measured as O₂ consumption. pH 6.5 at 28 days. Negative control (8 flasks). Positive control (6.7 mg/l, 8 flasks).

 Readily biodegradable according to EU criterion for this test, which requires 60% of theoretical O₂ consumed within 10-day window after the 10% mark is reached (OECD Guideline 301D).

Results

Kinetics Measured as: other

<i>Kinetics of Test Substance:</i>	Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
	5	day(s)	=	11	n/a
	15	day(s)	=	66	n/a
	28	day(s)	=	82	n/a
<i>Kinetics of Control Substance:</i>	Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
	5	day(s)	=	75	n/a
	28	day(s)	=	87	n/a

Half Life: *Mineralization:* not determined
Primary Biodegradation: n/a
Result: readily biodegradable
Degradation Products: not measured

Data Quality	2B (Klimisch) - Basic data given, comparable to guideline. It was not clear from the report whether oxygen consumption due to nitrification was taken into account, but this is would not be expected to change the results significantly. Critical study for SIDS endpoint
Reference	Akzo Nobel Chemicals, 1990I

4. ECOTOXICITY**4.1.1 TOXICITY TO FISH (ACUTE)****Test Substance**

CAS Number: 68955-55-5
Identity: Amines, C12-18-alkyldimethyl, N-oxides
Purity: 29.8%
Chain Length Distribution: C12-18
Remarks: Balance is water

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: CRL F90064
Method/Guideline Followed: Directive 92/69/EEC, C.1; OECD Guideline 203
Test Type: acute, semi-static, renewal at 48 hrs
Analytical Monitoring: no
Limit Test: no
Species: *Brachydanio rerio*
Exposure Period: 96 hours
Remarks: 10 fish per concentration. No aeration; Temp. 21-25 °C; hardness 232 mg/l as CaCO₃; pH 8.2; 12 hours light; unfed; loading probably 0.9 g fish/l. Positive control substance K₂Cr₂O₇. Nominal test concentrations 0.0 - 0.6 - 1.1 - 1.7 - 3.0 mg/l (active ingredient).

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
LC50:	c	=	1.5	n/a
LC50	c	=	1	2.1

Remarks: No analyses. Biodegradation study (Biodegradability of CAS RN 68955-55-5 showed decrease in test substance of 11% over 5 days. Therefore it is believed that the test substance was present at concentrations of at least 80% of nominal values during this 4 day test. Dissolved oxygen was at times lower than recommended but this had no effect on the study results. Individual fish weights reported as 2.8 grams probably should be 0.28 grams.

Data Quality 1A (Klimisch)
Critical study for SIDS endpoint

Reference Akzo Nobel Chemicals, 1990C

4.4 TOXICITY TO MICROORGANISMS e.g. BACTERIA**Test Substance**

CAS Number: 68955-55-5
Identity: Amines, C12-18-alkyldimethyl, N-oxides
Purity: 30%
Chain Length Distribution: C12-18
Remarks: Balance is water.
51% C12; 22% C14; 13% C16; 12% C18; 2% C20

Method

GLP: yes
Report/Study Year: 1993
Report/Study Number: 930601HM
Method/Guideline Followed: OECD Guideline 209
Analytical Monitoring: no
Species: activated sludge
Exposure Period: 3 hours
Remarks: Unadapted activated sludge biomass from municipal sewage treatment plant; test substance concentration range [58-1000 mg/l]; reference substance Cu(II)sulfate pentahydrate; room temperature 20 +/- 2°C; dark; measured endpoint is respiration inhibition; EC values determined by Probit analysis.

Results

Unit: mg/l

	Measured/Computed	Operator	
EC50:	c	=	214
EC20	c	=	100
EC80	c	=	457

Remarks: 95% confidence interval for EC50 was [77 - 595] mg/l; reference substance results as expected.

Data Quality 1A

Reference Hoechst AG, 1993B

6. REFERENCES

AISE 2002. Amine Oxide Survey of European Use and Exposure Information Provided by Member Companies.

AISE/HERA, 2002. HERA Task Forces Human Habits and Uses Tables.

AISE/HERA, 2005. Human & Environmental Risk Assessment on ingredients of European household cleaning products (HERA): Amine Oxides. (*in preparation*).

Akzo Nobel Chemicals, 1990I. Biodegradation of CAS RN 68955-55-5.

Akzo Nobel Chemicals, 1990C. Acute toxicity of CAS RN 68955-55-5 to fish.

CESIO Report, April 2003. CESIO Recommendation For The Classification And Labelling Of Surfactants As "Dangerous For The Environment"

CESIO Report, January 2000. CESIO recommendations for Anionic and Non-ionic surfactants (including 1990 recommendations on Quaternary Ammonium Compounds and Fatty Amines and Derivatives).

CTFA, 2003. Cosmetics, Toiletries, and Fragrance Association survey of amine oxide uses in personal care products

Hoechst AG, 1993B. Prüfung auf Bakterientoxizität im Belebtschlamm-Respirationshemmtest von (CAS RN 68955-55-5).

Japanese Soap and Detergent Association, 2002. Survey of amine oxide production, 2001- 02.

Kirk Othmer Encyclopedia of Chemical Technology, 2001, 4th edition, CD-ROM, John Wiley and Sons, ISBN: 0-471-15158-0

Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting

Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 2605-79-0

Decanamine, N,N-dimethyl-, N-oxide

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2571-88-2
2530-44-1
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

Sponsor Country: United States
Date: July, 2006

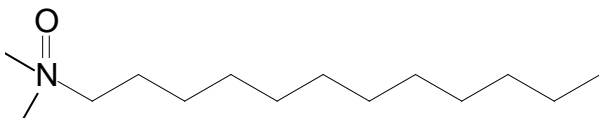
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number 2605-79-0
- B. Name (IUPAC name)
- C. Name (OECD name) Decanamine, N,N-dimethyl-, N-oxide
- D. CAS Descriptor
- E. EINECS-Number
- F. Molecular Formula C₁₂H₂₇NO
- G. Structural Formula

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

C₁₂ dimethyl amine oxide



- H. Substance Group Amine Oxides category
- I. Substance Remark None
- J. Molecular Weight 201 grams/mole
- ### 1.02 OECD INFORMATION
- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
- Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460
U.S.A.
Tel: (202) 564-7641
Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

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1500 K Street, N.W., Suite 300
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Tel: (202) 662-2523
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The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in

the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (*at 20°C and 1.013 hPa*)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

1-Decanamine, N,N-dimethyl-, N-oxide
1-Decanamine, N,N-dimethyl-, N-oxide
1-Decanamine, N,N-dimethyl-N-oxide
N,N-Dimethyldecylamine oxide
N,N-Dimethyldecylamine N-oxide

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

- (a) United States
26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)
Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.
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- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in other applications.

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The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
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spray)	
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

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It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion

of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS

A. Options for Disposal

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

2. PHYSICAL-CHEMICAL DATA**2.0.1 EPISuite™ ESTIMATION OF PHYSICAL/CHEMICAL PROPERTIES****Test Substance**

CAS Number: **2605-79-0**
Identity: N,N-dimethyldecylamine N-oxide
Purity: not relevant
Carbon Chain Length Distribution: C10
Remarks:

Method

GLP: n/a
Report/Study Year: n/a
Method/Guideline Followed: EPIWIN
Remarks: All estimates apply to the pure, dry substance and not their solutions in water.

Results

	Estimate	Exp. Database Match
Molecular Weight (grams/mole):	201.36	
Water Solubility (mg/l):	30.35	n/a
Octanol Water Partition Coefficient (Log Kow):	3.69	n/a
Bioconcentration Factor (Log BCF):	2.142	
Boiling Point (°C):	403.41	n/a
Melting Point (°C):	152.60	n/a
Vapor Pressure(Pa):	4.57E-5	n/a
Henry's Law Constant (atm/(mole/m ³)):	2.994E-9	n/a
Atmospheric Oxidation Half-Life (hours):	5.26	n/a
Soil Adsorption Coefficient (Log Koc):	3.739	

Remarks: Trends analysis, based on the N,N-Dimethyl Amine Oxides:
 For every extension of two –CH₂– units to the alkyl chain

- Water solubility decreases by 1 order of magnitude.
- The Log Kow increases by ~ 1 unit [or the octanol/water partition coefficient increases by 1 order of magnitude].
- The Log BCF increases by ~ 0.25 units [or the BCF nearly doubles; it increases by a factor of 1.8].
- The boiling point increases by ~ 23°C, although these are theoretical values, as most surfactants decompose before they boil.
- The melting point increases by ~ 15°C.

- The Log Koc increases by ~ 0.5 unit [or the soil adsorption coefficient increases by a factor of 3].

Trends are similar for the N,N-Dihydroxyethyl Amine Oxides - The substitution of the nitrogen with two hydroxyethyl groups (vs. the two methyl groups of the N,N-Dimethyl Amine Oxides) increases the hydrophilicity of the hydrophilic head group of the surfactant. This results in a higher water solubility, a lower Log Kow and a lower Koc.

CAS #	Chain Length	MW (g/mole)	Water Sol. (mg/l)	Log Kow	Log BCF	BP (°C)	MP (°C)	VP (Pa)	Log Koc	Atm Oxidation half-life (hours)
N,N-Dimethyl Amine Oxides										
2605-79-0	C10	201.36	30.35	3.69	2.142	403.41	152.60	4.57E-5	3.739	5.26
1643-20-5	C12	229.41	3.13	4.67	⁽¹⁾ 2.392	426.62	167.95	2.09E-5	4.271	4.71
3332-27-2	C14	257.46	0.32	5.66	2.655	449.82	183.30	1.48E-6	4.803	4.27
7128-91-8	C16	285.52	0.032	6.64	2.911	473.03	198.65	2.59E-7	5.334	3.90
N,N-Dihydroxyethyl Amine Oxides										
2530-44-1	C12	289.46	29.89	3.13	1.712	536.73	229.76	3.39E-12	2.360	2.36
14048-77-2	C18	373.63	0.029	6.08	2.481	606.35	262.28	7.45E-15	3.955	2.04
93962-62-0	C18:1	371.61	0.045	5.86	2.815	609.93	263.95	5.43E-15	3.955	2.95

⁽¹⁾The value obtained by KOWWIN is 1.989, which is an outlier. The expected value, based on linear extrapolation between C10, C14 and C16 amine oxide, is 2.392.

Data Quality

Reliability (Klimisch): 2D

Remarks: Reliable with restrictions.

Reference

Source Reference: EPIWIN, Version 3.0

2.1 MELTING POINT

Test Substance

CAS Number: **2605-79-0**

Identity: C10 amine oxide; decylamine oxide

Carbon Chain Length: C10

Distribution:

Remarks:

Method

GLP: n/a

Report/Study Year: 1985

Results

Value:		Lower (°C)	Upper (°C)
	=	133	136

Data Quality

*Reliability
(Klimisch):* 2A

Remarks: Reliable with restrictions. Acceptable, well-documented publication/study report, meets basic scientific principles.

Reference

Source Reference: Devinsky et al, 1985.

3. ENVIRONMENTAL FATE AND PATHWAYS**3.5 BIODEGRADATION****Test Substance**

CAS Number: **2605-79-0**

Identity: N,N-dimethyldecylamine N-oxide
decyldimethylaminoxide

Purity: 30.6%

Carbon Chain Length Distribution: C10

Remarks: Balance (69.4%) is water

Method

GLP: yes

Report/Study Year: 1997

Report/Study Number: 970303GS

Test Type: aerobic

Method/Guideline Followed: OECD Guideline 301 E

Inoculum: activated sludge, domestic, non-adapted

Inoculum Acclimated: no

Control Substance: Acetic acid, sodium salt

Value	Unit	Expressed as
29	mg/l	DOC

Remarks: Test duration 28 days. Biodegradation measured as DOC. pH 7.41. Temp. 24 °C. Negative control (2 flasks). Positive control (38 mg DOC/l, 1 flask). Constant stirring, no aeration.

Readily biodegradable according to EU criterion for this test, which requires 70% of DOC removed in 28 days (OECD Guideline 301E).

Results

Kinetics Measured as: DOC (Dissolved Organic Carbon)

Kinetics of Test Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
5	day(s)	=	18	n/a
7	day(s)	=	72	n/a
14	day(s)	=	89	n/a
21	day(s)	=	94	n/a
28	day(s)	=	97	n/a

	Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
<i>Kinetics of Control Substance:</i>	5	day(s)	=	93	n/a
	28	day(s)	=	96	n/a

*Half Life:**Mineralization:* not determined*Primary Biodegradation:* n/a*Result:*

readily biodegradable

Degradation Products:

not measured

Data Quality*Flags:* Critical study for SIDS endpoint*Reliability
(Klimisch):* 1A*Remarks:* No abiotic controls were included, but this did not affect the reliability rating because biodegradation is the only way that organic carbon could be removed under the test conditions.**Reference**

Source Reference: Th. Goldschmidt AG, 1997..

6. REFERENCES

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Cosmetics, Toiletries and Fragrances Association, 2003. Cosmetics, Toiletries, and Fragrance Association survey of amine oxide uses in personal care products.

Devinsky F, Leitmanova A, Lacko I, Krasnec L, 1985. Amine Oxides -XIII: Iodine complexes with non-aromatic amine oxides. *Tetrahedron* 41(23): 5707-5709.

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Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting.

Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

Th. Goldschmidt AG, 1997. Biologische Abbaubarkeit im modifizierten OECD Screening Test. Report # 970303GS.

SIDS DOSSIER

CAS NO. 7128-91-8

Hexadecanamine, N,N-dimethyl-, N-oxide

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2571-88-2
2530-44-1
2605-79-0
3332-27-2
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

Sponsor Country: United States

Date: July, 2006

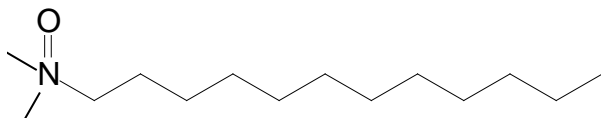
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number 7128-91-8
- B. Name (IUPAC name)
- C. Name (OECD name) Hexadecanamine, N,N-dimethyl-, N-oxide
- D. CAS Descriptor
- E. EINECS-Number 2304290
- F. Molecular Formula C₁₈H₃₉NO
- G. Structural Formula

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

C₁₂ dimethyl amine oxide



- H. Substance Group Amine Oxides category
- I. Substance Remark None
- J. Molecular Weight 285 grams/mole

1.02 OECD INFORMATION

- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
Address U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M

Washington, DC 20460
U.S.A.
Tel: (202) 564-7641
Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the

longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

1-Hexadecanamine, N,N-dimethyl-, N-oxide,
Hexadecyldimethylamine N-oxide,
N,N-Dimethylhexadecylamine N-oxide

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

- (a) United States
26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)
Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.
- (b) Europe
(i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tonnes (AISE, 2002)
- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in industrial, institutional and commercial applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%

Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion

of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS

A. Options for Disposal

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

2. PHYSICAL-CHEMICAL DATA

2.0.1 EPISuite™ ESTIMATION OF PHYSICAL/CHEMICAL PROPERTIES

Test Substance

CAS Number: 7128-91-8
Identity: hexadecyldimethylamine N-oxide
Purity: not relevant
Chain Length Distribution: C16
Remarks:

Method

GLP: n/a
Report/Study Year: n/a
Method/Guideline Followed: EPIWIN
Remarks: All estimates apply to the pure, dry substance and not their solutions in water.

Results

	Estimate
Molecular Weight (grams/mole):	285.52
Water Solubility (mg/l):	0.032
Octanol Water Partition Coefficient (Log Kow):	6.64
Bioconcentration Factor (Log BCF):	2.911
Boiling Point (°C):	473.03
Melting Point (°C):	198.65
Vapor Pressure(Pa):	2.59E-7
Henry's Law Constant (atm/(mole/m ³)):	2.28E-8
Atmospheric Oxidation Half-Life (hours):	3.90
Soil Adsorption Coefficient (Log Koc):	5.334

Remarks Trends analysis, based on the N,N-Dimethyl Amine Oxides:
: For every extension of two –CH₂– units to the alkyl chain

- Water solubility decreases by 1 order of magnitude.
- The Log Kow increases by ~ 1 unit [or the octanol/water partition coefficient increases by 1 order of magnitude].
- The Log BCF increases by ~ 0.25 units [or the BCF nearly doubles; it increases by a factor of 1.8].
- The boiling point increases by ~ 23°C, although these are theoretical values, as most surfactants decompose before they boil.
- The melting point increases by ~ 15°C.
- The Log Koc increases by ~ 0.5 unit [or the soil adsorption coefficient increases

by a factor of 3].

Trends are similar for the N,N-Dihydroxyethyl Amine Oxides - The substitution of the nitrogen with two hydroxyethyl groups (vs. the two methyl groups of the N,N-Dimethyl Amine Oxides) increases the hydrophilicity of the hydrophilic head group of the surfactant. This results in a higher water solubility, a lower Log Kow and a lower Koc.

CAS #	Chain Length	MW (g/mole)	Water Sol. (mg/l)	Log Kow	Log BCF	BP (°C)	MP (°C)	VP (Pa)	Log Koc	Atm Oxidation half-life (hours)
N,N-Dimethyl Amine Oxides										
2605-79-0	C10	201.36	30.35	3.69	2.142	403.41	152.60	4.57E-5	3.739	5.26
1643-20-5	C12	229.41	3.13	4.67	⁽¹⁾ 2.392	426.62	167.95	2.09E-5	4.271	4.71
3332-27-2	C14	257.46	0.32	5.66	2.655	449.82	183.30	1.48E-6	4.803	4.27
7128-91-8	C16	285.52	0.032	6.64	2.911	473.03	198.65	2.59E-7	5.334	3.90
N,N-Dihydroxyethyl Amine Oxides										
2530-44-1	C12	289.46	29.89	3.13	1.712	536.73	229.76	3.39E-12	2.360	2.36
14048-77-2	C18	373.63	0.029	6.08	2.481	606.35	262.28	7.45E-15	3.955	2.04
93962-62-0	C18:1	371.61	0.045	5.86	2.815	609.93	263.95	5.43E-15	3.955	2.95

⁽¹⁾The value obtained by KOWWIN is 1.989, which is an outlier. The expected value, based on linear extrapolation between C10, C14 and C16 amine oxide, is 2.392.

Data Quality

Reliability
(Klimisch): 2D

Remarks: Reliable with restrictions

Reference

Source: EPIWIN, Version
Reference: 3.0.

2.1 MELTING POINT

Test Substance

CAS Number: **7128-91-8**
Identity: C16 amine oxide; hexadecylamine oxide
Chain Length Distribution: C16
Remarks:

Method

GLP: n/a
Report/Study Year: 1985

Results

Value:

	Lower (°C)	Upper (°C)
=	126	130

Data Quality*Reliability (Klimisch):*

2A

Remarks:

Reliable with restrictions. Acceptable, well-documented publication/study report, meets basic scientific principles.

Reference

Source Reference:

Devinsky et al, 1985.

3. ENVIRONMENTAL FATE AND PATHWAYS**3.5 BIODEGRADATION**

(a)

Test Substance

CAS Number: **7128-91-8**
Identity: hexadecyldimethylamine N-oxide
Purity: 25%
Chain Length Distribution: >94% C16
Remarks: Balance (75%) is water

Method

GLP: no
Report/Study Year: 1995
Report/Study Number: 94-0100-41
Test Type: aerobic
Method/Guideline Followed: OECD Guideline 301 A (new version)
Inoculum: predominantly domestic sewage, non-adapted
Inoculum Acclimated: no
Control Substance: Benzoic acid, sodium salt

*Test Substance**Initial Concentration:*

Value	Unit	Expressed as
10	mg/l	DOC

Remarks: Test duration 11 days. Continuous shaking. Temp 20-22 °C. pH 7.2 at start. Negative control (2 flasks). Positive control (1 flask) Na benzoate 20 mg/l as DOC.

Results

Kinetics Measured as: DOC (Dissolved Organic Carbon)

Kinetics of Test Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
4	day(s)	=	0	n/a
7	day(s)	=	94	n/a
11	day(s)	=	100	n/a

Kinetics of Control Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
4	day(s)	=	98	n/a
7	day(s)	=	99	n/a

Half Life:

Mineralization: not determined

Primary Biodegradation: n/a

Result: other
Degradation Products: not measured

Data Quality

Reliability (Klimisch): 3B
Remarks: Report consisted of an abstract rather than a full report. The information was confined to what is included in this summary. No abiotic control, no toxicity control. Only 1 test flask.

Reference

Source Reference: Hoechst AG, 1995.

(b)

Test Substance

CAS Number: **7128-91-8**
Identity: hexadecyldimethylamine
N-oxide
Purity: 25%
Chain Length Distribution: >94% C16
Remarks: Balance (75%) is water.

Method

GLP: no
Report/Study Year: 1994
Report/Study Number: A 538 a
Test Type: aerobic
Method/Guideline Followed: OECD Guideline 301 E
Inoculum: predominantly domestic sewage, non-adapted
Inoculum Acclimated: no
Control Substance: Benzoic acid, sodium salt

Test Substance
Initial Concentration:

Value	Unit	Expressed as
68	mg/l	Test substance
7.6	mg/l	DOC

Remarks: Test duration 28 days. Continuous shaking. Temp. 202 °C. pH 7.2 at start. Negative control (2 flasks). Positive control (1 flask).

After 7 days the % biodegradation decreases, which indicates something wrong with the analyses.

Results

Kinetics Measured as: DOC (Dissolved Organic Carbon)

Kinetics of Test Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
4	day(s)	=	35	n/a
7	day(s)	=	44	n/a
14	day(s)	=	25	n/a
21	day(s)	=	17	n/a
28	day(s)	=	28	n/a

Kinetics of Control Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
4	day(s)	=	90	n/a
28	day(s)	=	93	n/a

*Half Life:**Mineralization:* not determined*Primary Biodegradation:* n/a*Result:*

other

Degradation Products:

not measured

Data Quality*Reliability (Klimisch):*

4C

Remarks:

Report consisted of an abstract rather than a full report. The information was confined to what is included in this summary. No abiotic control, no toxicity control. Only 1 test flask. The % biodegradation increases up until day 7, then decreases for the next 3 weeks (dissolved organic carbon increased?). It is not possible to draw any conclusions from this test, other than that the test substance biodegraded to some extent (44% DOC removed by day 7).

Reference

Source Reference:

Hoechst AG, 1994A.

4. ECOTOXICITY

4.1.1 TOXICITY TO FISH (ACUTE)

(a)

Test Substance

CAS Number: **7128-91-8**
Identity: hexadecyldimethylamine N-oxide
Purity: 24.9%
Chain Length Distribution: C16
Remarks: Balance is water

Method

GLP: yes
Report/Study Year: 1992
Report/Study Number: CRL F92041
Method/Guideline Followed: Directive 92/69/EEC, C.1
Test Type: acute, semi-static
Limit Test: no
Species: *Brachydanio rerio*

Exposure Period:

Value	Unit
96	hours

Remarks:

Method essentially same as OECD Guideline 203. Aeration. Seven fish per test concentration. Daily renewal of test solutions. Nominal test conc. 0 - 0.25 - 0.45 - 0.80 - 1.44 - 2.54 mg/l (active ingredient). Hardness 209 mg/l as CaCO₃. pH 8.0-8.2. O₂ > 91% saturated. Temp. 21-22 °C. 12 hours light. Loading 0.7 g fish/l. Statistics by Spearman Karber binomial test method.

Results*Unit:* mg/l

	Measured/Computed	Operator	Lower	Upper
LC50:	c	=	0.6	n/a
LC50	c	=	0.45	0.8

Remarks:

No analyses were done; results are reported as nominal concentrations. Biodegradation study (61788-90-7; Kurzbericht über die Prüfung der biologischen Abbaubarkeit gemäss dem modif. OECD Screening-Test 301 E und DIN ISO 7827 (1993) / A 538 a) showed decrease in test substance conc. of 35% over 4 days. The conc. of test subst. may have fallen below 80% in the course of this test.

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2B
Remarks: No information on renewal frequency or frequency of physical measurements (O₂, pH, temp.)

Reference

Source Reference: Akzo Nobel,
1992C.

(b)

Test Substance

CAS Number: **7128-91-8**
Identity: hexadecyldimethylamine N-oxide
Purity: 25%
Chain Length Distribution: >94% C16
Remarks: Balance (75%) is water

Method

GLP: no
Report/Study Year: 1994
Report/Study Number: 94.0656
Method/Guideline Followed: Directive 92/69/EEC, C.1
Test Type: acute, static
Analytical Monitoring: no
Limit Test: no
Species: *Brachydanio rerio*
Remarks: Method essentially same as OECD 203 (7 fish per concentration). Nominal test conc. 0 - 0.25 - 0.55 - 1.25 mg/l (active ingredient). pH 7.8-8.3. O₂ 76-108% of saturation. Temp. 21-23 °C.

Results

Unit: mg/l

	Measured/Computed	Operator	
LC50:	c	=	0.37

Data Quality

Reliability (Klimisch): 4A
Remarks: Only brief summary available.

Reference

Source Reference: Hoechst AG, 1994B.

4.2.1 AQUATIC INVERTEBRATES TOXICITY (ACUTE)

(a)

Test Substance

CAS Number: **7128-91-8**
Identity: hexadecyldimethylamine N-oxide
Purity: 24.9%
Chain Length Distribution: C16

Method

GLP: no
Report/Study Year: 1994
Report/Study Number: CRL F94174
Method/Guideline Followed: OECD Guideline 202
Test Type: acute, static
Analytical Monitoring: no
Limit Test: no
Species: *Daphnia magna*

Exposure Period:

Value	Unit
48	hour(s)

Remarks: Daphnids < 24h old; 4 reps./conc. x 5 daphnids/rep. = 20 daphnids per conc. Nominal conc. 0.0 - 0.26 - 0.47 - 0.83 - 1.51 - 2.73 mg/l (active ingredient). No vehicle. Hardness 214 mg/l as CaCO₃; pH 8.1-8.2; temp. 19-20 °C; O₂ 95-100% saturated. Observe immobility at 0, 24 and 48h.

Results*Unit:* mg/l

	Measured/Computed	Operator	Lower	Upper
EC50:	c	=	0.65	n/a
EC50	c	=	0.58	0.73

Remarks: No analyses. A biodegradation study (CAS RN 61788-90-7 Kurzbericht über die Prüfung der biologischen Abbaubarkeit gemäss dem modif. OECD Screening-Test 301 E und DIN ISO 7827 (1993) / A 538 a) showed decreasing conc. of 22-25% in 2 days. Test substance conc. may have fallen below 80% of nominal in course of test. No information about feeding.

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2B

Remarks: No analyses. No feeding information.

Reference

Source Reference: Akzo Nobel N.V., 1994.

4.3 TOXICITY TO AQUATIC PLANTS e.g. ALGAE

Test Substance

CAS Number: **7128-91-8**
 Identity: Hexadecyldimethylamine N-oxide
 Purity: 24.9%
 Carbon Chain Length Distribution: C16
 Remarks: Balance is water

Method

GLP: no
 Report/Study Year: 1992
 Report/Study Number: CRL F92121
 Method/Guideline Followed: OECD Guideline 201
 Analytical Monitoring: no
 Species: *Selenastrum capricornutum*
 Endpoint: other

Exposure Period:	Value	Unit
	72	hour(s)

Remarks: Endpoints are biomass and growth rate. 3 reps./conc. and 6 controls. Initial cell density 25000 cells/ml. Nominal conc. 0.0 - 0.015 - 0.03 - 0.06- 0.12 - 0.24 mg/l (active ingredient). Temp. 20-22 °C. Continuous illumination. Shaken. Observe cell density at 0, 24, 48 and 72h spectrophotometrically. Statistics: least squares method, Fieller's theorem.

Results

Unit: mg/l

	Measured/Computed	Operator	
EC10:	c	=	0.016
EC50:	c	=	0.060
EC20	c	=	0.025

Remarks: EC50 in table stands for ErC50. NOEC not determined. No analyses. Biodegradation study (CAS RN 61788-90-7; Kurzbericht über die Prüfung der biologischen Abbaubarkeit gemäss dem modif. OECD Screening-Test 301 E und DIN ISO 7827

(1993)/A 538 a) showed decrease in test subst. of 22-35% in 2-4 days. Individual cell counts, growth in controls and pH not reported.

Results calculated according to Bruce and Versteeg (1992), in mg/l:

	EC50	EC20	EC10
Biomass	0.060	0.025	0.016
Growth Rate	0.11	0.05	0.032

Data Quality

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 2C

Remarks: Reliable with restrictions. Comparable to guideline study with acceptable restrictions. Individual cell counts, pH and growth in controls not reported. Test concentrations probably stable, but some degradation may have occurred.

Reference

Source Reference: Akzo Nobel Chemicals, 1992F.

Other Reference: Bruce and Versteeg, 1992

4.4 TOXICITY TO MICROORGANISMS e.g. BACTERIA

Test Substance

CAS Number: 7128-91-8

Identity: Hexadecyldimethylamine N-oxide

Purity: 25%

Carbon Chain Length Distribution: C16

Remarks: Balance is water

Method

GLP: not stated

Report/Study Year: 1994

Report/Study Number: 94-0100-13

*Method/Guideline
Followed:* DIN 38 412 Part 8

Species: *Pseudomonas putida*

Exposure Period:

Value	Unit
16.25	hours

Remarks: Concentration range tested was [500-1000] mg/l; 20-22°C; shaken continuously at 220 rpm; reference substance 2,4-dichlorophenol at 30 and 90 mg/l; negative (water) control; unacclimated biomass; endpoint is growth inhibition

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC10:	c	>	1000	n/a
EC50:	c	>	1000	n/a
EC90	c	>	1000	n/a

Data Quality*Reliability (Klimisch):* 2A*Remarks:* Results of control substance not reported. Summary report.**Reference**

Source Reference: Hoechst AG, 1994C.

6. REFERENCES

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- Hoechst AG, 1994B. Kurzbericht CAS RN 7128-91-8; Prüfung der akuten Toxizität am Fisch Zebraabärbling über 96 Stunden (*Brachydanio rerio*).
- Hoechst AG, 1994C. Prüfung der Schadwirkung von (CAS RN 7128-91-8) gegenüber Bakterien (Bakterientoxizität).
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- Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting.
- Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.
- Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 2571-88-2

Octadecanamine, N,N-dimethyl-, N-oxide

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2530-44-1
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

Sponsor Country: United States
Date: July, 2006

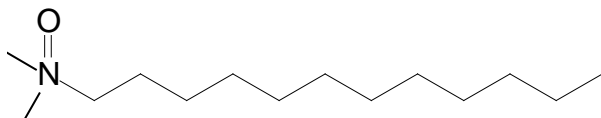
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number 2571-88-2
- B. Name (IUPAC name)
- C. Name (OECD name) Octadecanamine, N,N-dimethyl-, N-oxide
- D. CAS Descriptor
- E. EINECS-Number 2199195
- F. Molecular Formula C₂₀H₄₃NO
- G. Structural Formula

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

C₁₂ dimethyl amine oxide



- H. Substance Group Amine Oxides category
- I. Substance Remark None
- J. Molecular Weight

1.02 OECD INFORMATION

- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460

U.S.A.
Tel: (202) 564-7641
Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical

properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyl oxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

N,N, Dimethyloctadecylamine N-oxide
Octadecyldimethylamine oxide
Steryldimethylamine oxide

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

(a) United States

26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)

Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.

- (b) Europe
 - (i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
 - (ii) 21,570 metric tonnes (AISE, 2002)
- (c) Japan
 - 6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in industrial, institutional and commercial applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%

Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur

with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS

A. Options for Disposal

Remarks: Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

Reference:

B. Last Literature Search

Remarks: 2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

4. ECOTOXICITY

4.1.1 TOXICITY TO FISH (ACUTE)

(a)

Test Substance

CAS Number: 2571-88-2
Identity: N,N-dimethyloctadecylamine N-oxide
Purity: 24.4%
Carbon Chain Length Distribution: C18
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1992
Report/Study Number: CRL F92040
Method/Guideline Followed: Directive 92/69/EEC, C.1 and OECD Guideline 203
Test Type: acute, semi-static
Analytical Monitoring: no
Limit Test: no
Species: *Brachydanio rerio*

Exposure Period:

Value	Unit
96	hour(s)

Remarks: Method essentially same as OECD Guideline 203. Seven fish per test concentration. Aeration. Nominal test conc. 0 - 0.24 - 0.44 - 0.78 - 1.41 - 2.56 mg/l (active ingredient). Hardness 209 mg/l as CaCO₃. pH 7.9-8.2. O₂ > 90% saturated. Temp. 22-23 °C. 12 hours light. Loading 0.7 g fish/l. Statistics by Spearman Karber binomial test method.

Results

Unit: mg/l

	Measured/ Computed	Operator	Lower	Upper
LC50:	c	=	1.4	n/a
LC50	c	=	1	1.8

Remarks: No analyses; conc. of test substance may have decreased during test.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2B*Remarks:* No information on frequency of physical measurements (O₂, pH, temp.)**Reference**

Source Reference: Akzo Nobel, 1992A.

(b)

Test Substance*CAS Number:* **2571-88-2***Identity:* N,N-dimethyloctadecylamine N-oxide*Purity:* 24.4%*Carbon Chain Length Distribution:* C16*Remarks:* Balance is water**Method***GLP:* No*Report/Study Year:* 1992*Report/Study
Number:* CRL F92122*Method/Guideline
Followed:* OECD Guideline 201*Analytical
Monitoring:* No*Species:* *Selenastrum capricornutum**Endpoint:* Other

<i>Exposure Period:</i>	Value	Unit
	72	hour(s)

Remarks: 3 reps./conc. and 6 controls. Initial cell density 25,000 cells/ml. Standard OECD algal growth medium (OECD Guideline 201); hardness (Ca + Mg) dH 0.6 mmol/l. Nominal test concentrations 0.0 - 0.024 - 0.044 - 0.078 - 0.14 - 0.26 mg/l (active ingredient). Temp. 20-22 °C. Continuous illumination. Shaken. Cell density measurements at 0, 24, 48 and 72h (spectrophotometrically).

Results*Unit:* mg/l

	Measured/Computed	Operator	
EC10:	c	=	0.06
EC50:	c	=	0.10
EC20:	c	=	0.07

Remarks: NOEC not determined. No analyses. Individual cell counts not reported. No pH measurements reported. Growth in controls not reported.

Results calculated according to Bruce & Versteeg (1992), in mg/l:

	EC50	EC20	EC10
Growth Rate	0.14	0.10	0.08
Biomass	0.10	0.07	0.06

Data Quality

Flags: Critical study for SIDS endpoint

Reliability
(Klimisch): 2B

Remarks: Individual cell counts not reported. Growth in controls not reported. pH not reported. Concentrations were probably stable, but may have decreased during this test.

Reference

Source Reference: Akzo Nobel Chemicals, 1992E.

Other Reference Bruce and Versteeg, 1992

5. TOXICITY

5.2.1 SKIN IRRITATION

Test Substance

CAS Number: **2571-88-2**

Identity: Stearyl dimethylamine oxide; N,N-dimethyloctadecanamine N-oxide; C18 DMAO

Purity: 2.5% (w/w) amine oxide

Carbon Chain Length: C18

Distribution:

Remarks: Four skin lotions were tested, containing 2.5% C18 DMAO. Other ingredients were: 35% of either mineral oil or isopropyl palmitate, 1% cetyl alcohol, 1% lanolin, with or without 0.2% quaternary preservative (50:50 mixture of alkyl dimethyl benzyl ammonium chloride and alkyl dimethyl ethylbenzyl ammonium chloride); the balance was water. This test was designed to investigate the skin irritation that could be attributed to the quaternary preservatives.

Method

GLP: n/a

Report/Study Year: 1975

Report/Study Number: SDA198

Method/Guideline Followed: Draize method

Analytical Monitoring: no

Species: rabbits

Vehicle: skin lotion

Number of Animals: as specified in Draize method

Concentration: 2.5%

Exposure: 72 hours

Results

Result: not irritating

Classification: not irritating

Primary Dermal Irritation Index (PDII): 0

Remarks: Primary irritation index (PII) of the 4 lotions:
Lotion 1 (mineral oil, no quat) PII = 4
Lotion 2 (mineral oil, quat) PII = 6
Lotion 3 (isopropyl palmitate, no quat) PII = 0
Lotion 4 (isopropyl palmitate, quat) PII = 0
2.5% C18 Amine Oxide did not impact the irritation profile of these skin lotions.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; comparable to guideline study.

Reference

Source Reference: Like et al, 1975.

5.2.2 EYE IRRITATION**Test Substance**

CAS Number: **2571-88-2**

Identity: octadecyldimethylamine oxide; C18 DMAO

Purity: 2.5% (w/w)

Carbon Chain Length Distribution: C18

Remarks: Skin lotion containing 2.5% C18 DMAO. Other ingredients were: 35% isopropyl palmitate, 1% cetyl alcohol and 1% lanolin; the balance was water.

Method

GLP: n/a

Report/Study Year: 1975

Report/Study Number: SDA198

Method/Guideline Followed: Draize method

Species: Rabbits

Vehicle: skin lotion

Number of Animals: as specified in Draize method

Remarks: For rabbits with washed eye treatment, washing occurred 4 seconds after application.

Results

Result: not irritating

Classification: not irritating

Remarks: No irritation was observed in rabbits with washed or unwashed eyes.

Data Quality

Reliability (Klimisch): 1A

Remarks: Reliable without restriction; comparable to guideline study.

Reference

Source Reference: Like et al, 1975.

6. REFERENCES

AISE 2002. Amine Oxide Survey of European Use and Exposure Information Provided by Member Companies.

AISE/HERA 2002. HERA Task Forces Human Habits and Uses Tables.

AISE/HERA 2005. Human & Environmental Risk Assessment on ingredients of European household cleaning products (HERA): Amine Oxides. (*in preparation*).

Akzo Nobel Chemicals, 1992A. Acute toxicity of CAS RN 2530-44-1 to *Brachydanio rerio*.

Akzo Nobel Chemicals, 1992E. Toxicity of CAS RN 2571-88-2 to the freshwater alga *Selenastrum capricornutum*.

Bruce and Versteeg, 1992. Env. Toxicol. Chem. 11: 1485

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Japan Soap and Detergent Association, 2002. Japanese Soap and Detergent Association survey of amine oxide production, 2001-2002.

Kirk Othmer Encyclopedia of Chemical Technology, 2001, 4th edition, CD-ROM, John Wiley and Sons, ISBN: 0-471-15158-0

Like B, Sorrentino R, Petrocci A. 1975. Utility of amine oxides in oil/water cosmetic systems. J. Soc. Cosmet. Chem. 26: 155-168.

Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting.

Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 61788-90-7

Amine oxides, cocoalkyldimethyl

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2571-88-2
2530-44-1
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

Sponsor Country: United States
Date: July, 2006

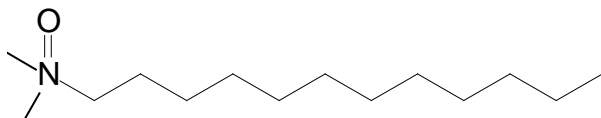
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number 61788-90-7
- B. Name (IUPAC name)
- C. Name (OECD name) Amine oxides, cocoalkyldimethyl
- D. CAS Descriptor
- E. EINECS-Number 2630169
- F. Molecular Formula Unspecified
- G. Structural Formula

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

C₁₂ dimethyl amine oxide



- H. Substance Group Amine Oxides category
- I. Substance Remark None
- J. Molecular Weight Unspecified
- 1.02 OECD INFORMATION
- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
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C. Name of Responder

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Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-(9Z)-

9-octadecenyloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [**X**]; organometallic []; petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [**X**] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

Amines, coco alkyldimethyl, N-oxides,
Amine oxides, cocoalkyldimethyl,
Amines, coco alkyldimethyl, N-oxide,
Coco alkyldimethylamines, N-oxides
N,N-dimethyl (coconut oil alkyl) amine oxide

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

- (a) United States
26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)
Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.
- (b) Europe
(i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tonnes (AISE, 2002)
- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in other applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%

Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use,

and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS

A. Options for Disposal

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

3. ENVIRONMENTAL FATE AND PATHWAYS

3.5 BIODEGRADATION

(a)

Test Substance

CAS Number: **61788-90-7**

Identity: Amines, coco alkyltrimethyl, N-oxides (C12-C14)alkyltrimethylamine oxide

Purity: 29.8%

Chain Length Distribution: C12-C14

Remarks: Balance (70.2%) is water.

Method

GLP: no

Report/Study Year: 1987

Test Type: aerobic

Method/Guideline Followed: OECD Guideline 301 D

Inoculum: domestic sewage, non-adapted

Inoculum Acclimated: no

Control Substance: Acetic acid, sodium salt

Test Substance Initial Concentration: 6.8 mg/l (as test substance)

Remarks: Continuously shaken. Duration 42 days. pH 6.7-7.1. Control without test substance. Negative control. Positive control Na acetate 14.6 mg/l, 3 flasks, 7 days. Toxicity control, Na acetate 6.8 mg/l + test substance 20.5 mg/l, 3 flasks each, 7 days.

Readily biodegradable according to EU criteria for this test, which would require at least 60% of theoretical O₂ consumed in 28 days (OECD Guideline 301D).

Results

Kinetics Measured as: COD (Chemical Oxygen Demand)

<i>Kinetics of Test Substance:</i>	Exposure Period	Exposure Unit	Operator	Lower (%)
	14	day(s)	=	89
	28	day(s)	=	93
	42	day(s)	=	94

<i>Kinetics of Control Substance:</i>	Exposure Period	Exposure Unit	Operator	Lower (%)
	7	day(s)	=	42

Result: readily biodegradable

Data Quality 2C (Klimisch) - Limited information on the controls. Compliance with OECD 301D could not be fully verified. Incubation temperature not given.
Critical study for SIDS endpoint

Reference Akzo Chemie, 1987

(b)

Test Substance

CAS Number: 61788-90-7

Identity: Amines, coco alkyldimethyl, N-oxides

Purity: not given

Chain Length Distribution: C12-18

Method

GLP: no

Report/Study Year: 1989

Report/Study Number: 41-89B

Test Type: aerobic

Method/Guideline Followed: OECD Guideline 301 E

Inoculum: domestic sewage, non-adapted

Inoculum Acclimated: no

Control Substance: Benzoic acid, sodium salt

Test Substance Initial Concentration:

Value	Unit	Expressed as
5	mg/l	DOC
40	mg/l	DOC

Remarks: Initial conc. was a range [5-40 mg/l as DOC]. Continuously shaken. Duration 28 days. Temp. 20-25 °C. Control without test substance.

Results

Kinetics Measured as: DOC (Dissolved Organic Carbon)

Kinetics of Test Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)
7	day(s)	=	15
14	day(s)	=	41
21	day(s)	=	53
27	day(s)	=	55
28	day(s)	=	57

Not readily biodegradable according to EU criteria for this test,

which would require at least 70% DOC removal in 28 days (OECD Guideline 301A).

Kinetics of Control Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)
14	day(s)	=	94
28	day(s)	=	98

Half Life:

Mineralization: not determined

Primary Biodegradation: n/a

Result:

other

Data Quality

4A (Klimisch) - The report consisted of an abstract of the test rather than a full report. The information was essentially confined to what is included in this summary. Protocol deviations: no abiotic control and no toxicity control. Only 1 flask with test substance.

Reference

Hoechst AG, 1989C

(c)

Test Substance

CAS Number:

61788-90-7

Identity:

Amines, coco alkyldimethyl, N-oxides

Purity:

25%

Chain Length Distribution:

C12-C18 (C12: 70%; C14: 30%)

Remarks:

Balance (75%) is water

Method

GLP:

no

Report/Study Year:

1995

Report/Study Number:

B152-2

Test Type:

aerobic

Method/Guideline Followed:

OECD Guideline 301 E

Inoculum:

domestic sewage, non-adapted

Inoculum Acclimated:

no

Control Substance:

Benzoic acid, sodium salt

Test Substance Initial Concentration:

55 mg/l (expressed as test substance)
14.3 mg/l DOC

Remarks:

Method equivalent to Directive 84/449 EEC. Water quality parameters pH 7.2 Temp. 28-22 °C. Continuous shaking. Test duration 28 days. Control without test substance (2 flasks). Positive control Na-benzoate at 20 mg DOC/l (1 flask).

Results

Kinetics Measured as:

DOC (Dissolved Organic Carbon)

Kinetics of Test Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)
4	day(s)	=	8.1
7	day(s)	=	18
14	day(s)	=	44
21	day(s)	=	47
28	day(s)	=	47

Under the conditions of this test, the substance was not readily biodegradable. The EU criterion for ready biodegradability requires at least 70% DOC removal in the modified OECD screening test (OECD Guideline 301 E).

Kinetics of Control Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)
4	day(s)	=	90
28	day(s)	n/a	93

Result:

other

Data Quality

4A (Klimisch) - The report consisted of an abstract of the test rather than a full report. Only 1 flask with test substance.

Reference

Hoechst AG, 1993A

4. ECOTOXICITY**4.1.1 TOXICITY TO FISH (ACUTE)**

(a)

Test Substance

CAS Number: **61788-90-7**
Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 30%
Chain Length Distribution: C10-16
Remarks: Balance (70%) is water

Method

GLP: yes
Report/Study Year: 1987
Report/Study Number: NA 86-9835/1
Method/Guideline Followed: OECD Guideline 203
Test Type: acute, static
Analytical Monitoring: no
Limit Test: no
Species: *Salmo gairdneri*
Exposure Period: 96 hours
Remarks: Ten fish per concentration. Reconstituted water prepared from city water supply after dechlorination by passage through active charcoal filters. Nominal test concentrations were 2 - 3 - 4.5 - 6.7 - 10.0 - 15.0 - 22.5 - 33.5 and 50 mg/l. LC50 determined graphically. A biodegradation study (CAS RN 61788-90-7; Kurzbericht über die Prüfung der biologischen Abbaubarkeit gemäss dem modif. OECD Screening-Test 301 E und DIN ISO 7827 (1993) / B 152-2) showed that the test substance concentration may have fallen below 80% of initial conc. during this test.

Results

Unit: mg/l

	Measured/Computed	Operator	
LC50:	c	=	13

Data Quality

1A (Klimisch) – Reliable with restriction; comparable to guideline study.
 Critical study for SIDS endpoint

Reference

Akzo Nobel, 1987

(b)

Test Substance

CAS Number: 61788-90-7
Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 30%
Chain Length Distribution: C10-16
Remarks: Balance (70%) is water

Method

GLP: yes
Report/Study Year: 1983
Report/Study Number: 83.0520
Method/Guideline Followed: OECD Guideline 203
Test Type: acute, static
Analytical Monitoring: no
Limit Test: no
Species: *Brachydanio rerio*
Exposure Period: 96 hours
Remarks: Ten fish per test conc. Nominal test concentrations were 0 - 1 - 2.5 - 3.55 - 5.0 - 7.1 - 10 and 100 mg/l. Water hardness approx. equivalent to 200 mg/l CaCO₃ + 42 mg/l MgCO₃. Biodegradation study (CAS RN 61788-90-7); Kurzbericht über die Prüfung der biologischen Abbaubarkeit gemäss dem modifizierten OECD Screening-Test 301 E und DIN ISO 7827 (1993) / B 152-2) showed decrease of test substance conc. of 80% of nominal in this test. The 4 tests were conducted in the time-span of 1 month. Results were comparable, combined and reported as one test.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
LC50:	c	=	0.9	1.1
LC50	c	=	1	n/a

Data Quality

2A (Klimisch) – Reliable with restriction; acceptable, well-documented publication/study report.
 Critical study for SIDS endpoint

Reference

Hoechst AG, 1983D

(c)

Test Substance

CAS Number: 61788-90-7

Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 30%
Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1977
Report/Study Number: 477/77
Method/Guideline Followed: OECD Guideline 203
Test Type: acute, static
Analytical Monitoring: no
Species: *Leuciscus idus f. melanotus*
Exposure Period: 96 hours
Remarks: Fish were fasted for 113 hours before the test, which could lead to higher sensitivity. Nominal test concentrations: 0.0 - 0.03 - 0.24 - 0.3 - 0.6 - 1.5 - 3 - 3.75 - 10.5 - 24 - 30 mg/l (active ingredient). Dechlorinated water, hardness 255 mg/l CaCO₃, pH 7.1-8.1, oxygen 66-96% saturated.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	>	1.5	n/a
LC100:	m	<	10.5	n/a
LC50	c	=	4.3	n/a
LC50	c	=	3.5	5.5

Remarks: A biodegradation study (report # B152-2) showed less than 10% decrease over 96 hours. Test concentrations therefore believed to be >80% of nominal during this test. Light regime not reported. Probably this test was two separate tests, reported as one: one with 5 fish per conc. and test concentrations 0, 0.03, 0.3, 3 and 30 mg/l and one with 10 fish per conc. and test concentrations 0, 0.24, 0.6, 1.5, 10.5 and 24 mg/l.

Data Quality

2B (Klimisch) – Reliable with restriction; basic data given, comparable to guidelines/standards. Incompletely documented test conditions.

Reference

Hoechst, 1977

(d)

Test Substance

CAS Number: 61788-90-7
Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 30%
Chain Length Distribution: C12-14
Remarks: Balance (70%) is water

Method

GLP: no
Report/Study Year: 1987
Report/Study Number: 87.1178
Method/Guideline Followed: Directive 84/449/EEC, C.1; OECD Guideline 203
Test Type: acute, static
Analytical Monitoring: no
Limit Test: no
Species: *Brachydanio rerio*
Exposure Period: 96 hours
Remarks: Zebrafish. Nominal concentrations 0, 3 and 30 mg/l (a.i.)

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	3	n/a
LC50:	m	=	3	30

Data Quality 4A (Klimisch) – Full report not available. The available information consisted of a brief abstract. Test conditions were incompletely documented.

Reference Hoechst AG, 1987C

4.2.1 AQUATIC INVERTEBRATES TOXICITY (ACUTE)**Test Substance**

CAS Number: 61788-90-7
Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 31%
Chain Length Distribution: C10-16
Remarks: Balance is water.

Method

GLP: yes

Report/Study Year: 1990
Report/Study Number: CRL F90069
Method/Guideline Followed: OECD Guideline 202
Test Type: static
Analytical Monitoring: no
Limit Test: no
Species: *Daphnia magna*
Exposure Period: 48 hours
Remarks: A.k.a. EEC C.2 method. Statistics: Griffioen, based on model of Kooyman. Daphnids less than 24 hours old. 5/vessel; 4 reps. per conc.; 6 reps. for control. Nominal test conc. 0.0 - 0.3 - 0.65 - 1.4 - 3.1 - 6.5 mg/l (active ingredient). No vehicle. Temp. 19 °C; pH 8.2; hardness 232 mg/l CaCO₃; O₂ 96-98% saturated. Phys. meas. at 0h and 48h. Observed for immobility at 0, 24 and 48h. No analyses. A biodegradation study (CAS RN 61788-90-7) showed decrease in test substance of 80% of nominal during this test.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC50	c	=	2.9	n/a
EC50	c	=	2.4	3.6

Remarks: EC50 = 2.9 [95% confidence interval 2.4 - 3.6] mg/l.

Data Quality

1B (Klimisch) – No information about feeding during the study.
 Statistical method not fully referenced.
 Critical study for SIDS endpoint

Reference

Akzo Nobel Chemicals, 1990A

4.3 TOXICITY TO AQUATIC PLANTS e.g. ALGAE

Test Substance

CAS Number: **61788-90-7**
Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 31%
Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: yes
Report/Study Year: 1990

Report/Study Number: CRL F90062
Method/Guideline Followed: OECD Guideline 201
Analytical Monitoring: yes
Species: *Selenastrum capricornutum*
Endpoint: other
Exposure Period: 72 hours
Remarks: Endpoints are biomass and growth rate. Initial cell conc. 12000 cells/ml. 3 reps./conc. and 6 controls. Standard OECD algal growth medium (OECD Guideline 201); hardness (Ca + Mg) 0.6 mmol/l. Nominal conc. 0.0 – 0.02 – 0.04 – 0.08 – 0.16 – 3.1 mg/l (active ingredient). Cont. illumination 6000-10000 lux; shaken 100 rpm. Phys. Meas. At 0 and 72h; pH 6.9-7.9; Temp. 23 °C. Observations cell density at 0, 24, 48 and 72h spectrophotometrically. Pos. control K₂Cr₂O₇: EbC50 = 0.69 mg/l; ErC50 = 0.56 mg/l.

Results

Unit: mg/l

	Measured/Computed		
NOEC:	c	=	0.08
LOEC:	n/a	n/a	0.16
EC50:	c	=	0.20
ErC50	c	=	0.29
ErC20	c	=	0.14
ErC10	c	=	0.09

Remarks: EC50 in table stands for EbC50 (effects on biomass). Concentrations were probably stable during the test, but some degradation is possible.

Ecrxx values (effects on growth rate) calculated according to Bruce & Versteeg (1992), in mg/l:

		EC50	EC20	EC10
Growth Rate	0.29	0.14	0.09	
Biomass	Ecxx values could not be calculated			

Data Quality

2C (Klimisch) – Comparable to guideline study with acceptable restrictions.
 Critical study for SIDS endpoint

Reference

Other reference

Akzo Nobel Chemicals, 1990E
 Bruce and Versteeg, 1992

4.4 TOXICITY TO MICROORGANISMS e.g. BACTERIA

(a)

Test Substance

CAS Number: **61788-90-7**
Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 29-31%
Carbon Chain Length Distribution: C10-16
Remarks: Balance (69%) is water

Method

GLP: no
Report/Study Year: 1992
Report/Study Number: 8.686
Method/Guideline Followed: OECD Guideline 209
Analytical Monitoring: no
Species: *Pseudomonas putida*
Exposure Period: 3 hours
Remarks: Respiration inhibition test with activated sludge from municipal sewage treatment plant, sludge conc. 1.6 g/l, synthetic sewage feed and test substance conc. 100 – 200 – 300 – 400 – 500 mg/l. O₂ measured continuously. Pos. control K₂Cr₂O₇ (60 mg/l) and duplicate untreated controls.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC50:	c	=	240	n/a
EC50	c	=	52	1112

Remarks: Pos. control 34% inhibited.
 K₂Cr₂O₇ used instead of 3,5-dichlorophenol as pos. control. The pos. control should have been 40-60% inhibited but was only 34% inhibited, pointing to an insensitive study design and likely overestimation of the EC50 value.
 Balance (69-71%) of test substance not given; believed to be water.
 Limited information in report.

Data Quality

Reliability (Klimisch): 3B
Remarks: Secondary literature.

Reference

Source Reference: Hoechst AG, 1989B.

(b)

Test Substance

CAS Number: **61788-90-7**
Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 31%
Carbon Chain Length Distribution: C12 and 14 (C12:70%; C14:30%)
Remarks: Balance (69%) is water

Method

GLP: no
Report/Study Year: 1992
Report/Study Number: 91-P159-P1
Method/Guideline Followed: DIN 38412, part 8
Analytical Monitoring: no
Species: *Pseudomonas putida*
Exposure Period: 16 hours
Remarks: *Pseudomonas putida* Migula.
Test conc. ranged from 62.5 - 1000 mg/l. Blank and reference controls (2,4 dichlorophenol). Shaken (220 rpm). Temp. 20-22 °C.

Results

Unit: mg/l

	Measured/Computed		
EC10:	c	=	76
EC50:	c	=	189

Remarks: Summary report. No experimental details given.

Data Quality

Reliability (Klimisch): 4B
Remarks: Secondary literature.

Reference

Source Reference: Hoechst AG, 1992.

5. TOXOCITY

5.1.1 ACUTE ORAL TOXICITY

(a)

Test Substance

CAS Number: **61788-90-7**
Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 30%
Carbon Chain Length Distribution: C10-16
Remarks: Balance (70%) is water

Method

GLP: no
Report/Study Year: 1983
Report/Study Number: 83.0662
Method/Guideline Followed: OECD Guideline 401
Test type: LD50
Species: rat
Strain: Wistar
Sex: male/female
Vehicle: water
Number of Animals per Dose: 5
Doses: 375; 600; 750; 945; 1200; 1500 mg a.i./kg. bw (in deionized water)
Remarks: 5 females per dose in 4 lowest dose groups; 5 males per dose in 3 highest dose groups; this resulted in 10 animals in the 945 mg a.i./kg bw dose group; no controls; feeding at libitum; food was withheld as of 16 h prior to until 2 hours after dosing.

Results

Value:		Females	Males	Unit
	=	846	1236	mg a.i./kg bw

Remarks: Calculation of a combined gender LD50 could not be justified based on statistical considerations. Data in parentheses are 95% confidence intervals.

Oral LD50 (males) = 1236 (1020 - 1503) mg a.i./kg bw

Oral LD50 (males) = 4120 (3400 - 5010) mg test substance/kg bw

Oral LD50 (females) = 846 (708 - 1062) mg a.i./kg bw

Oral LD50 (females) = 2820(2360 - 3540)mg test substance/kg bw

Clinical symptoms: rough coat, hunched posture, calmness, diarrhea, ptosis, ventro-lateral recumbency, flat body posture, lowered breathing frequency, stretched legs, rashes, laying on back. Necropsy findings: yellow and/or red fluid in GI tract, full

stomach, pink fluid in thorax, pale liver (partial), intestines filled with yellow/green fluid and (starting or partial) autolysis.

Mortalities:

Females - 375 mg/kg(0/5); 600 mg/kg(0/5); 750 mg/kg(1/5); 945 mg/kg(4/5)

Males - 945 mg/kg(0/5); 1200 mg/kg(3/5); 1500 mg/kg(4/5)

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Reference

Source Reference: Hoechst AG, 1983C.

(b)

Test Substance

CAS Number: 61788-90-7

Identity: Amines, coco alkyldimethyl, N-oxides

Purity: 30%

Carbon Chain Length Distribution: C10-16

Remarks: Balance (70%) is water

Method

GLP: no

Report/Study Year: 1978

Report/Study Number: 157/78

Test type: LD50

Species: rat

Strain: Wistar

Sex: female

Vehicle: water

Number of Animals per Dose: 10

Doses: 3000 and 5000 mg a.i./kg. bw (as 25% aqueous solution)

Remarks: Method not indicated; no controls; feeding at libitum; no food given as of 16 h prior to dosing.

Results

Value:	Operator		Unit
	=	3873	mg/kg bw

Remarks: Symptoms in animals that died included decreased breathing frequency and ptosis. At 3000 mg a.i./kg bw, 1/10 animals died. At 5000 mg a.i./kg bw, all (10) animals died.

Data Quality

*Reliability
(Klimisch):* 3B

Remarks: Limited information in summary report. No individual animal data reported. LD50 calculated by the reviewer using the 20%-Trimmed Spearman-Kärber method was 3873 mg a.i./kg bw. Only females were tested, therefore it cannot be excluded that sex differences may occur. It is not clear whether the LD50 was corrected for the concentration of the test substance (25%) in water prior to dosing.

Reference

Source Reference: Hoechst AG, 1978A.

5.2.1 SKIN IRRITATION

(a)

Test Substance

CAS Number: **61788-90-7**
Identity: Amines, coco alkyldimethyl, N-oxides HOE S3406
Alkyldimethylamine oxide
Purity: 30%
Carbon Chain Length
Distribution: C10-16
Remarks: Balance is water

Method

GLP: yes
Report/Study Year: 1983
Report/Study Number: 83.0514
Method/Guideline
Followed: OECD Guideline 404
Species: rabbit
Number of Animals: 3
Concentration: undiluted
Exposure: 4 hours
Remarks: New Zealand White rabbits; weight 2.6-3.4 kg; application of 0.5 ml of the test substance on clipped skin (2.5x2.5 cm²) during 4 h under semi-occlusion. Observations at 30-60 min., 24, 48 and 72 h and after 7 and 14 days.

Results

Result: irritating
Classification: irritating
Remarks: No data on individual animal weights was reported.

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 1A

Reference

Source Reference: Hoechst AG, 1983E.

(b)

Test Substance

CAS Number: **61788-90-7**

Identity: Amines, coco alkyldimethyl, N-oxides
Dimethylcocosfettaminoxid, 30%ig

Purity: 30%

Carbon Chain Length Distribution: C10-16

Remarks: Balance is water

Method

GLP: no

Report/Study Year: 1978

*Report/Study
Number:* 158/78

Species: rabbit

Vehicle: physiological saline

Number of Animals: 6

Concentration: 30%, 3%, 0.3% active

Exposure: 24 hours

Remarks: Guideline not indicated; 2 rabbits per treatment; sex not indicated; application of 0.5 ml of undiluted test substance and a 1% and 10% solution in physiological saline on the clipped skin of the flank (6.25 cm²) under occlusion for 24 h. Observations at 24, 48 and 72 h after patch removal.

Results

Result: irritating

Classification: irritating

Remarks: Undiluted treatment resulted in well defined erythma and moderate-strong edema, also grey-green discoloration and hardened skin. The 10% treatment resulted in well defined erythema, light edema, grey-green discoloration and hardened skin. The 1% treatment resulted in light erythema, minimal edema and no discoloration.

Data Quality

*Reliability
(Klimisch):* 2A

Remarks: Limited information. No individual animal data were reported. It is inconclusive whether or not the test substance is corrosive. The undiluted treatment under occlusion for 24 hours is a very high exposure (worst case). Number of animals too small.

Reference

Source Reference: Hoechst AG. 1978B.

(c)

Test Substance

CAS Number: **61788-90-7**
Identity: Amines, coco alkyl dimethyl, N-oxides
Alkyldimethylaminoxide
Purity: 30%
Carbon Chain Length Distribution: C12/14
C12:70%; C14:30%
Remarks: Balance (70%) is water

Method

GLP: no
Report/Study Year: 1987
Report/Study Number: 87.1204
Method/Guideline Followed: OECD Guideline 404
Species: rabbit
Vehicle: None
Concentration: undiluted
Exposure: 3 minutes and 4 hours
Remarks: New Zealand rabbits; no vehicle; application of 0.5 ml. of 100% solution of the test substance on the skin of the flank during 3 minutes and 4 hours.
Number of animals not stated.

Results

Result: corrosive
Classification: corrosive (causes burns)
Remarks: The information in the report is limited to what is given in this summary.

Data Quality

Reliability (Klimisch): 4A
Remarks: Insufficiently documented.

Reference

Source Reference: Hoechst AG, 1987B.

5.2.2 EYE IRRITATION

(a)

Test Substance

CAS Number: **61788-90-7**
Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 30%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: yes
Report/Study Year: 1983
Report/Study Number: 83.0524
Method/Guideline Followed: OECD Guideline 405
Species: rabbit
Vehicle: water
Number of Animals: 6

Dose:

Value	Unit
0.1	ml

Remarks: Observations: 1, 24, 48, 72 hours and 7, 14 and 21 days (rinsed 24h after application; fluorescein treatment before 48 and after 72 hour observations).

Results

Result: irritating
Classification: irritating

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 1A

Reference

Source Reference: Hoechst AG, 1983B.

(b)

Test Substance

CAS Number: **61788-90-7**

Identity: Amines, coco alkyldimethyl, N-oxides
Purity: 30%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1978
Report/Study Number: 158/78
Method/Guideline Followed: other
Species: rabbit
Vehicle: physiological saline
Number of Animals: 6

Dose:

Value	Unit
0.1	ml

Remarks: Guideline not indicated. Application of 0.1 ml of undiluted test substance and a 1% and 10% solution. Observations: 1, 7, 24, 48, 72 hours; rinsed after 24 h observation; fluorescein treatment before 48 and after 72 hour observations.

Results

Result: irritating
Classification: irritating

Remarks: Undiluted treatment resulted in light corneal opacity, diffuse redness, moderate-strong chemosis of conjunctivae and strong discharge.
10% treatment resulted in light corneal opacity, diffuse redness, moderate chemosis of conjunctivae and strong discharge.
1% treatment did not cause corneal opacity or redness; light (slight hyperaemia) chemosis of conjunctivae; no discharge.

Data Quality

Reliability (Klimisch): 2A

Remarks: Limited report. No individual data were reported. Number of animals tested was too small.

Reference

Source Reference: Hoechst AG, 1978B.

5.5 GENETIC TOXICITY *in vitro*

Test Substance

CAS Number:	61788-90-7
Identity:	Amines, coco alkyl dimethyl, N-oxides
Purity:	30%
Carbon Chain Length Distribution:	C12/14 C12:70%; C14:30%
Remarks:	Balance (70%) is water

Method

GLP:	yes
Report/Study Year:	1989
Report/Study Number:	88.1427
Method/Guideline Followed:	OECD Guideline 471
Test Type:	Ames test
System:	Strains TA98, TA100, TA1535, TA1537, TA1538. Liver S9 mix (Aroclor induced).
Test Concentration:	Expt. 1: 4, 20, 100, 500, 2500 and 10,000 µg/plate. Expt. 2: 0.8, 4, 20, 100, 500 and 2500 µg/plate.
Species/strain:	n/a
Metabolic Activation:	Yes
Remarks:	Negative control: vehicle (DMSO) Positive controls: 2-aminoanthracene, benzo-a-pyrene (both with S9); sodium azide (TA100, TA1535), 2-nitrofluorene (TA98, TA1538), 9-aminoacridine (TA 1537), all without S9. Doses in experiment 2 based on toxicity in experiment 1.

Results

Result:	negative
Cytotoxic Concentration:	no data
Remarks:	No information on incubation time, initial number of bacteria and their growth phase. It was stated that toxicity observed in 1st experiment without S9 was high at conc. of 20 µg/plate and above, but this was not confirmed by individual data on colonies per plate nor by the concentrations chosen in the 2nd experiment. For TA1535 the benzo[a]pyrene control (with S9) was not clearly positive, however the 2-aminoanthracene control was positive. This renders the results for this strain less reliable, because a reduced sensitivity of the bacteria used in the test cannot be fully excluded.

Data Quality

Flags:	Critical study for SIDS endpoint
--------	----------------------------------

Reliability (Klimisch): 2C

Remarks: Limited information on test design.

Reference

Source Reference: Hoechst AG, 1989A.

6. REFERENCES

- AISE 2002. Amine Oxide Survey of European Use and Exposure Information Provided by Member Companies.
- AISE/HERA 2002. HERA Task Forces Human Habits and Uses Tables.
- AISE/HERA 2002. HERA Task Forces Human Habits and Uses Tables.
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- Akzo Chemie, 1987. Biodegradability of a number of nitrogen derivatives (MU-30).
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- Akzo Nobel Chemicals, 1990E. Algal growth inhibition test with CAS RN 61788-90-7.
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- Hoechst AG, 1978A. Akute orientierende orale Toxizität von CAS RN 61788-90-7 (dimethylcocosfettaminoxid 30%ig in Wasser), an weiblichen SPF-Wistar-Ratten
- Hoechst AG, 1978B. Orientierende Prüfung auf Haut- und Schleimhautverträglichkeit von CAS RN 61788-90-7 (dimethylcocosfettaminoxid 30%ig) an Kaninchen.
- Hoechst AG, 1983B. CAS RN 61788-90-7; Prüfung auf Acute dermale Reizwirkung / Ätzwirkung am Kaninchen.
- Hoechst AG, 1983C. CAS RN 61788-90-7; Prüfung der akuten oralen Toxizität an der männlichen und weiblichen Wistar-Ratte.
- Hoechst AG, 1983D. CAS RN 61788-90-7; Prüfung der akuten Toxizität am Fisch Zebra barling (*Brachydario rerio*) über 96 Stunden.
- Hoechst AG, 1983E. Hoe S 3406; Prüfung auf akute dermale Reizwirkung/Ätzwirkung am Kaninchen.
- Hoechst AG, 1987B. Kurzbericht Nr. 87.1204.
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- Hoechst AG, 1989A. CAS RN 61788-90-7 study of the mutagenic potential in strains of *Salmonella typhimurium* (Ames test). Feb. 27, 1989.
- Hoechst AG, 1989B. Prüfung auf Bakterientoxizität. OECD 209/8.686
- Hoechst AG, 1989C. Untersuchung des biologischen Abbaus nach dem OECD-Screening-Test 301 E 12 (modifiziert); Alkyl(C12-18)dimethylaminoxid

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Hoechst AG, 1993A. CAS RN 61788-90-7. Kurzbericht über die Prüfung der biologischen Abbaubarkeit gemäss dem modifizierten OECD Screening-Test 301E und DIN ISO 7827.

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Japan Soap and Detergent Association, 2002. Japanese Soap and Detergent Association survey of amine oxide production, 2001-2002.

Kirk Othmer Encyclopedia of Chemical Technology, 2001, 4th edition, CD-ROM, John Wiley and Sons, ISBN: 0-471-15158-0

Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting.

Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 85408-48-6

Amines, C10-18-alkyldimethyl, N-oxides

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2530-44-1
2571-88-2
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
93962-62-0

Sponsor Country: United States
Date: July, 2006

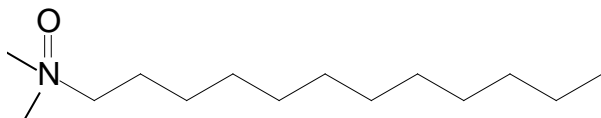
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number 85408-48-6
- B. Name (IUPAC name)
- C. Name (OECD name) Amines, C10-18-alkyldimethyl, N-oxides
- D. CAS Descriptor
- E. EINECS-Number 287-010-0
- F. Molecular Formula Unspecified
- G. Structural Formula

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

C₁₂ dimethyl amine oxide



- H. Substance Group Amine Oxides category
- I. Substance Remark None
- J. Molecular Weight Unspecified

1.02 OECD INFORMATION

- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460

U.S.A.
Tel: (202) 564-7641
Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical

properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyl oxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic []; petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

None

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

(a) United States

26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)

Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.

(b) Europe

- (i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tonnes (AISE, 2002)

- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000 and 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000 and 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or other applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%

Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS**A. Options for Disposal**

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

6. REFERENCES

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Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 85408-49-7

Amines, C12-16-alkyldimethyl, N-oxides

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2530-44-1
2571-88-2
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-6
93962-62-0

Sponsor Country: United States
Date: July, 2006

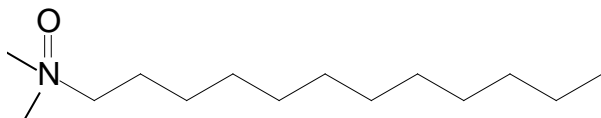
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number 85408-49-7
- B. Name (IUPAC name)
- C. Name (OECD name) Amines, C12-16-alkyldimethyl, N-oxides
- D. CAS Descriptor
- E. EINECS-Number 287-011-6
- F. Molecular Formula Unspecified
- G. Structural Formula

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

C₁₂ dimethyl amine oxide



- H. Substance Group Amine Oxides category
- I. Substance Remark None
- J. Molecular Weight Unspecified

1.02 OECD INFORMATION

- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
- Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460

U.S.A.
Tel: (202) 564-7641
Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical

properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyl oxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

None

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

(a) United States

26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)

Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.

(b) Europe

- (i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tonnes (AISE, 2002)

- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000 and 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000 and 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or other applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%

Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS**A. Options for Disposal**

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

3. ENVIRONMENTAL FATE AND PATHWAYS

3.5 BIODEGRADATION

Test Substance

CAS Number: **85408-49-7**
Identity: Amines, C12-16-alkyldimethyl, N-oxides
Purity: 29%
 C10:0.3%; C12:40-62%; C14:20-50%; C16:9-13%; C18:5-9%
Chain Length Distribution: C12-16
Remarks: Balance (71%) is water

Method

GLP: no
Report/Study Year: 1987
Report/Study Number: R 0001279
Test Type: aerobic
Method/Guideline Followed: OECD Guideline 301 D
Inoculum: activated sludge, domestic, non-adapted
Inoculum Acclimated: no
Control Substance: Benzoic acid, sodium salt
Test Substance Initial Concentration: 2 mg/l as test substance
 10 mg/l as test substance
Control Substance Initial Concentration: 2 mg/l as test substance
Remarks: Temp. 20 °C. Test duration 30 days. Negative control (no test substance). Positive control (Na benzoate). Concentrations tested were 2, 5 and 10 mg/l test substance. Biodegradation is measured as O₂ consumption as a percentage of COD.

Results

Kinetics Measured as: other

Kinetics of Test Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
5	day(s)	=	0	0
15	day(s)	=	42	51
30	day(s)	=	41	48

Kinetics of Control Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
5	day(s)	=	62	n/a
30	day(s)	=	90	n/a

<i>Half Life:</i>	<i>Mineralization:</i> not determined
	<i>Primary Biodegradation:</i> n/a
<i>Result:</i>	Inherently biodegradable
<i>Degradation Products:</i>	not measured
<i>Remarks:</i>	<p>The lower and upper % biodegradation in "kinetics of test substance" indicate the range observed among the three concentrations tested. Results for individual test concentrations are as follows:</p> <p>test conc. - % degradation after 5, 15 and 30 days:</p> <p>2 mg/l - 0, 51, 41</p> <p>5 mg/l - 0, 42, 41</p> <p>10 mg/l - 0, 45, 48</p> <p>At the two lower test concentrations, the % biodegradation was lower at 30 days compared to 15 days. This could be due to leakage of oxygen back into the bottles. Since the kinetics were measured by O₂ determination, leakage could result in an apparent decrease in the extent of biodegradation over time.</p> <p>Not readily biodegradable according to the EU criterion for ready biodegradability, which requires 60% of theoretical O₂ consumption within 10-day window after 10% mark is reached (OECD Guideline 301D).</p>
Data Quality	<p>2B (Klimisch) - Basic data given; comparable to guideline study. No individual BOD-data for test substance/controls are given in the report.</p> <p>Critical study for SIDS endpoint</p>
Reference	Henkel KGaA, 2000A

4. ECOTOXICITY

4.1.1 TOXICITY TO FISH (ACUTE)

Test Substance

CAS Number: 85408-49-7

Identity: Amines, C12-16-alkyldimethyl, N-oxides

Purity: 30% active

Chain Length Distribution: C12-16; 2% C10, 91% C12-16, 7% C18

Remarks: Balance (70%) is water

Method

GLP: no data

Report/Study Year: 2000

Report/Study Number: R-0000994

Method/Guideline Followed: ISO 7346/3

Test Type: acute, flow-through

Analytical Monitoring: no

Limit Test: no

Species: *Brachydanio rerio*

Exposure Period: 96 hours

Remarks: Method corresponds to ISO 7346/3 or "Water quality - Determination of the acute lethal toxicity of substances to a freshwater fish (*Brachydanio rerio*) - Part 3: Flow-through method" of January 12, 1984. Ten fish per concentration; insufficient experimental details are given.

Results

Unit: mg/l

	Measured/Computed		
LC50:	c	=	1.7
LC100:	m	=	2.5
LC50	c	=	3.5

Data Quality

3B (Klimisch) - Insufficient information to assess. Information is from a one-page summary report

Reference

Henkel KGaA, 2000B

6. REFERENCES

AISE 2002. Amine Oxide Survey of European Use and Exposure Information Provided by Member Companies.

AISE/HERA 2002. HERA Task Forces Human Habits and Uses Tables.

AISE/HERA 2005. Human & Environmental Risk Assessment on ingredients of European household cleaning products (HERA): Amine Oxides. (*in preparation*).

CESIO, 2003. CESIO Recommendation For The Classification And Labelling Of Surfactants As “Dangerous For The Environment”. CESIO report, April 2003.

Cosmetics, Toiletries and Fragrances Association, 2003. Cosmetics, Toiletries, and Fragrance Association survey of amine oxide uses in personal care products.

Henkel KGaA, 2000A. (CAS RN 85408-49-7), Ultimate biodegradability in the closed bottle test.

Henkel KGaA, 2000B. Acute toxicity: Fish. Summary sheet R 0000994.

Japan Soap and Detergent Association, 2002. Japanese Soap and Detergent Association survey of amine oxide production, 2001-2002.

Kirk Othmer Encyclopedia of Chemical Technology, 2001, 4th edition, CD-ROM, John Wiley and Sons, ISBN: 0-471-15158-0

Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting.

Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 61791-47-7

Ethanol, 2,2'-iminobis-, N-coco alkyl derivs., N-oxides

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2571-88-2
2530-44-1
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

Sponsor Country: United States
Date: July, 2006

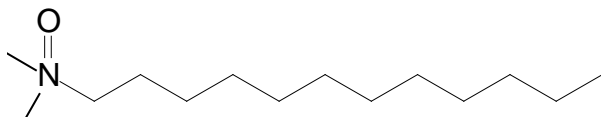
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number 61791-47-7
- B. Name (IUPAC name)
- C. Name (OECD name) Ethanol, 2,2'-iminobis-, N-coco alkyl derives., N-oxides
- D. CAS Descriptor
- E. EINECS-Number
- F. Molecular Formula Unspecified
- G. Structural Formula

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

Representative C₁₂ dimethyl amine oxide



- H. Substance Group Amine Oxides category
- I. Substance Remark None
- J. Molecular Weight Unspecified

1.02 OECD INFORMATION

- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460
U.S.A.

Tel: (202) 564-7641

Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association

1500 K Street, N.W., Suite 300

Washington, D.C. 20005

USA

Tel: (202) 662-2523

Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.

Goldschmidt Chemical Corporation

Rhodia Inc.

Stepan Company

The Procter & Gamble Company

Akzo Nobel Surface Chemistry AB

Clariant GmbH

Cognis Deutschland GmbH

Huntsman Surface Sciences UK Limited

KAO Chemical

Stepan Europe

Degussa AG (Goldschmidt)

Kao Corporation

Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-

9-octadecenyloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

(a) United States

26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)

Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.

(b) Europe

(i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)

(ii) 21,570 metric tonnes (AISE, 2002)

- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in other applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%

Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also "Use and Exposure Information on Amine oxides", available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA 2002.

1.10 ADDITIONAL REMARKS**A. Options for Disposal**

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

3. ENVIRONMENTAL FATE AND PATHWAYS

3.5 BIODEGRADATION

Test Substance

CAS Number: **61791-47-7**
Identity: Ethanol, 2,2'-iminobis-, N-coco alkyl derivs., N-oxides
Purity: 30.5%
Chain Length Distribution: C12-14
Remarks: Balance is water (69.5%)

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: CRL F90055
Test Type: aerobic
Method/Guideline Followed: OECD Guideline 301D
Inoculum: activated sludge, domestic, non-adapted
Inoculum Acclimated: no
Control Substance: Acetic acid, sodium salt
Remarks: Method was slightly modified version of OECD Guideline 301D.
 Test duration 35 days. Test substance conc. not given. Positive control Na acetate.
 Biodegradation measured as O₂ consumption.

Results

Kinetics Measured as: other

<i>Kinetics of Test Substance:</i>	Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
	5	day(s)	=	17	n/a
	15	day(s)	=	46	n/a
	28	day(s)	=	57	n/a
	35	day(s)	=	69	n/a

<i>Kinetics of Control Substance:</i>	Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
	5	day(s)	=	75	n/a
	28	day(s)	=	87	n/a

Half Life: *Mineralization:* not determined

Primary Biodegradation: n/a

Result: inherently biodegradable

Degradation Products: not measured

Remarks: According to the EU criterion of ready biodegradability in this test, O₂ consumption should reach 60% of the theoretical value within 10

days after the 10% mark is reached (OECD Guideline 301D). The test results are inconclusive in this regard.

Data Quality

2B (Klimisch) – Basic data given; comparable to guideline study.

Reference

Akzo Nobel Chemicals, 1990H

4. ECOTOXICITY**4.1.1 TOXICITY TO FISH (ACUTE)****Test Substance**

CAS Number: 61791-47-7
Identity: Ethanol, 2,2'-iminobis-, N-coco alkyl derivs., N-oxides
Purity: 30.5%
Chain Length Distribution: C10-16
Remarks: Balance is water, free amine (0.3%) and peroxide (0.13%)

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: CRL F90059
Method/Guideline Followed: Directive 84/449/EEC, C.1; OECD Guideline 203
Test Type: acute, semi-static, renewal at 48 hrs
Species: *Brachydanio rerio*
Exposure Period: 96 hours
Remarks: No aeration. No feed. 10 fish per vessel. 1 vessel/conc. Nominal test conc. 0 - 2.0 - 2.80 - 3.54 - 5.5 - 6.9 mg/l (active ingredient). pH 7.3 - 7.7. O₂ > 60 saturated except at 24h in highest conc. and at 48h in 0.58 and 1.22 mg/l treatments where O₂ was [43-55%] of saturation. Temp. 22-23 °C. Hardness 230 mg/l as CaCO₃. Statistics: LC50 program of Griffioen (RIZA) based on model of Kooyman (1981).

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	2.5	n/a
LC50:	c	=	3.4	n/a
LC50	c	=	3	3.8

Remarks: O₂ concentrations below 60% of saturation during part of study, at all conc. except highest conc. at 24h, but no relationship with mortality so outcome of study is not affected. No analyses. A biodegradation study (Biodegradability of CAS RN 61791-47-7; Report # CRL F90055) showed a decrease in test substance conc. of 18% over 5 days. In this 4-day test, conc. most likely remained >80%.

Data Quality

2B (Klimisch) – No analyses.
 Critical study for SIDS endpoint

References

Akzo Chemicals International B.V., 1990D

4.2.1 AQUATIC INVERTEBRATES TOXICITY (ACUTE)**Test Substance**

CAS Number: **61791-47-7**
Identity: Ethanol, 2,2'-iminobis-, N-coco alkyl derivs., N-oxides
Purity: 30.5%
Chain Length Distribution: C10-16
Remarks: Balance is water

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: CRL F90068
Method/Guideline Followed: OECD Guideline 202
Test Type: static
Analytical Monitoring: no
Limit Test: no
Species: *Daphnia magna*
Exposure Period: 48 hours
Remarks: 5 daphnids/vessel x 4 reps./conc. = 20 daphnids per conc. Six control flasks. Nominal test conc. 0.0 - 0.14 - 0.30 - 0.64 - 1.40 - 3.05 mg/l (active ingredient). No aeration. Phys. meas. at 0 and 48h; Temp. 19-20 °C; pH 8.0-8.1; O₂ 94-97% saturated; hardness 230 mg/l as CaCO₃; no feeding. Biol. observ. immobility at 24 and 48h.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
48h EC50	c	=	1.1	n/a
48h EC50	c	=	0.88	1.3

Remarks: EC50 = 1.1 (95% confidence interval 0.88 - 1.3) mg/l.
Results of a biodegradation study (Biodegradability of CAS RN 61791-47-7; Report # CRL F90055) showed that concentrations probably remained at >80% of nominal during the test.

Data Quality

1A (Klimisch) – Reliable without restriction; comparable to guideline study.
Critical study for SIDS endpoint

Reference

Akzo Chemicals International B.V., 1990C

4.3 TOXICITY TO AQUATIC PLANTS e.g. ALGAE**Test Substance**

CAS Number: 61791-47-7
Identity: Ethanol, 2,2'-iminobis-, N-coco alkyl derivs., N-oxides
Purity: 30.5%
Chain Length Distribution: C10-16
Remarks: Balance is water.

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: CRL F90063
Method/Guideline Followed: OECD Guideline 201
Analytical Monitoring: no
Species: *Selenastrum capricornutum*
Endpoint: other
Exposure Period: 72 hours
Remarks: Endpoints are biomass and growth rate. 3 reps./conc. and 6 controls. Initial cell density 12000 cells/ml. Nominal conc. 0.0 - 0.02 - 0.04 - 0.08 - 0.15 - 0.30 mg/l (active ingredient). Phys. meas. at 0 and 72h. Temp. 23°C. pH 6.3-7.8. Continuous illumination 6000-10000 lux. Shaken 100 rpm. Observe cell density at 0, 24, 48 and 72h spectrophotometrically.
 Pos. control K₂Cr₂O₇: EbC50 = 0.20 mg/l; ErC50 = 0.77 mg/l.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
NOEC:	m	=	0.1	n/a
EC10:	c	=	0.12	n/a
EC50:	c	=	0.25	n/a
EC20	c	=	0.15	n/a

Remarks: A biodegradation study (Biodegradability of CAS RN 61791-47-7; Report # CRL F90055) showed decrease in conc. to below 80% of nominal during test period.

Results calculated according to Bruce & Versteeg (1992), in mg/l:

	EC50	EC20	EC10
Growth Rate	0.29 [0.24-0.35]	0.17 [0.12-0.25]	0.13 [0.07-0.22]
Biomass	0.25 [0.18-0.35]	0.15 [0.07-0.30]	0.12 [0.04-0.30]

Data Quality	1A (Klimisch) – Reliable; guideline study Critical study for SIDS endpoint
Reference	Akzo Chemicals International B.V., 1990E
Other reference	Bruce and Versteeg, 1992

6. REFERENCES

AISE 2002. Amine Oxide Survey of European Use and Exposure Information Provided by Member Companies.

AISE/HERA 2002. HERA Task Forces Human Habits and Uses Tables.

AISE/HERA 2005. Human & Environmental Risk Assessment on ingredients of European household cleaning products (HERA): Amine Oxides. (*in preparation*).

Akzo Chemicals International B.V., 1990C. Acute Toxicity of CAS RN 61791-47-7 to *Daphnia magna*.

Akzo Chemicals International B.V., 1990D. Acute Toxicity of CAS RN 61791-47-7 to Fish.

Akzo Nobel Chemicals, 1990H. Biodegradability of CAS RN 61791-47-7

Bruce and Versteeg, 1992. Env. Toxicol. Chem. 11: 1485

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Kirk Othmer Encyclopedia of Chemical Technology, 2001, 4th edition, CD-ROM, John Wiley and Sons, ISBN: 0-471-15158-0

Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting.

Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 2530-44-1

Ethanol, 2,2'-(dodecyloxidoimino)bis-

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2571-88-2
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

Sponsor Country: United States
Date: July, 2006

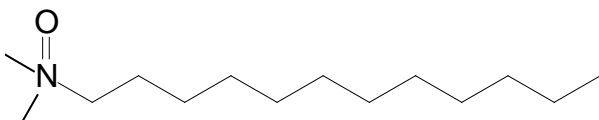
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number** 2530-44-1
- B. Name (IUPAC name)**
- C. Name (OECD name)** Ethanol, 2,2'-(dodecyloxidoimino)bis-
- D. CAS Descriptor**
- E. EINECS-Number**
- F. Molecular Formula**
- G. Structural Formula**

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

C₁₂ dimethyl amine oxide



- H. Substance Group** Amine Oxides category
- I. Substance Remark** None
- J. Molecular Weight** 289 grams/mole
- 1.02 OECD INFORMATION**
- A. Sponsor Country:** United States
- B. Lead Organization:** Environmental Protection Agency (EPA)

Contact person: Oscar Hernandez
Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460
U.S.A.
Tel: (202) 564-7641

Fax: (202) 564-7450**C. Name of Responder**

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is

expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (*at 20°C and 1.013 hPa*)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

None

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

(a) United States

26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)

Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.

- (b) Europe
(i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tonnes (AISE, 2002)
- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in other applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%

Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also "Use and Exposure Information on Amine oxides", available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS

A. Options for Disposal

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

2. PHYSICAL-CHEMICAL DATA

2.0.1 EPISuite™ ESTIMATION OF PHYSICAL/CHEMICAL PROPERTIES

Test Substance

CAS Number: 2530-44-1
Identity: Ethanol, 2,2'-iminobis-,N-coco alkyl derivatives, N-oxides
Purity: not relevant
Carbon Chain Length Distribution: C12
Remarks:

Method

GLP: n/a
Method/Guideline Followed: EPIWIN
Remarks: All estimates apply to the pure, dry substance and not their solutions in water.

Results

	Estimate	Exp. Database Match
Molecular Weight (grams/mole):	289.46	
Water Solubility (mg/l):	29.89	n/a
Octanol Water Partition Coefficient (Log Kow):	3.13	n/a
Bioconcentration Factor (Log BCF):	1.712	
Boiling Point (°C):	536.73	n/a
Melting Point (°C):	229.76	n/a
Vapor Pressure(Pa):	3.39E-12	n/a
Henry's Law Constant (atm/(mole/m ³)):	3.237E-16	n/a
Atmospheric Oxidation Half-Life (hours):	2.36	n/a
Soil Adsorption Coefficient (Log Koc):	2.360	

Remarks: Trends analysis, based on the N,N-Dimethyl Amine Oxides:
For every extension of two –CH₂– units to the alkyl chain

- Water solubility decreases by 1 order of magnitude.
- The Log Kow increases by ~ 1 unit [or the octanol/water partition coefficient increases by 1 order of magnitude].
- The Log BCF increases by ~ 0.25 units [or the BCF nearly doubles; it increases by a factor of 1.8].
- The boiling point increases by ~ 23°C, although these are theoretical values, as most surfactants decompose before they boil.
- The melting point increases by ~ 15°C.
- The Log Koc increases by ~ 0.5 unit [or the soil adsorption coefficient increases by a factor of 3].

Trends are similar for the N,N-Dihydroxyethyl Amine Oxides - The substitution of the nitrogen with two hydroxyethyl groups (vs. the two methyl groups of the N,N-Dimethyl Amine Oxides) increases the hydrophilicity of the hydrophilic head group of the surfactant. This results in a higher water solubility, a lower Log Kow and a lower Koc.

CAS #	Chain Length	MW (g/mole)	Water Sol. (mg/l)	Log Kow	Log BCF	BP (°C)	MP (°C)	VP (Pa)	Log Koc	Atm Oxidation half-life (hours)
N,N-Dimethyl Amine Oxides										
2605-79-0	C10	201.36	30.35	3.69	2.142	403.41	152.60	4.57E-5	3.739	5.26
1643-20-5	C12	229.41	3.13	4.67	⁽¹⁾ 2.392	426.62	167.95	2.09E-5	4.271	4.71
3332-27-2	C14	257.46	0.32	5.66	2.655	449.82	183.30	1.48E-6	4.803	4.27
7128-91-8	C16	285.52	0.032	6.64	2.911	473.03	198.65	2.59E-7	5.334	3.90
N,N-Dihydroxyethyl Amine Oxides										
2530-44-1	C12	289.46	29.89	3.13	1.712	536.73	229.76	3.39E-12	2.360	2.36
14048-77-2	C18	373.63	0.029	6.08	2.481	606.35	262.28	7.45E-15	3.955	2.04
93962-62-0	C18:1	371.61	0.045	5.86	2.815	609.93	263.95	5.43E-15	3.955	2.95

⁽¹⁾The Log BCF value obtained by KOWWIN is 1.989, which is an outlier. The expected value, based on linear extrapolation between C10, C14 and C16 AO, is 2.392.

Data Quality

Reliability (Klimisch): 2D

Remarks: Reliable with restrictions.

Reference

Source Reference: EPIWIN, Version 3.0.

4. ECOTOXICITY

4.1.1 TOXICITY TO FISH (ACUTE)

Test Substance

CAS Number: **2530-44-1**
Identity: Ethanol, 2,2'-iminobis-,N-coco alkyl derivs., N-oxides
Purity: 24.8%
Carbon Chain Length Distribution: C12
Remarks: Balance is water.

Method

GLP: no
Report/Study Year: 1992
Report/Study Number: CRL F92169
Method/Guideline Followed: Directive 84/449/EEC, C.1; OECD Guideline 203
Test Type: acute, semi-static, renewal at 48 hrs
Analytical Monitoring: no
Species: *Brachydanio rerio*

Value	Unit
96	hour(s)

Remarks: 7 fish per vessel and 1 vessel per treatment. Nominal test conc. 0.0 - 2.5 - 4.5 - 7.9 - 13.9 - 24.8 mg/l (active ingredient). pH 7.7-8.1. O₂ >82% saturated. Hardness 209 mg/l as CaCO₃. Temp 22 °C. Statistics by Spearman Karber binomial test method.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
LC50:	c	=	10.5	n/a
LC50	c	=	7.9	13.9

Remarks: No analyses. Test substance conc. may have decreased somewhat in the course of the test due to biodegradation.

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2B
Remarks: Summary report only. No information about fish size/loading or feeding

regime during the test.

Reference

Source Reference: Akzo Nobel Chemicals. 1992A.

4.2.1 AQUATIC INVERTEBRATES TOXICITY (ACUTE)

Test Substance

CAS Number: 2530-44-1
Identity: Ethanol, 2,2'-iminobis-,N-coco alkyl derivs., N-oxides
Purity: 24.8%
Carbon Chain Length Distribution: C10-16
Remarks: Balance is water.

Method

GLP: yes
Report/Study Year: 1994
Report/Study Number: CRL F94116
Method/Guideline Followed: OECD Guideline 202
Test Type: static
Analytical Monitoring: no
Limit Test: no
Species: *Daphnia magna*
Exposure Period: 48 hours
Remarks: Statistics by Spearman-Kärber, binomial method. Conditions: hardness 214 mg/l CaCO₃; pH 8.0-8.1; 16h light; oxygen 90-101%; temp. 19-21 °C. *Daphnia magna*

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC50	c	=	10.8	n/a
EC50	c	=	9.6	12.1

Remarks: EC50 = 10.8 [95% confidence interval 9.6 - 12.1] mg/l.
 Test substance conc. may have decreased due to biodegradation during the test.

Data Quality

Flags: Critical study for SIDS endpoint
Reliability (Klimisch): 2A
Remarks: No analyses. Daphnids may have been fed.

Reference

Source Reference: Akzo Nobel Chemicals, 1994A.

4.3 TOXICITY TO AQUATIC PLANTS e.g. ALGAE**Test Substance**

CAS Number: 2530-44-1
Identity: Ethanol, 2,2'-iminobis-, N-coco alkyl derivatives, N-oxides
Purity: 24.8%
Carbon Chain Length
Distribution: C10-16
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1990
Report/Study Number: CRL F92138
Method/Guideline Followed: OECD Guideline 201
Analytical Monitoring: no
Species: *Selenastrum capricornutum*
Endpoint: other

Exposure Period:	Value	Unit
	72	hour(s)

Remarks: Endpoints are the effects on biomass (EbCx) and growth rate (ErCx). Three replicates per concentration and 6 controls. Initial cell density 25000 cells/ml. Standard OECD algal growth medium (OECD Guideline 201); hardness (Ca + Mg) dH 0.6 mmol/l. Nominal conc. 0.0 - 0.012 - 0.025 - 0.055 - 0.22 - 0.26 mg/l (active ingredient). Phys. meas. at 0 and 72h. Temp. 20-22 °C. Continuous illumination. Shaken. Observe cell density at 0, 24, 48 and 72h spectrophotometrically. Statistics: Probit analysis. Pos. control K₂Cr₂O₇: EbC₅₀ = 0.20 mg/l; ErC₅₀ = 0.77 mg/l.

Results

Unit: mg/l

	Measured/Computed	Operator	
EC10:	c	=	0.01
EC50:	c	=	0.07
EC20	c	=	0.02

Remarks: Individual cell counts reported. pH not reported. Test concentrations were probably

stable but may have decreased in the course of the test.

Results were calculated according to Bruce & Versteeg (1992), in mg/l:

	EC50	EC20	EC10
Growth Rate	0.18	0.06	0.03
Biomass	0.07	0.02	0.01

Data Quality

Flags: Critical study for SIDS endpoint

Reliability (Klimisch): 2B

Remarks: Basic data given, comparable to guidelines/standards.

Reference

Source Reference: Akzo Nobel Chemicals, 1992D.

Other Reference Bruce and Versteeg, 1992.

6. REFERENCES

AISE 2002. Amine Oxide Survey of European Use and Exposure Information Provided by Member Companies.

AISE/HERA 2002. HERA Task Forces Human Habits and Uses Tables.

AISE/HERA 2005. Human & Environmental Risk Assessment on ingredients of European household cleaning products (HERA): Amine Oxides. (*in preparation*).

Akzo Nobel Chemicals, 1992A. Acute toxicity of CAS RN 2530-44-1 to *Brachydanio rerio*.

Akzo Nobel Chemicals, 1992D. Toxicity of CAS RN 2530-44-1 to the freshwater alga *Selenastrum capricornutum*.

Akzo Nobel Chemicals, 1994A. Acute toxicity of CAS RN 2530-44-1 to *Daphnia magna*.

Bruce and Versteeg, 1992. Env. Toxicol. Chem. 11: 1485

CESIO, 2003. CESIO Recommendation For The Classification And Labelling Of Surfactants As "Dangerous For The Environment". CESIO report, April 2003.

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EPIWIN: Physical/chemical property estimation methods, Version 3.0, from Syracuse Research Corporation, Syracuse, NY.

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Kirk Othmer Encyclopedia of Chemical Technology, 2001, 4th edition, CD-ROM, John Wiley and Sons, ISBN: 0-471-15158-0

Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting.

Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 14048-77-2

Ethanol, 2,2'-(octadecyloxidoimino)bis-

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2571-88-2
2530-44-1
2605-79-0
3332-27-2
7128-91-8
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

Sponsor Country: United States

Date: July, 2006

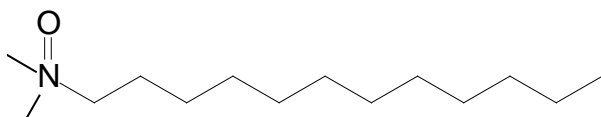
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number** 14048-77-2
- B. Name (IUPAC name)**
- C. Name (OECD name)** Ethanol, 2,2'-(octadecyloxidoimino)bis-
- D. CAS Descriptor**
- E. EINECS-Number**
- F. Molecular Formula** Unspecified
- G. Structural Formula**

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

Representative C₁₂ dimethyl amine oxide



- H. Substance Group** Amine Oxides category
- I. Substance Remark** None
- J. Molecular Weight** Unspecified

1.02 OECD INFORMATION

- A. Sponsor Country:** United States
- B. Lead Organization:** Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.

Mail Code 7403M
Washington, DC 20460
U.S.A.
Tel: (202) 564-7641
Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and

the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-9-octadecenyloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

None

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

- (a) United States
26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)

Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.

- (b) Europe
 - (i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
 - (ii) 21,570 metric tonnes (AISE, 2002)
- (c) Japan
 - 6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
 Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or in industrial, institutional and commercial applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%

Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS

A. Options for Disposal

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

2. PHYSICAL-CHEMICAL DATA

2.0.1 EPISuite™ ESTIMATION OF PHYSICAL/CHEMICAL PROPERTIES

Test Substance

CAS Number: **14048-77-2**
Identity: N,N-Dihydroxyethyl C18 Amine
Oxide
Purity: not relevant
Chain Length Distribution: C18
Remarks:

Method

GLP: n/a
Method/Guideline Followed: EPIWIN
Remarks: All estimates apply to the pure, dry substance and not its solutions in water.

Results

	Estimate
Molecular Weight (grams/mole):	373.63
Water Solubility (mg/l):	0.029
Octanol Water Partition Coefficient (Log Kow):	6.08
Bioconcentration Factor (Log BCF):	2.481
Boiling Point (°C):	606.35
Melting Point (°C):	262.28
Vapor Pressure(Pa):	7.45E-15
Henry's Law Constant (atm/(mole/m ³)):	9.59E-16
Atmospheric Oxidation Half-Life (hours):	2.04
Soil Adsorption Coefficient (Log Koc):	3.955

Remarks Trends analysis, based on the N,N-Dimethyl Amine Oxides:
: For every extension of two –CH₂– units to the alkyl chain

- Water solubility decreases by 1 order of magnitude.
- The Log Kow increases by ~ 1 unit [or the octanol/water partition coefficient increases by 1 order of magnitude].
- The Log BCF increases by ~ 0.25 units [or the BCF nearly doubles; it increases by a factor of 1.8].
- The boiling point increases by ~ 23°C, although these are theoretical values, as most surfactants decompose before they boil.
- The melting point increases by ~ 15°C.

- The Log K_{oc} increases by ~ 0.5 unit [or the soil adsorption coefficient increases by a factor of 3].

Trends are similar for the N,N-Dihydroxyethyl Amine Oxides - The substitution of the nitrogen with two hydroxyethyl groups (vs. the two methyl groups of the N,N-Dimethyl Amine Oxides) increases the hydrophilicity of the hydrophilic head group of the surfactant. This results in a higher water solubility, a lower Log K_{ow} and a lower K_{oc}.

CAS #	Chain Length	MW (g/mole)	Water Sol. (mg/l)	Log K _{ow}	Log BCF	BP (°C)	MP (°C)	VP (Pa)	Log K _{oc}	Atm Oxidation half-life (hours)
N,N-Dimethyl Amine Oxides										
2605-79-0	C10	201.36	30.35	3.69	2.142	403.41	152.60	4.57E-5	3.739	5.26
1643-20-5	C12	229.41	3.13	4.67	⁽¹⁾ 2.392	426.62	167.95	2.09E-5	4.271	4.71
3332-27-2	C14	257.46	0.32	5.66	2.655	449.82	183.30	1.48E-6	4.803	4.27
7128-91-8	C16	285.52	0.032	6.64	2.911	473.03	198.65	2.59E-7	5.334	3.90
N,N-Dihydroxyethyl Amine Oxides										
2530-44-1	C12	289.46	29.89	3.13	1.712	536.73	229.76	3.39E-12	2.360	2.36
14048-77-2	C18	373.63	0.029	6.08	2.481	606.35	262.28	7.45E-15	3.955	2.04
93962-62-0	C18:1	371.61	0.045	5.86	2.815	609.93	263.95	5.43E-15	3.955	2.95

⁽¹⁾ Value obtained by KOWWIN is 1.989, which is an outlier. The expected value, based on linear extrapolation between C10, C14 and C16 amine oxide is 2.392.

Data Quality

2D (Klimisch) – Reliable with restrictions

References

EPIWIN, Version 3.0

6. REFERENCES

AISE 2002. Amine Oxide Survey of European Use and Exposure Information Provided by Member Companies.

AISE/HERA 2002. HERA Task Forces Human Habits and Uses Tables.

AISE/HERA 2005. Human & Environmental Risk Assessment on ingredients of European household cleaning products (HERA): Amine Oxides. (*in preparation*).

CESIO, 2003. CESIO Recommendation For The Classification And Labelling Of Surfactants As "Dangerous For The Environment". CESIO report, April 2003.

Cosmetics, Toiletries and Fragrances Association, 2003. Cosmetics, Toiletries, and Fragrance Association survey of amine oxide uses in personal care products.

EPIWIN: Physical/chemical property estimation methods, Version 3.0, from Syracuse Research Corporation, Syracuse, NY.

Japan Soap and Detergent Association, 2002. Japanese Soap and Detergent Association survey of amine oxide production, 2001-2002.

Kirk Othmer Encyclopedia of Chemical Technology, 2001, 4th edition, CD-ROM, John Wiley and Sons, ISBN: 0-471-15158-0

Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting.

Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 61791-46-6

Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2571-88-2
2530-44-1
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
68955-55-5
70592-80-2
85408-49-7
85408-48-6
93962-62-0

Sponsor Country: United States

Date: July, 2006

1. GENERAL INFORMATION

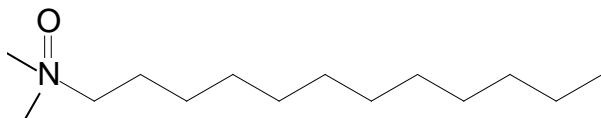
1.01 SUBSTANCE INFORMATION

- A. CAS number 61791-46-6
- B. Name (IUPAC name)
- C. Name (OECD name) Ethanol, 2,2'-iminobis-, N-tallow alkyl derives., N-oxides
- D. CAS Descriptor
- E. EINECS-Number 2631796
- F. Molecular Formula Unspecified

G. Structural Formula

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

Representative C₁₂ dimethyl amine oxide



- H. Substance Group Amine Oxides category
- I. Substance Remark None
- J. Molecular Weight Unspecified
- ### 1.02 OECD INFORMATION
- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
Address U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460
U.S.A.

Tel: (202) 564-7641

Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association

1500 K Street, N.W., Suite 300

Washington, D.C. 20005

USA

Tel: (202) 662-2523

Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.

Goldschmidt Chemical Corporation

Rhodia Inc.

Stepan Company

The Procter & Gamble Company

Akzo Nobel Surface Chemistry AB

Clariant GmbH

Cognis Deutschland GmbH

Huntsman Surface Sciences UK Limited

KAO Chemical

Stepan Europe

Degussa AG (Goldschmidt)

Kao Corporation

Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-

9-octadecenyloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

2,2'-Iminobisethanol, N-tallow alkyl derivs., N-oxides

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

(a) United States

26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)

Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.

- (b) Europe
(i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tonnes (AISE, 2002)
- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000; CESIO, 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or other applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%
Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%

Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also "Use and Exposure Information on Amine oxides", available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA 2002.

1.10 ADDITIONAL REMARKS**A. Options for Disposal**

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases.

3. ENVIRONMENTAL FATE AND PATHWAYS

3.5 BIODEGRADATION

(a)

Test Substance

CAS Number: **61791-46-6**
Identity: Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides
Purity: 50%
Chain Length Distribution: C16-18
Remarks: Balance is water (25%) and diethyleneglycol (25%)

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: CRL F90066
Test Type: aerobic
Method/Guideline Followed: Directive 84/449/EEC, C.6
Inoculum: activated sludge, domestic, non-adapted
Inoculum Acclimated: no
Control Substance: Acetic acid, sodium salt
Test Substance Initial Concentration: 2 mg/l as test substance
Remarks: Method essentially same as OECD Guideline 301D. Because of low solubility, test substance was added as coating of silica gel, prepared by mixing silica gel with test substance dissolved in dichloromethane, followed by evaporation of dichloromethane. Test duration 28 days. pH at end 7.4. Negative control (without test substance, 8 flasks), control without test substance but with silica gel (8 flasks), positive control (6.7 mg/l, 8 flasks).

Biodegradation measured as O₂ consumption. 1. Degradation was stated to have been calculated as the ratio between BOD/ThOD-NH₃. Nitrification was not measured. Kinetics shown represent worst-case assumptions namely that a) DEG is degraded readily and before any of the test substance is degraded and b. nitrification does occur so ThOD-NH₃ must be used in the calculations. This resulted in a degradation of >60% after 15 days.

Results

Kinetics Measured as: other

Kinetics of Test Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
5	day(s)	=	8	n/a

Kinetics of Control Substance:

15	day(s)	=	68	n/a
28	day(s)	=	79	n/a
Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
5	day(s)	=	79	n/a
28	day(s)	=	88	n/a

Result: readily biodegradable

Data Quality

2B (Klimisch) – Test conditions not fully documented.
Critical study for SIDS endpoint

Reference

Akzo Nobel Chemicals, 1990G

(b)

Test Substance

CAS Number: **61791-46-6**

Identity: Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides

Purity: not given

Chain Length Distribution: C10-16

Remarks: No CAS # given; assigned by reviewer.

Method

GLP: no

Report/Study Year: 1983

Report/Study Number: SDA101

Test Type: aerobic

Method/Guideline Followed: other

Inoculum: activated sludge, non-adapted

Inoculum Acclimated: no

Remarks: Literature review.

Test substances partition to water-organic interfaces and biodegrade rapidly. Approximately 15% is adsorbed to raw wastewater solids. Degradation reached 100% with 20 ppm coco-dimethylamine oxide within 23 hours in aerated synthetic sewage.

Degradation reached 99% at an unspecified concentration within 5 days in activated sludge.

Degradation reached 97% at an unspecified concentration within 5 days in activated sludge.

This summary report does not specify whether these results were primary biodegradation or mineralization, however mineralization test are more common.

Results

<i>Half Life:</i>	<i>Mineralization:</i> n/a
	<i>Primary Biodegradation:</i> n/a
<i>Degradation Products:</i>	not measured
Data Quality	4B (Klimisch) – Secondary literature
Reference	TSCA ITC, 1983

4. ECOTOXICITY

4.1.1 TOXICITY TO FISH (ACUTE)

Test Substance

CAS Number: **61791-46-6**
Identity: Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides
Purity: 50.1%
Chain Length Distribution: C12-18
Remarks: Balance is water

Method

GLP: no
Report/Study Year: 1991
Report/Study Number: CRL F90216
Method/Guideline Followed: Directive 92/69/EEC, C.1
Limit Test: no
Species: *Brachydanio rerio*
Exposure Period: 96 hours
Remarks: Method essentially same as OECD Guideline 203. 7 fish per vessel and 1 vessel per treatment. Aeration. Renewal after 2 days. Nominal test conc. 0 - 0.38 - 0.50 - 0.65 - 0.90 - 1.2 mg/l (active ingredient). Hardness 232 mg/l as CaCO₃. pH 8.0-8.2. O₂ 92 - 108% saturated. Temp 24 °C. 12 hours light. Loading 0.42 fish/l. Positive control K₂Cr₂O₇, 180 mg/l. Statistics by Spearman Karber binomial test method.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
LC50:	c	=	0.95	n/a
LC50	c	=	0.86	1.1

Remarks: No analyses. A biodegradation study (Biodegradability of CAS RN 61791-46-6) showed a decrease of test substance conc. of 8% over 5 days. The test substance concentrations were probably > 80% of nominal in the courser of this test. LC50 for K₂Cr₂O₇ not given.

Data Quality

1A (Klimisch) – No information on frequency of physical measurements (O₂, pH, temp.)
Critical study for SIDS endpoint

Reference

Akzo Nobel Chemicals, 1990B

4.2.1 AQUATIC INVERTEBRATES TOXICITY (ACUTE)**Test Substance**

CAS Number: 61791-46-6
Identity: Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides
Purity: 50.1%
Chain Length Distribution: C16
Remarks: Balance is 25% water and 25% diethyleneglycol

Method

GLP: yes
Report/Study Year: 1991
Report/Study Number: CRL F90214
Method/Guideline Followed: OECD Guideline 202
Test Type: static
Analytical Monitoring: no
Limit Test: no
Species: *Daphnia magna*
Exposure Period: 48 hours
Remarks: Daphnids < 24h old; 4 reps./conc. x 5 daphnids/rep. = 20 daphnids per conc. Nominal conc. 0.0 - 0.05 - 0.11 - 0.23 - 0.5 - 1.1 mg/l (active ingredient). No vehicle. Hardness 232 mg/l as CaCO₃; pH 8.2; temp. 19-20 °C; O₂ 96-102% saturated; 16h light. Observe immobility at 0, 24 and 48h. Statistics by Spearman-Kärber, binomial method.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
48h EC50	c	=	0.47	n/a
48h EC50	c	=	0.38	0.59

Remarks: EC50 = 0.47 (95% confidence interval 0.38 - 0.59) mg/l.
No analyses. A biodegradation study (CAS RN 61791-46-6; Report # CRL F90066) showed decreasing conc. of 8% in 2 days. Test substance conc. probably remained at >80% of nominal in this test. No information about feeding.

Data Quality

1A (Klimisch) – No feeding information.
Critical study for SIDS endpoint

Reference

Akzo Nobel Chemicals, 1991

4.3 TOXICITY TO AQUATIC PLANTS e.g. ALGAE**Test Substance**

CAS Number: 61791-46-6
Identity: Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides
Purity: 50.1%
Chain Length Distribution: C16
Remarks: Balance is 25% water and 25% diethyleneglycol

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: CRL F90154
Method/Guideline Followed: OECD Guideline 201
Analytical Monitoring: no
Species: *Selenastrum capricornutum*
Exposure Period: 72 hours
Remarks: 3 reps./conc. and 6 controls. Initial cell density 24000-42000 cells/ml. Standard OECD algal growth medium (OECD Guideline 201); hardness (Ca + Mg) dH 0.6 mmol/l. Nominal conc. 0.0 - 0.05 - 0.10 - 0.20 - 0.40 - 0.80 mg/l (active ingredient). Phys. meas. at 0 and 72h. Temp. 22-23 °C. pH 6.8-8.3. Continuous illumination 6000-10000 lux. Shaken. Observe cell density at 0, 24, 48 and 72h spectrophotometrically.
 Pos. control K₂Cr₂O₇: EbC50 = 0.20 mg/l; ErC50 = 0.77 mg/l.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower
NOEC:	m	=	0.1
EC10:	c	=	0.086
EC50:	c	=	0.19
EC20	c	=	0.11

Remarks: EC50 in table stands for EbC50. pH rose from 6.9 at initiation to (7.3 - 8.3) after 72 hours. pH increase was highest in the control and decreased as a function of test conc. Rise in pH was probably associated with strong cell growth, due to CO₂ depletion from test media. A biodegradation study (study report # CRL F90066) showed decrease in conc. of 8% in 5 days. Test conc. probably remained at >80% of nominal in this test.

Results calculated according to Bruce & Versteeg (1992) in mg/l:

	EC50	EC20	EC10
Growth Rate	0.30	0.15	0.21

	[0.27-0.33]	[0.13-0.18]	[0.08-0.13]
Biomass	0.19 [0.18-0.21]	0.11 [0.10-0.13]	0.086 [0.073-0.102]

Data Quality

1A (Klimisch)
Critical study for SIDS endpoint

Reference

Other reference

Akzo Nobel Chemicals, 1990F
Bruce and Versteeg, 1992

6. REFERENCES

AISE 2002. Amine Oxide Survey of European Use and Exposure Information Provided by Member Companies.

AISE/HERA 2002. HERA Task Forces Human Habits and Uses Tables.

AISE/HERA 2005. Human & Environmental Risk Assessment on ingredients of European household cleaning products (HERA): Amine Oxides. (*in preparation*).

Akzo Nobel Chemicals, 1990B. Acute toxicity of CAS RN 61791-46-6 to *Brachydanio rerio*. CRL F90216.

Akzo Nobel Chemicals, 1990F. Algal growth inhibition test with CAS RN 61791-46-6.

Akzo Nobel Chemicals, 1990G. Biodegradability of CAS RN 61791-46-6

Akzo Nobel Chemicals, 1991. Acute toxicity of CAS RN 61791-46-6 to *Daphnia magna*.

Bruce and Versteeg, 1992. Env. Toxicol. Chem. 11: 1485

CESIO, 2003. CESIO Recommendation For The Classification And Labelling Of Surfactants As "Dangerous For The Environment". CESIO report, April 2003.

Cosmetics, Toiletries and Fragrances Association, 2003. Cosmetics, Toiletries, and Fragrance Association survey of amine oxide uses in personal care products.

Japan Soap and Detergent Association, 2002. Japanese Soap and Detergent Association survey of amine oxide production, 2001-2002.

Kirk Othmer Encyclopedia of Chemical Technology, 2001, 4th edition, CD-ROM, John Wiley and Sons, ISBN: 0-471-15158-0

Modler R and Inoguchi Y., 2004. Surfactants, Household Detergents and their Raw Materials. Chemical Economic Handbook Marketing Research Report, SRI Consulting.

Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.

Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

TSCA ITC, 1983. Information Review Dimethyl (C10-C16 Alkyl) Amine N-Oxides. EPA Contract No. 68-01-6650. CRCS Inc., Reston, Virginia., USA & Dynamac Corporation, Rockville, Maryland, USA. 1983. TSCA Interagency Testing Committee, USA.

SIDS DOSSIER

CAS NO. 93962-62-0

Ethanol, 2,2'-[(9Z)-9-octadecenyloxidoimino]bis-

Chemical Category: Amine Oxides

Other CAS Nos. in the Category:

1643-20-5
2530-44-1
2571-88-2
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-48-6
85408-49-7

Sponsor Country: United States

Date: July, 2006

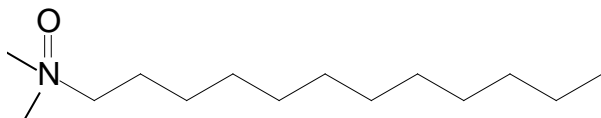
1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number 93962-62-0
- B. Name (IUPAC name)
- C. Name (OECD name) Ethanol, 2,2'-[(9Z)-9-octadecenyl oxidoimino]bis-
- D. CAS Descriptor
- E. EINECS-Number 3006955
- F. Molecular Formula C₂₂H₄₅NO₃
- G. Structural Formula

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

C₁₂ dimethyl amine oxide



- H. Substance Group Amine Oxides category
- I. Substance Remark None
- J. Molecular Weight 371 grams/mole
- 1.02 OECD INFORMATION
- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)
- Contact person: Oscar Hernandez
Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460
U.S.A.

Tel: (202) 564-7641
Fax: (202) 564-7450

C. Name of Responder

Name: Richard Sedlak, Consortium Manager

Address:

The Soap and Detergent Association
1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

1.03 CATEGORY JUSTIFICATION

The amine oxides category includes 15 substances as defined by 15 CAS numbers. Four of the chemical substances have High Production Volume (HPV) chemical status in one or more OECD regions. The justification for grouping the amine oxides into a category is based on their structural and functional similarity. All of the substances in this category are surfactants, consisting of a polar “head” (the amine oxide) and a relatively inert, hydrophobic “tail” (the long alkyl substituent). The structural variations in the category are three-fold: 1) the nature of the second and third substituents on the amine are either methyl groups or hydroxyethyl groups; 2) the long alkyl chain ranges in length from 8 to 20 carbons; and 3) the long alkyl chain may contain one or two double bonds (i.e. unsaturation) as in C18:1 (oleyl) or C18:2 (linoleyl).

Commercial amine oxides are either alkyl dimethyl amine oxides or alkyl dihydroxyethyl amine oxides which contain 2 methyl groups or 2 hydroxyethyl groups, respectively, attached to the tertiary nitrogen. Alkyl chain lengths range from 8 to 20 with 12 and 14 being predominant. Average chain lengths for the mixtures are 12.9 to 13.5, with the exception of one tallow-derived compound.

The chemical behaviors of the amine oxides are expected to be very similar. Differences relate to the alkyl substituents: their nature (methyl, hydroxyethyl) and the number of carbon atoms in the alkyl chain (8 to 20). These structural variances impact the physical and chemical properties of these surfactants. The presence of methyl- vs. hydroxyethyl-substituents affects the basicity of the nitrogen only marginally, and the hydroxyethyl group lends more bulk to the hydrophilic head-group of the surfactant. The length of the longest alkyl substituent does not alter the chemical reactivity of the molecule, but does affect its physical properties. The influence of unsaturation in the alkyl chain (as in CAS Nos. 93962-62-0 Ethanol, 2,2'-[(9Z)-

9-octadecenyloxidoimino]bis- and 61791-46-6 Ethanol, 2,2'-iminobis-, N-tallow alkyl derivs., N-oxides) is expected to make the molecule prone to reactions as typical for unsaturated fatty alkyl chains. Nevertheless, their overall chemical behavior fits within that of the group of C8-20 alkyl dihydroxy ethyl amine oxides.

1.1 GENERAL SUBSTANCE INFORMATION

A. Type of Substance

element []; inorganic []; natural substance []; organic [X]; organometallic [];
petroleum product []

B. Physical State (at 20°C and 1.013 hPa)

gaseous []; liquid []; solid [X] for pure substance

C. Purity

The chemicals of the amine oxides category do not exist as 'pure' substances, but are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity. Depending on method of manufacture, trace levels of stabilizers, processing aids or other impurities may be present.

D. Manufacturing Process

The fatty alkyl amine oxides are produced by reacting trialkylamines with hydrogen peroxide in water. In turn, the trialkylamines are derived from either linear alpha-olefins or detergent-range alcohols. Linear alpha-olefins are the source of the largest volume of fatty amine oxides. There are nine AO Manufacturing facilities in the U.S. All substances in the category are produced, transported and used as aqueous solutions, typically at a 25-35% level of activity.

1.2 SYNONYMS

2,2'-(Z)Octadec-9-en-1-ylimino)bis ethanol N-oxide

1.3 IMPURITIES

Impurities such as, hydrogen peroxide (trace levels) and free amine (<1%) may be present.

1.4 ADDITIVES

None

1.5 QUANTITY

This is for all amine oxides manufactured and/or imported; values for individual CAS numbers and substances are not available.

(a) United States

26,000 metric tonnes/year (Soap and Detergent Association, 2002A.)

Value is consistent with the USEPA 2002 IUR (Inventory Update Rule) database.

- (b) Europe
(i) 16,000 metric tonnes/year (Modler and Inoguchi, 2004)
(ii) 21,570 metric tonnes (AISE, 2002)
- (c) Japan
6,800 metric tonnes/year. (Japanese Soap and Detergent Association, 2002)

1.6 LABELLING AND CLASSIFICATION

Labelling dangerous for the environment ; irritating
Remarks: following CESIO recommendations (CESIO, 2000 and 2003)

Classification Very toxic to aquatic organisms (R50); Irritating to skin (R38);
Risk of serious damage to eyes (R41)
Remarks: following CESIO recommendations (CESIO, 2000 and 2003)

1.7 USE PATTERN

A. General

Type of Use:	Category:
main	Wide dispersive use
industrial	Personal and domestic use
use	Cleaning/Washing agent

Amine oxides are amphoteric surfactants that are used in cleaning and personal care products, usually in conjunction with other surfactants. They function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents in liquid dishwashing detergents, hard surface cleaners, fine fabric/laundry detergents, shampoos, hair conditioners, moisturizers, bar soaps, cleansing and other personal care products. There are no commercial uses or industrial process intermediate uses of the amine oxides. Some other less common uses of AOs have been reported in the patent literature, e.g., phase-transfer catalysts, bleaching agents and photography (Kirk Othmer Encyclopedia of Chemical Technology, 2001). These do not appear to be in widespread use. According to Modler and Inoguchi (2004), the majority AOs in North America, 95%, are used in household cleaning products. Much smaller volumes (<5%) are used in personal care or other applications.

B. Uses in Consumer, Institutional and Industrial Products

The following table shows the percentage of amine oxides that occurs in various types of consumer laundry/cleaning and personal care products globally.

Consumer Product Type	Range of Composition that is Amine Oxide
Laundry Liquid Detergents	1-5%
Hard Surface Cleaners (liquid)	0.05-5.2%
Hard Surface Cleaners (liquid / spray)	0.5-5%
Hand Dishwashing Liquid Detergents	0.1-10%

Hand / face soaps (bar)	0.1-5%
Shampoo	0.09-5%
Hair Conditioner	0.6-0.7%
Hair Styling tonic / gel	0.1-2%
Cleansing Products	0.04-9%
Skin Creams / Moisturizers	0.2-0.6%
After Shaves	0.5-1%
Home Dry Cleaning Products	0.1-0.5%
Douches	1-2%
Face/Eye Foundations (liquid)	<0.1%
Hair Coloring Preparations	<0.1%
Permanent Waves	1-2%

Sources: Soap and Detergent Association, 2002B; CTFA, 2003; AISE/HERA, 2002 and 2005; and Japanese Soap and Detergent Association, 2002.

See also “Use and Exposure Information on Amine oxides”, available from U.S. SDA website at www.sdahq.org/amineoxides

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUE

Exposure limit value

Type: None established

Short term exposure limit value

Value: None established

1.9 SOURCES OF EXPOSURE

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous material. The potential for human exposure to amine oxides by inhalation is minimized by its low volatility and because the production, formulation and industrial end use of products are in aqueous solutions. Dermal exposure is possible. Engineering controls (e.g., closed system operations and exhaust ventilation) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for amine oxides category.

Amine oxides are used primarily in household laundry and cleaning products and in personal care products. After use, these products are discharged into the wastewater treatment system. The exposure of the general human population and of environmental organisms depends on the application of amine oxides, the local sewage treatment practices, and on the characteristics of the receiving environment.

It is reasonable to consider that the greatest exposure to the consumer is dermal exposure following use of personal care products. The personal care products can be applied as is, diluted during use, and may be rinsed off. Dermal contact does occur with personal care products and may also occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, and/or eye contact with, product during handling and use. Low volatility minimizes the potential for inhalation.

Sources: Soap and Detergent Association, 2002A and 2002B; AISE/HERA, 2002.

1.10 ADDITIONAL REMARKS

A. Options for Disposal

Unused amine oxide may be recovered for reprocessing or disposed of by incineration or landfill or by flushing to sewage system; used material enters sewage system and is treated at WWTP. Spills may be recovered for reprocessing or disposal. Disposal is to be performed in compliance with all federal, state/provincial and local regulations. Do not dispose of via sinks, drains or into the immediate environment.

B. Last Literature Search

2003. Including survey of Amine Oxide Consortium member companies for quantity, uses, and unpublished studies on physical/chemical properties, environmental fate, environmental effects and mammalian toxicity. Also literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases

2. PHYSICAL-CHEMICAL DATA

2.0.1 EPISuite™ ESTIMATION OF PHYSICAL/CHEMICAL PROPERTIES

Test Substance

CAS Number: **93962-62-0**
Identity: 2,2'-(Z)-octadec-9-en-1-ylimino)bisethanol N-oxide
Purity: not relevant
Chain Length Distribution: C18:1

Method

GLP: n/a
Report/Study Year: n/a
Method/Guideline Followed: EPIWIN
Remarks: All estimates apply to the pure, dry substance and not their solutions in water.

Results

	Estimate
Molecular Weight (grams/mole):	371.61
Water Solubility (mg/l):	0.045
Octanol Water Partition Coefficient (Log Kow):	5.86
Bioconcentration Factor (Log BCF):	2.815
Boiling Point (°C):	609.93
Melting Point (°C):	263.95
Vapor Pressure (Pa):	5.43E-15
Henry's Law Constant (atm/(mole/m ³)):	4.42E-16
Atmospheric Oxidation Half-Life (hours):	3.95
Soil Adsorption Coefficient (Log Koc):	3.955

Remarks: Trends analysis, based on the N,N-Dimethyl Amine Oxides:
For every extension of two –CH₂– units to the alkyl chain

- Water solubility decreases by 1 order of magnitude.
- The Log Kow increases by ~ 1 unit [or the octanol/water partition coefficient increases by 1 order of magnitude].
- The Log BCF increases by ~ 0.25 units [or the BCF nearly doubles; it increases by a factor of 1.8].
- The boiling point increases by ~ 23°C, although these are theoretical values, as most surfactants decompose before they boil.
- The melting point increases by ~ 15°C.
- The Log Koc increases by ~ 0.5 unit [or the soil adsorption coefficient increases by a factor of 3].

Trends are similar for the N,N-Dihydroxyethyl Amine Oxides - The substitution of the nitrogen with two hydroxyethyl groups (vs. the two methyl groups of the N,N-Dimethyl Amine Oxides) increases the hydrophilicity of the hydrophilic head group of the surfactant. This results in a higher water solubility, a lower Log Kow and a lower Koc.

CAS #	Chain Length	MW (g/mole)	Water Sol. (mg/l)	Log Kow	Log BCF	BP (°C)	MP (°C)	VP (Pa)	Log Koc	Atm Oxidation half-life (hours)
N,N-Dimethyl Amine Oxides										
2605-79-0	C10	201.36	30.35	3.69	2.142	403.41	152.60	4.57E-5	3.739	5.26
1643-20-5	C12	229.41	3.13	4.67	⁽¹⁾ 2.392	426.62	167.95	2.09E-5	4.271	4.71
3332-27-2	C14	257.46	0.32	5.66	2.655	449.82	183.30	1.48E-6	4.803	4.27
7128-91-8	C16	285.52	0.032	6.64	2.911	473.03	198.65	2.59E-7	5.334	3.90
N,N-Dihydroxyethyl Amine Oxides										
2530-44-1	C12	289.46	29.89	3.13	1.712	536.73	229.76	3.39E-12	2.360	2.36
14048-77-2	C18	373.63	0.029	6.08	2.481	606.35	262.28	7.45E-15	3.955	2.04
93962-62-0	C18:1	371.61	0.045	5.86	2.815	609.93	263.95	5.43E-15	3.955	2.95

⁽¹⁾The value obtained by KOWWIN is 1.989, which is an outlier. The expected value, based on linear extrapolation between C10, C14 and C16 amine oxide, is 2.392.

Data Quality 2D (Klimisch) – Reliable with restrictions

Reference EPIWIN, Version 3.0.

3. ENVIRONMENTAL FATE AND PATHWAYS

3.5 BIODEGRADATION

Test Substance

CAS Number: **93962-62-0**
Identity: 2,2'-(Z)-octadec-9-en-1-ylimino)bisethanol N-oxide
Purity: 58.2%
Chain Length Distribution: C18:1
Remarks: Balance is water (8.9%), diethylene glycol (33%), free amine (0.3%) and H₂O₂ (0.07%)

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: CRL F90067
Test Type: aerobic
Method/Guideline Followed: Directive 92/69/EEC, C.4-E
Inoculum: activated sludge, domestic, non-adapted
Inoculum Acclimated: no
Control Substance: Acetic acid, sodium salt
Test Substance Initial Concentration: 500 mg/l as test substance
Remarks: Method essentially identical to Guideline OECD 301D. Test substance at 1 g/l was added in dichloromethane; 0.56 ml of this mixture was added to 2 grams silica gel. The solvent was evaporated for 3 hours. Thereafter the total content was added to 280 ml bottle, containing 2 mg (dry wt.) sludge/l. Initial test substance conc. calculated as 500 mg/l. by author of this summary. Biodegradation measured as O₂ consumption. All treatments in triplicate. The test substance is known to be toxic at high concentrations, and the test concentration is quite high at 500 mg/l. Therefore silica was used to:
a) facilitate dosing of the substance and
b) reduce its toxicity to the sludge as the test substance would be on the silica carrier material.

Kinetics given in this summary are for the substance dosed with the silica carrier material.

Results

Kinetics Measured as: other

Kinetics of Test Substance:

Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
5	day(s)	=	12	n/a

*Kinetics of Control
Substance:*

15	day(s)	=	45	n/a
28	day(s)	=	60	n/a
Exposure Period	Exposure Unit	Operator	Lower (%)	Upper (%)
5	day(s)	=	75	n/a
28	day(s)	=	87	n/a

*Half Life:**Mineralization:* not determined*Primary Biodegradation:* n/a*Result:*

Ultimately biodegradable

Remarks:

In order to classify a material as "readily biodegradable", the OECD 301D protocol (closed bottle test) requires that 60% of theoretical oxygen is consumed within a 10-day window after the 10% mark is reached. This requirement was not met in this test. It is possible that this is due to low bio-availability of the test compound, due to its low water solubility and/or its tendency to sorb to solids. In order to determine whether this might have been the case, it would be necessary to repeat the test and use a dosing vehicle to overcome this constraint.

Data Quality

2B (Klimisch) – Comparable to guideline study
Critical study for SIDS endpoint

Reference

Akzo Chemicals International B.V., 1990G.

4. ECOTOXICITY

4.1.1 TOXICITY TO FISH (ACUTE)

Test Substance

CAS Number: 93962-62-0
Identity: 2,2'-(Z)-octadec-9-en-1-ylimino)bisethanol N-oxide
Purity: 58.27%
Chain Length Distribution: C18:1
Remarks: Balance is water (8.9%), diethyleneglycol (33%), free amine (0.28%), H₂O₂ (0.07%)

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: CRL F90065
Method/Guideline Followed: Directive 84/449/EEC, C.1; OECD Guideline 203
Test Type: acute, semi-static, renewal at 48 hrs
Analytical Monitoring: no
Limit Test: no
Species: *Brachydanio rerio*
Exposure Period: 96 hours
Remarks: No aeration. No feed. 10 fish/vessel; 1 vessel/conc. Nominal test conc. 0.0 - 0.12 - 0.27 - 0.58 - 1.22 - 2.68 mg/l (active ingredient). Physical measurements daily; pH 7.3-8.2. O₂ > 60% saturated except as 24h in highest conc. and at 48h in 0.58 and 1.22 mg/l treatments where O₂ was [43-55%] of saturation. Temp 21-24 °C. Hardness 230 mg/l as CaCO₃.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
LC50:	c	=	0.81	n/a
LC50	c	=	0.58	1.2

Remarks: At 24h the water was turbid in the highest conc. due to bacterial growth. All fish had died. A biodegradation study (Biodegradability of CAS RN 93962-62-0; Report # CRL F90067) showed a decrease in test substance conc. of up to 12% in 5 days. The test concentrations probably remained at or above 80% of nominal during the test. Mortality at highest treatment might be due to lack of oxygen, but low oxygen conc. not expected to affect the calculated LC50. 100% mortality at 2.7 mg/l. After 24 hours, water turbid due to bacterial growth.

Data Quality 2B (Klimisch) – Basic data given, comparable to guidelines/standards. Deaths due to possible oxygen shortage. No analyses
Critical study for SIDS endpoint

Reference Akzo Chemicals International B.V., 1990B.

4.2.1 AQUATIC INVERTEBRATES TOXICITY (ACUTE)

Test Substance

CAS Number: **93962-62-0**

Identity: 2,2'-(Z)-octadec-9-en-1-ylimino)bisethanol N-oxide
N-oleyl-N,N-dihydroxyethylamine oxide

Purity: 58.2%

Chain Length Distribution: C18:1

Remarks: Balance is water (8.9%), diethylene glycol (33%), free amine (0.3%) and H₂O₂ (0.07%)

Method

GLP: yes

Report/Study Year: 1991

Report/Study Number: CRL F90144

Method/Guideline Followed: OECD Guideline 202

Test Type: acute, static

Analytical Monitoring: no

Species: *Daphnia magna*

Exposure Period: 48 hours

Remarks: Daphnids < 24h old; no feeding; 5 daphnids/rep. x 4 reps./conc. = 20 daphnids per conc. Nominal conc. 0.0 - 0.33 - 0.58 - 1.05 - 1.86 - 3.26 mg/l (active ingredient). No aeration. 16 h light; Phys. meas. at 0 and 48h. pH 8.2; Temp. 19-21 °C; O₂ 96-102% saturated; hardness 230 mg/l as CaCO₃. Statistics: Trimmed Spearman-Kärber method.

Results

Unit: mg/l

	Measured/Computed	Operator	Lower	Upper
EC50:	c	=	0.64	n/a
EC50	c	=	0.55	0.76

Remarks: No analyses. A biodegradation study (CAS RN 93962-62-0; Report # CRL F90067) showed decrease in conc. of 80% of nominal in this test.

Data Quality 1A
Critical study for SIDS endpoint

Reference Akzo Chemicals International, 1991.

4.3 TOXICITY TO AQUATIC PLANTS e.g. ALGAE

Test Substance

CAS Number: 93962-62-0

Identity: 2,2'-(Z)-octadec-9-en-1-ylimino)bisethanol N-oxide

Purity: 58.2%

Chain Length Distribution: C18:1

Remarks: Balance is water (8.9%), diethylene glycol (33%), free amine (0.3%) and H₂O₂ (0.07%)

Method

GLP: yes

Report/Study Year: 1990

Report/Study Number: CRL F90156

Method/Guideline Followed: OECD Guideline 201

Analytical Monitoring: no

Species: *Selenastrum capricornutum*

Endpoint: other

Exposure Period: 72 hours

Remarks: 3 reps./conc. and 6 controls. Initial cell density 6000-28000 cells/ml. Nominal conc. 0.0 - 0.06 - 0.12 - 0.23 - 0.46 - 0.93 mg/l (active ingredient). Physical measurements at 0 and 72h. Temp. 22-23°C. pH 6.8-6.3. Continuous illumination 6000-10000 lux. Shaken 100 rpm. Pos. control K₂Cr₂O₇; EbC50 = 0.2 mg/l and ErC50 = 0.77 mg/l. Observe cell density at 0, 24, 48 and 72h (spectrophotometrically). Statistics: Probit analysis.

Results

Unit: mg/l

	Measured/Computed	Operator	
NOEC:	m	=	0.12
EC10:	c	=	0.069
EC50:	c	=	0.16
EC20	c	=	0.091

Remarks: Rises in pH of > 1 unit probably associated with strong cell growth due to CO₂ depletion from test media. Controls unaffected by lack of CO₂.
A biodegradation study (report # CRL F90067) showed decrease in concentration of 12% in 5 days.

Results calculated according to Bruce and Versteeg (1992), in mg/l:

	EC50	EC20	EC10
Growth Rate	0.25 [0.212-0.285]	0.11 [0.0881-0.144]	0.074 [0.0554-0.101]
Biomass	0.16 [0.127-0.195]	0.091 [0.0657-0.127]	0.069 [0.0462-0.102]

Data Quality

1A - Reliable; guideline study
Critical study for SIDS endpoint

Reference

Other reference

Akzo Nobel Chemicals, 1990D
Bruce and Versteeg, 1992

5. TOXOCITY

5.1.1 ACUTE ORAL TOXICITY

Test Substance

CAS Number: **93962-62-0**
Identity: 2,2'-(Z)-Octadec-9-en-1-ylimino)bisethanol N-oxide
Purity: 58.2%
Chain Length Distribution: C18:1
Remarks: Balance is water (8.9%), diethylene glycol (33%), free amine (0.3%) and H₂O₂ (0.07%)

Method

GLP: yes
Report/Study Year: 1990
Report/Study Number: 031409
Method/Guideline Followed: OECD Guideline 401; EEC Dir. 84/449/EEC, Part B.1.
Test type: LD50
Species: rat
Strain: Wistar Albino rats
Sex: male/female
Vehicle: No vehicle; single dose by gavage
Number of Animals per Dose: 10 (5 males + 5 females)
Doses: 757, 1397 and 2444 mg a.i./kg bw
Remarks: No vehicle; weight 163-197 g (females) and 199-251 g (males). Animals were fasted overnight before dosing.

Results

Value: 2395 mg/kg bw
Remarks: Estimated, combined LD50 2395 mg/kg bw
Males LD50 7489 mg/kg bw
Females LD50 1706 mg/kg bw

Exact LD50 could not be calculated due to the distribution of the mortalities.

From high to low dose, the mortalities among the males were: 1/5, 0/5 and 0/5 and among the females they were: 5/5, 0/5 and 0/5. Mortality (males and females combined): low dose group 0/10; mid dose group 0/10; high dose group 6/10.

Clinical symptoms: lethargy, piloerection and emaciation in the highest dose. Necropsy findings: stomach enlargement, red coloration of stomach and/or thymus, gaseous accumulation in

stomach, yellow intestine content, stomach and/or intestines filled with bloody fluid, irregular grey/white areas in forestomach epithelium, small thymus, deep/bright red or light tan lungs sometimes with liver-colored areas or petechiae. Macroscopic changes from 90% mortality level. Salivation, nasal and/or ocular haemorrhage.

Data Quality

1A
Critical study for SIDS endpoint

Reference

Akzo Chemicals International B.V., 1990F

5.5 GENETIC TOXICITY *in vitro***Test Substance**

CAS Number: 93962-62-0

Identity: 2,2'-(Z)-octadec-9-en-1-ylimino)bisethanol N-oxide

Purity: 58.2%

Chain Length Distribution: C18:1

Remarks: Balance is water (8.9%), diethylene glycol (33%), free amine (0.3%) and H₂O₂ (0.07%)

Method

GLP: yes

Report/Study Year: 1990

Report/Study Number: NOTOX 031433

Method/Guideline Followed: OECD Guideline 471

Test Type: Ames test

System: Bacterial strains TA1535; TA1537; TA98, TA100. Rat liver S9 mix (Aroclor 1254-induced).

Test Concentration: see remarks

Species/strain: n/a

Metabolic Activation: with and without

Remarks: Ames *Salmonella*/microsome test. Initial and repeat test, based on toxicity. -S9: 0.33, 1.0, 3.3, 10.0 and 33.3 µg a.i./plate. +S9: 1.0, 3.3, 10.0, 33.3 and 100.0 µg a.i./plate. Negative control DMSO. Positive control 2-aminoanthracene (+S9); sodium azide (TA1535); 9-aminoacridine (TA1537); daunomycin (TA98); methylmethanesulfonate (TA100), all without S9.

Results

Result: negative

Cytotoxic Concentration: no data

Remarks: Positive controls gave expected results.

Data Quality

1A
Critical study for SIDS endpoint

Reference

Akzo Chemicals International BV, 1990A

6. REFERENCES

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- Akzo Chemicals International B.V., 1990B. Acute Toxicity of (CAS RN 93962-62-0) to Fish.
- Akzo Nobel Chemicals, 1990D. Algal growth inhibition test with (CAS RN 93962-62-0).
- Akzo Chemicals International B.V., 1990F. Assessment of acute oral toxicity with (CAS RN 93962-62-0) in the rat.
- Akzo Chemicals International B.V., 1990G. Biodegradability of CAS RN 93962-62-0.
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- Soap and Detergent Association, 2002A. Amine Oxide Survey: Survey of use and exposure information provided by the member companies of the Amine Oxides Consortium and the SDA HPV Task Force.
- Soap and Detergent Association, 2002B. Habit and Practice Survey. Survey conducted by the U.S. Soap and Detergent Association and its member companies.

SIDS DOSSIER

CAS NO. 60729-78-5

1-(methyldodecyl)dimethylamine-N-oxide

supporting chemical for

Chemical Category: Amine Oxides

CAS Nos. in the Category:

1643-20-5
2530-44-1
2571-88-2
2605-79-0
3332-27-2
7128-91-8
14048-77-2
61788-90-7
61791-47-7
61791-46-6
68955-55-5
70592-80-2
85408-48-6
85408-49-7
93962-62-0

Sponsor Country: United States
Date: July, 2006

1. GENERAL INFORMATION

1.01 SUBSTANCE INFORMATION

- A. CAS number 60729-78-4
- B. Name (IUPAC name)
- C. Name (OECD name) 1-(methyldodecyl)dimethylamine-N-oxide
- D. CAS Descriptor
- E. EINECS-Number
- F. Molecular Formula C₁₅H₃₃NO
- G. Structural Formula



- H. Substance Group
- I. Substance Remark
- J. Molecular Weight

1.02 OECD INFORMATION

- A. Sponsor Country: United States
- B. Lead Organization: Environmental Protection Agency (EPA)

Contact person: Oscar Hernandez
Address: U.S. Environmental Protection Agency
1200 Pennsylvania Ave.
Mail Code 7403M
Washington, DC 20460
U.S.A.
Tel: (202) 564-7641
Fax: (202) 564-7450

- C. Name of Responder
- Name: Richard Sedlak, Consortium Manager
Address:
The Soap and Detergent Association

1500 K Street, N.W., Suite 300
Washington, D.C. 20005
USA
Tel: (202) 662-2523
Fax: (202) 347-4110

Consortium Participants:

Akzo Nobel Chemicals Inc.
Goldschmidt Chemical Corporation
Rhodia Inc.
Stepan Company
The Procter & Gamble Company
Akzo Nobel Surface Chemistry AB
Clariant GmbH
Cognis Deutschland GmbH
Huntsman Surface Sciences UK Limited
KAO Chemical
Stepan Europe
Degussa AG (Goldschmidt)
Kao Corporation
Lion Akzo Co., Ltd.

5. TOXICITY

5.6 GENETIC TOXICITY *in vivo*

Test Substance

CAS Number: 60729-78-4

Identity: 1-(methyldodecyl)dimethylamine-N-oxide

Purity: n/a

Carbon Chain Length: C12

Distribution:

Remarks: CAS No. added by reviewer based on chemical identity provided in publication.

Method

GLP: unknown

Report/Study Year: 1986

Method/Guideline Followed: similar to OECD474

Test Type: Mammalian Erythrocyte Micronucleus test

Species: mouse

Strain: ICR-SPF

Sex: male / females (3 males / 4 females)

Route of Administration: gavage

Exposure Period: n/a

Doses: 235 mg/kg

Remarks: Material (abbreviated as 2-ATDNO) dissolved in water. Administered to 8 week old animals weighing 25-30 g as 0.1 mL/10g single dose p.o. Dose selection based on 1/5 LD50. Harvest time at 6, 24, 48 and 72 hours post exposure. 500 PCE analyzed for the incidence of micronuclei according to Schmid (1976).

Results

Result: negative

Remarks: No statistical increase in micronuclei by t-test at p
Positive control not reported for this study.

time	incidence of micronuclei (%)			
	negative control males	negative control females	2-ATDNO males	2-ATDNO females
6 hr	-	-	0.2	0.2
24 hr	0.16	0.15	0.2	0.2
48 hr	-	-	0.07	0.15
72 hr	-	-	0.13	0.05

Data Quality

Flags: Critical study for SIDS endpoint

*Reliability
(Klimisch):* 2D

Remarks: Reliable with restrictions. No positive control included in report. No PCE/NCE ratio reported. Only 500 cells/animal scored. Only one dose tested. No discussion of toxicity for this test material (2 other materials were included in the study: 1-dodecylpiperidine-N-oxide (DPNO) and 1-dodecyl-1-methylpiperidine bromide (DMPBr). The authors reported 20% mortality within 3 hours of dosing DMPBr at 235mg/kg).

Reference

Source Szabova E. and Devinsky F. (1988) Cytogenetic effect of some amine oxides and
Reference: organic ammonium salts on mouse somatic cells. Casopis Pre Farmaceuticku Vedu A Prax. 57(1)1-5. [SLOVAK]

Test Substance

CAS Number: 60729-78-4

Identity: 1-(methyldodecyl)dimethylamine-N-oxide

Purity: n/a

*Carbon Chain Length
Distribution:* C12

Remarks: CAS No. added by reviewer based on chemical identity provided in publication.

Method

GLP: unknown

Report/Study Year: 1987

*Method/Guideline
Followed:* similar to OECD 474

Test Type: Mammalian Erythrocyte Micronucleus test

Species: hamster

Strain: Chinese hamster

Sex: males (5 / dose)

*Route of
Administration:* i.p.

Exposure Period: 2 administrations, 24 hr apart, 6 hr harvest after last dose

Doses: 160, 300, and 700 mg/kg

Remarks: Animals 8-10 weeks old, 25-30 g. Included negative control (water) and positive control (cyclophosphamide). Bone marrow was collected from both femurs, prepared separately for each animal. Performed according to the method described by Schmid (1975). Test substance abbreviated as 2-ATDNO.

Results

Result: negative

Remarks:

Substance	Dose (mg/kg)	# PCE	incidence of cells with micronuclei
2-ATDNO	160	1000	2
2-ATDNO	300	1000	3
2-ATDNO	700	1000	4
cyclophosphamide	66	1000	52
water		1000	4

Data Quality

Flags: Critical study for SIDS endpoint

Reliability
(Klimisch): 2D

Remarks: Reliable with restrictions. Individual animal data not provided. Presumably 1000 PCE/animal, but unclear in publication. Males only (should not affect validity of the study). Included positive control that showed an appropriate response.

Reference

Source Karasova, M., Catar, G., Kieferova, L., Devinsky, F. and Leitmanova, A. (1987)
Reference: Effect of an Amine Oxide Iodophor on Mammalian Chromosomes. Bratisl. lek. Listy. 87(2)204-209. [SLOVAK]

Test Substance

CAS Number: 60729-78-4

Identity: 1-(methyldodecyl)dimethylamine-N-oxide

Purity: n/a

Carbon Chain Length
Distribution: C12

Remarks: CAS No. provided by reviewer based on chemical identity provided in publication.

Method

GLP: unknown

Report/Study Year: 1987

Method/Guideline
Followed: similar to OECD 475

Test Type: Mammalian bone marrow chromosome aberration test

Species: hamster

Strain: Chinese hamster

Sex: males (5 / group)

Route of i.p.

Administration:

Exposure Period: 1mL i.p. every 24 hr.

Doses: 160, 300, and 700 mg/kg

Remarks: Animals were 8-10 weeks old, 25-30g. Dose selection based on LD50 mentioned in introduction of article (1004 - 1379 mg/kg p.o.); high dose is approximately 50% LD50. Analyzed 250 metaphase cells / concentration. Mitotic index not provided. Colchicine administered two hours prior to sacrifice. Slide preparations for cytogenetic analysis prepared using a modification of Tjio and Whang (1962). Test substance abbreviated as 2-ATDNO.

Results

Result: negative

Remarks: Evaluated 250 mitoses for each concentration, counted less than 2% aberrant cells. Cyclophosphamide (positive control) showed an appropriate response.

Substance	Dose	# cells evaluated	# aberrant cells	# chromatid breaks	# chromosome breaks	exchanges	partially pulverized	gaps
2-ATDNO	160	250	1	0	1	0	0	0
2-ATDNO	300	250	2	1	1	0	0	3
2-ATDNO	700	250	5	4	1	0	0	5
cyclophosphamide	66	250	85	43	0	36	6	15
water		250	1	1	0	0	0	0

Data Quality**Flags:** Critical study for SIDS endpoint

Reliability (Klimisch): 2D

Remarks: Reliable with restrictions. Lacks some details. Not clear how many cells were analyzed per animal.

Reference

Source Karasova, M., Catar, G., Kieferova, L., Devinsky, F. and Leitmanova, A. (1987)
Reference: Effect of an Amine Oxide Iodophor on Mammalian Chromosomes. Bratisl. lek. Listy. 87(2)204-209. [SLOVAK]