AMINES, TALLOW ALKYL

CAS No: 61790-33-8

EINECS No: 263-125-1

(2nd Priority List)

(Z)-OCTADEC-9-ENYLAMINE

CAS No: 112-90-3

EINECS No: 204-015-5

OCTADECYLAMINE

CAS No: 124-30-1

EINECS No: 204-695-3

AMINES, HYDROGENATED TALLOW ALKYL

CAS No: 61788-45-2

EINECS No: 262-976-6

AMINES, COCO ALKYL

CAS No: 61788-46-3

EINECS No: 262-977-1

(all 4th Priority List)

Strategy For Limiting Risks

Human Health

Draft of November 2008

The rapporteur for the primary alkyl amines is the Federal Institute for Occupational Safety and Health.

Contact point:

Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA)

Anmeldestelle Chemikalien / Zulassungsstelle Biozide

(Federal Institute for Occupational Safety and Health

Division for Chemicals and Biocides Regulation)

Friedrich-Henkel-Weg 1-25

44149 Dortmund (Germany)

fax: +49(231)9071-2679

e-mail: chemg@baua.bund.de

CONTENT

0 Summary

The five primary alkyl amines **Amines, tallow alkyl, (Z)-Octadec-9-enylamine, Octadecylamine, Amines, hydrogenated tallow alkyl and Amines, coco alkyl** are produced and/or imported by eight companies in the European Union (State 1999/2000) (see also Tab. 1.2: Production and import of primary alkyl amines).

Starting materials in the manufacture of long-chain, primary alkyl amines are natural fats and oils, or synthetic products of the petrochemical industry. Intermediates are alkyl nitriles, which are formed from carboxylic acids and ammonia over dehydrating catalysts (Al_2O_3, ZnO, or salts of Mn or Co) in liquid-phase reactors or liquid- and vapor-phase reactors at 280-360°C. The nitriles are hydrogenated at a temperature of 80-180°C and a pressure of 1 - >10 MPa in the presence of nickel or cobalt catalysts.

According to the data supplied by the producers and importers 5172 t/a Coco, 12119 t/a Tallow, 7555 t/a Hydr. Tall., 462 t/a Octadecyl and 4022 t/a Octadecenyl are consumed within Europe for the period 1999/2000 (see also Tab. 1.3: Production volume, imports and exports).

Major amounts of the amines are used as intermediate in chemical industry: 97% of Coco, 98% of Tallow, 34% of Hydr. Tall., 69% of Octadecyl and 84% of Octadecenyl.

Further uses are fertilizers, anticaking, metal ind., floatation agent, metal proc. ind., lubricants, fuel additive, formulations (metal, corrosion inhibitors), formulations (textiles), paints, antistatic agent and rubber additive (see also Tab. 1.4: Uses of primary alkyl amines)

The primary alkyl amines are currently not classified in the Annex I of Directive 67/548/EEC.

Industry labels some of them as follows (GESTIS, 2008):

(Z)-Octadec-9-enylamine:	C,N; R22-35-50; S26-28-36/37/39-45-61
Octadecylamine:	Xi,N; R38- 41-51/53; S26-39-61
Amines, hydrogenated tallow alkyl:	Xi,N; R38-41-50; S26-28-37/39-61.

The primary alky amines have not been discussed in the TC C&L, but directly in the TC NES (Technical Committee of New and Existing Chemical Substances). In the year 2007 the following proposal for a harmonised classification and labelling with respect to the Human Health classification was laid down in an Annex XV –Dossier:

Proposed classification based on Directive 67/548/EEC:

Amines, tallow alkyl:	Xn; R22 - C; R35 - Xn; R48/22
(Z)-Octadec-9-enylamine:	Xn; R22 - C; R34 - Xn; R48/22
Octadecylamine:	Xi; R38 - Xi; R41 - Xn; R48/22
Amines, hydrogenated tallow alkyl	Xi, R38 - Xi; R41 - Xn; R48/22
Amines, coco alkyl:	Xn; R22 - C; R35 - Xi; R37 - Xn; R48/22

Furthermore, it was proposed in the RAR to classify primary alkyl amines as: N, R 50/R53.

Workers

It has been concluded from the risk assessment that there is a need for limiting the risks. The primary alkyl amines have been and are proposed to be classified and labelled as skin irritants or corrosives. Skin irritation and corrosive lesions need to be avoided by adequate skin-related risk management measures.

As a result of the Risk Assessment measures have to be implemented to reduce inhalative exposure to dust. Inhalative exposures caused concern for repeated dose toxicity (systemic effects) because they exceeded the critical exposure limit (CEL) of 0.15mg/m^3. For those primary alkyl amines (octadecyl amine and hydrogenated tallow alkyl amine) that will be classifised only as irritant (not corrosive) dermal exposures were assessed to be high and resulted in concern for repeated dose toxicity (systemic effects) (CEL 0.04 mg/kg/day) and also in concern for fertility impairment (CEL 0.4 mg/kg/day). By convention, dermal exposure to corrosive substances is not assessed.

To prevent chronic systemic health effects while handling primary alkyl amines, occupational exposure by inhalation is proposed to be controlled down to a level of 0.15 mg/m³ (8-hour time-weighted average). The corresponding health-based reference level for controlling repeated dermal exposure is calculated to be 0.04 mg/kg/day.

The risk reduction strategy recommends the following measures f**or Workers:**

- to establish at community level an occupational exposure limit value according to Directive 98/24/EEC for :

  Amines, coco alkyl (CAS 61788-46-3),
  Amines, tallow alkyl (CAS 61790-33-8),
  Amines, hydrogenated tallow alkyl (CAS 61788-45-2),
  Octadecylamine (CAS 124-30-1),
  (Z)-Octadec-9-enylamine (112-90-3)

- to apply the following revised classification and labelling in the forefront of a future Adaption to Technical Progress of Directive 67/548/EEC:

  Amines, coco alkyl (CAS 61788-46-3)
  Xn; R22
  C; R35
  Xi; R37
  Xn; R48/22

  Amines, tallow alkyl (CAS 61790-33-8)
  Xn; R22
  C; R35
  Xn; R48/22

  Amines, hydrogenated tallow alkyl (CAS 61788-45-2)
  Xi, R38
  Xi; R 41
  Xn; R48/22

Octadecylamine (CAS 124-30-1)
Xi; R38
Xi; R41
Xn; R48/22

(Z)-Octadec-9-enylamine (112-90-3)
Xn; R22
C; R34
Xn; R48/22

- to transfer the classification into the Inventory according to Article 114 of Regulation (EC) 1907/2006

- information on the need of specific training, organisational measures and occupational hygiene in the framework of Directive 98/24 in order to reduce dermal exposure in scenario 1 and 3

1 Background

In the framework of EU Regulation 793/93 on the evaluation and control of the risks of existing substances data are gathered, priority substances are selected, their risks are assessed and, if necessary, strategies for limiting the risks are developed. The risk assessments cover the risks to man exposed directly at the workplace or as a consumer and indirectly through the environment and the risks to the environment. Tallow alkyl amine is a substance on the second priority list (Regulation (EC) No. 2268/95 of the Commission of 28 September 1995), while (Z)-Octadec-9-enylamine, 1-Octadecanamine, Hydrogenated tallow alkyl amine and Cocos alkyl amine are substances on the fourth priority list (Regulation (EC) No. 2364/2000 of the Commission of 25 October 2000).

Tallow alkyl amine is a white waxy solid with a pungent amine-like smell at 20 °C.
(Z)-Octadec-9-enylamine is a light yellow paste-like liquid with amine-like odour at 20 °C.
1-Octadecanamine is a colourless solid with amine-like odour at 20 °C.
Hydrogenated tallow alkyl amine is a white wax with amine-like odour at 20 °C.
Cocos alkyl amine is a slightly yellow liquid with amine-like odour at 20 °C.

Data on further physical and chemical properties of the five substances are given in table 1.1.

Tab. 1.1: Summary of physico-chemical properties

Substance	Property	Value	Reference
	Melting point		
Amines, tallow alkyl		32 – 40 °C	Ullmann, 1985
(Z)-Octadec-9-enylamine		15 – 30 °C	Clariant, 2000
Octadecylamine		49 – 52 °C	Richardson et al., 1994
Amines, hydrogenated tallow alkyl		48-56 °C	Ullmann, 1985
Amines, coco alkyl		12 – 17 °C	Ullmann, 1985
	Boiling point		
Amines, tallow alkyl		200 – 230 °C at 36 hPa	Ullmann, 1985
(Z)-Octadec-9-enylamine		128 – 174 °C at 4 hPa 345.55 °C (calculated) 353 – 355 °C at 1013 Pa	Kao, 2001 Hoechst, 1996c Siemens Axiva, 2002b
Octadecylamine		348.8 °C at 1013 hPa	Ralston et al., 1959
Amines, hydrogenated tallow alkyl		348 - 351 °C at 1013 hPa	Siemens Axiva, 2003
Amines, coco alkyl		130 - 227 °C at 133 hPa	Ullmann, 1985
	Relative density		
Amines, tallow alkyl		0.79 g/cm^3 at 60 °C	Hoechst, 1980a
(Z)-Octadec-9-enylamine		0.8 g/cm^3 at 60 °C	Clariant, 2000
Octadecylamine		0.8618 at 20 °C	Richardson et al., 1994
Amines, hydrogenated tallow alkyl		0.94 at 23.2 °C	Siemens Axiva, 2003
Amines, coco alkyl		0.8 g/cm^3 at 25 °C	Akzo, 2000

Substance	Property	Value	Reference
	Vapour pressure		
Amines, tallow alkyl		not conducted	
(Z)-Octadec-9-enylamine		0.005 hPa at 20 °C (calculated)	Hoechst, 1996c
Octadecylamine		$4.38 \cdot 10^{-5}$ mm Hg at 25 °C (≡ 0.006 Pa at 25 °C) (calc.)	Clariant, 2001a
Amines, hydrogenated tallow alkyl		not conducted	
Amines, coco alkyl		not conducted	
	Water solubility		
Amines, tallow alkyl		0.12 mg/l at 25 °C (calc.)	Clariant, 1998
(Z)-Octadec-9-enylamine		insoluble at 25 °C 0.07639 at 25 °C (calculated)	CECA, 2000 Hoechst, 1996c
Octadecylamine		insoluble at 25 °C 0.04875 mg/l at 25 °C (calc.)	Kao, 2000 Clariant, 2001a
Amines, hydrogenated tallow alkyl		insoluble at 25 °C	Clariant, 2001b
Amines, coco alkyl		insoluble at 25 °C	Clariant, 2001c
	Partition coefficient n-octanol/water (log value)		
Amines, tallow alkyl		log Pow 7.1 at 20 °C (calculated)	APAG, 2003a
(Z)-Octadec-9-enylamine		log Pow 7.5 at 20 °C (calculated)	Hoechst, 1996c
Octadecylamine		log Pow 7.71 (calc.)	Clariant, 2001a
Amines, hydrogenated tallow alkyl		7.3 (calc.)	Clariant, 2001a
Amines, coco alkyl		not conducted	
	Flash point		
Amines, tallow alkyl		159 °C	Hoechst, 1997
(Z)-Octadec-9-enylamine		156 °C	Siemens Axiva, 2002b
Octadecylamine		not conducted (solid)	
Amines, hydrogenated tallow alkyl		not conducted (solid)	
Amines, coco alkyl		> 100 °C	Akzo, 2000
	Autoflammability		
Amines, tallow alkyl		no selfignition up to the melting range	Chemsafe, 2001
(Z)-Octadec-9-enylamine		265 °C	Siemens Axiva, 2002a
Octadecylamine		no selfignition up to the melting range	Chemsafe, 2001
Amines, hydrogenated tallow alkyl		no selfignition up to the melting range	Chemsafe, 2001
Amines, coco alkyl		255 °C	Siemens Axiva, 2002a

Production processes

Starting materials in the manufacture of long-chain, primary alkyl amines are natural fats and oils, or synthetic products of the petrochemical industry. Intermediates are alkyl nitriles, which are formed from carboxylic acids and ammonia over dehydrating catalysts (Al_2O_3, ZnO, or salts of Mn or Co) in liquid-phase reactors or liquid- and vapor-phase reactors at 280-360°C. The nitriles are hydrogenated at a temperature of 80-180°C and a pressure of 1 - >10 MPa in the presence of nickel or cobalt catalysts.

$$R - CN + 2\ H_2 \rightarrow R - CH_2 - NH_2$$

The formation of secondary and tertiary amines as by-products is generally inhibited by addition of ammonia. Conversion is usually carried out in autoclaves operated in batch process, although there are also plants which operate in continuous process. Depending on the use, alkyl amines are used as such or purified by distillation under reduced pressure (BUA, 1994; Heilen et al., 1985).

Production, Import and Export

According to the information supplied by industry, primary alkyl amines are produced and/or imported by the following companies in the European Union (State 1999/2000, EU 15). One of the production sites listed in table 1.2 has been closed in the meanwhile. A further site was an importer without own production, the import has been stopped in the meanwhile:

Tab. 1.2: Production and import of primary alkyl amines (1999)

Company	Coco	Tallow	Hydr. Tall.	Octadecyl	Octadecenyl
Akzo Nobel Chemicals S.A., Ghlin (Belgium)	+	+	+	+	+
Akzo Nobel Chemicals Ltd., Littleborough (UK)	+	+	+		+
Akzo Nobel Surface Chemistry AB, Stockviksverken (Sweden)	+	+	+		+
CECA S.A., Feuchy les Arras (France)	+	+	+		+
Clariant GmbH, Gendorf (Germany)	+	+	+	+	+
Ecogreen Oleochemicals, Rodleben (Germany)	+	+	+		+
Infineum UK Ltd., Oxfordshire (UK)					+
Kao Corporation S.A., Barbera del Valles (Spain)	+	+	+	+	+

In the following table the market data received from producers and importers are summarized. The European consumption volumes (EU 15) are calculated from the figures on production, import and export:

Tab. 1.3: Production volume, imports and exports for the period 1999/2000 [t/a] (APAG, 2003b)

	Coco	Tallow	Hydr. Tall.	Octadecyl	Octadecenyl
Production	5760	13339	10620	474	4415
Import	0	394	164	0	12
Export	588	1614	3229	12	405
European Consumption	5172	12119	7555	462	4022

Uses

Introduction

Table 1.4 details the uses of primary alkyl amines within the EU. The use pattern was generated based on manufacturer's data reflecting the European market.

Tab. 1.4: Uses of primary alkyl amines [t/a] (APAG, 2003b)

	Coco	Tallow	Hydr. Tall.	Octadecyl	Octadecenyl
Intermediate (IC 3 / UC 33)	5020 (97%)	11901 (98%)	2577 (34%)	319 (69%)	3385 (84%)
Fertilizers, anticaking (IC 1 / UC 7)		13 (0.1%)	4178 (55%)		
Metal ind., floatation agent (IC 8 / UC 23) *	87 (1.7%)	193 (1.6%)	664 (8.8%)		65 (1.6%)
Metal proc. ind., lubricants		13 (0.1%)	72 (1%)		306 (8%)
Fuel additive				78 (17%)	111 (3%)
Formulations (metal, corrosion inhibitors)	43 (0.8%)				8 (0.2%)
Formulations (textiles)			64 (0.8%)		

	Coco	Tallow	Hydr. Tall.	Octadecyl	Octadecenyl
Paints, antistatic agent	22 (0.4%)				147 (3.6%)
Rubber additive				65 (14%)	
Total EU consumption	**5172**	**12119**	**7555**	**462**	**4022**

* According to APAG (2005b), about 300 t/a used in floatation agents are exported outside the EU. Considering this amount, the total European consumption of all 5 amines amounts to 29,030 t/a.

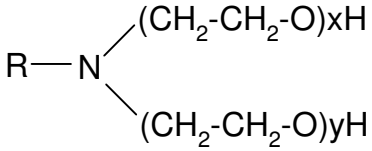
From the table it can be observed that major amounts of the amines are used as intermediate in chemical industry. A further breakdown of this use was generated focusing on major customers, while smaller outlets were omitted. Therefore, the amounts are not quite identical with those referred in table 1.4, but the relative importance of the most important daughter products is shown.

Tab. 1.5: Daughter products from processing of primary alkyl amines [t/a] (APAG, 2001)

	Coco	Tallow	Hydr. Tall.	Octadecyl	Octadecenyl
Ethoxylates	2995 t	5396 t	957 t		1864 t
Amine derivatives	459 t	4491 t	470 t		955 t
Sulphosuccinamate		1216 t			
Amides	32 t		27 t	110 t	85 t
Other intermediates	314 t		104 t	208 t	330 t
Total	**3800 t**	**11103 t**	**1558 t**	**318 t**	**3234 t**

Amino ethoxylates:

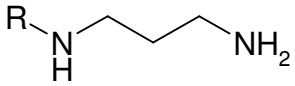
The most important products manufactured from primary alkyl amines are amino ethoxylates. Ethoxylation is carried out through the addition of ethylene oxide to the alkyl amine. At a ratio of 1 mol alkyl amine to 2 mol ethylene oxide, N,N-bis(2-hydroxyethyl)-alkyl amines (2,2'-(alkyl imino)-diethanoles) are formed, while with a ratio of more than 2 mol ethylene oxide per mol alkyl amine, N,N-bis(polyoxyethyl)-alkyl amines are yielded with the following general formula (x,y = number of attached molecules of ethylene oxide):

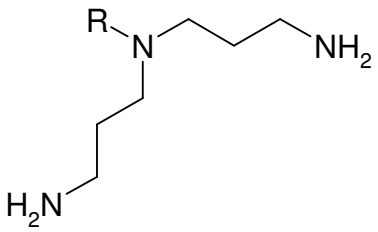


Alkyl amino ethoxylates are surface-active substances, which can be combined with other surfactants, are used as they are or in the form of their salts, as key components or as additional ingredients in a wide range of chemotechnical products. For example, they can be used as an additive in viscose, plastics and mineral oils, as auxiliary agents in the dyeing and textile industries, as wetting agents in pesticide and plant protection products, and as emulsifiers and binding agents (BUA, 1994; Hoechst AG, 1980b, 1989a).

Amine derivatives:

At a molar ratio of 1:1, alkyl amines react with acrylonitrile to form N-(2-cyanoethyl)-alkyl amines, from which N-alkyl-1,3-propyl diamines are formed through catalytic hydrogenation. At a ratio of 1 mol alkyl amine to 2 mol acrylonitrile, N,N-bis(2-cyanoethyl)-alkyl amines are formed, the hydrogenation of which yields N-alkyl-N-(3-aminopropyl)-1,3-propyl diamines (BUA, 1994).





Amine derivatives serve as intermediates for further chemical conversion to disinfectants and other products, for example, to anticarious agents, or are used as they are, mainly in the preparation of diaryl yellow pigments, which are used particularly for intaglio printing of illustrations in short-lived printed matter such as catalogues and illustrated magazines, but also, although to a lesser extent, in colouring plastics. Another area of amine derivatives use is as a lubricant in water-based, spray preparations for the hinge-plate chains of conveying plant, for example, in a bottle-filling plant, and as a cationic emulsifier and auxiliary agent in the production of universal, rapidly breaking, acidic bitumen emulsions with good binding properties towards all kinds of filling materials, even in the presence of moisture, for use in road building (Hoechst AG, 1980b; BUA, 1994).

Sulphosuccinamates and other amides:

Primary alkyl amines react with carboxylic acids or their derivatives to amides substituted with long-chained alkyl groups. The following groups with amide structure are of importance:

Sulphosuccinamates (sulphosuccinamic acids) on the basis of tallow alkyl amine are used mainly as emulsifiers in latex emulsions for carpet backings, and to a lesser extent as a component in washing agents for wool. Condensation products with urea and formaldehyde are applied as water-repelling softener for leather and textiles. Alkyl isocyanate is, for example, used as a catalyst in the manufacture of polyamides. Ethylene diamino tetraacetic monoalkyl amide is a complex-forming detergent (BUA, 1994).

Uses without chemical conversion:

To a minor extent, alkyl amines or their salts are applied directly without chemical conversion. Because of the low water solubility, alkyl amines are only exceptionally used as free bases. More frequently they are used as salts which belong to the group of cationic surfactants. The majority of the uses is based on the strong adsorption onto the surface of many different materials like proteins, cellulose, synthetic fabrics, polymers, silicates, pigments, metals or potassium salts (Hoechst AG, 1980b). The most important applications are:

Floatation:

Floatation involves the separation of a certain mineral from a mineral mix, whereby suspended mineral particles adhering to air bubbles are carried to the surface of the slurry, where they are skimmed off in the laden froth. Selective adhesion to the air bubbles is achieved by hydrophobing agents like alkyl amines and their salts (chloride and acetate), which are suitable in the floatation of halogenides (KCl and NaCl), silicates and zinc ores. In Germany, production of potassium salts for the use in fertilizers is of high importance in this area (BUA, 1994; Hoechst AG, 1978a).

Fertilizers:

Alkyl amines, mainly the potassium salts are used as soil fertilizers in agriculture. In addition to that, acetate and stearyl salts of hydrogenated tallow amine are used by the potash and fertilizer industry as an anticaking agent. On account to their water-repelling properties, they prevent caking during storage and transport, maintaining flowability of the potash or fertilizer in crystal or granular form (BUA, 1994; Hoechst AG, 1978b).

Other direct uses:

In table 1.4 other direct uses of alkyl amines are described (e.g. fuel additive, paints, formulations for textiles…). These uses are regarded to be of minor importance based on the consumption volumes. No relevant environmental releases are expected from these areas and no emission scenarios are calculated for these uses.

2 The Risk Assessment

2.1 Workers

Introductory remarks

The term primary alkyl amines stands for a group of substances which share essential chemical key aspects so that it seems appropriate to perform a joint risk assessment for all the members of the group. Occupational exposure may be different for the individual substances because of differing physico-chemical properties and varying areas application. As basis for the risk assessment in this report the occupational exposure assessment (chapter 4.1.1.2) does not solely follow the group approach but gives differentiated information on the individual substances where necessary.

From toxicological aspects, however, there is indication that the primary alkyl amines may have a closely related effect spectrum. On that background read across of data from one substance to another is broadly accepted. As a consequence the data base for some endpoints becomes rather small because few studies are available which are used as basis for the assessment of the whole group. The toxicological profile of primary alkyl amines (chapter 4.1.2) and the threshold levels identified in the hazard assessment are taken forward to characterise the risks at the workplace and give indication for concern according to the MOS approach as outlined in the TGD (Human Health Risk Characterisation, Final Draft).

Systemic availability for different routes of exposure

Very little is known on the absorption and bioavailability of the primary alkyl amines in question. For this report information on absorption mainly comes from considerations on physico-chemical properties in combination with some data on alkylamines with shorter chain length. On that background a value of 100 % for oral and inhalative absorption is taken forward to worker risk assessment. For dermal absorption a value of 60 % is considered reasonable based on absorption data for 1-dodecanamine.

Occupational exposure and internal body burden

In table 2.1.A. the exposure levels of the RAR-table 4.1 which concern primary alkyl amines are summarised and the route-specific internal body burdens are identified. To this end the route-specific percentages for absorption (100 % for inhalation and 60 % for dermal exposure) are taken into account. For combined exposure the internal budy burdens by inhalation and dermal contact are summed up to give a total internal body burden.

There are five primary alkyl amines to assess, two liquids (coco alkyl amine and octadecenyl amine), a paste (tallow alkyl amine) and two solids (octadecyl amine and hydrogenated tallow alkyl amine). The liquid and paste primary alkyl amines are corrosive (labelled with R 35). The solid amines are skin-irritating substances (R 38).

For the liquids and the paste primary alkyl amines inhalation exposure is only assumed via vapour, and because the vapour pressure is less than 1 Pa the inhalation exposure is considered to be low (no quantitative assessment). These three substances are also corrosive substances. For corrosive substances, it is the convention not to perform quantitative dermal exposure assessment.

The remaining two, octadecyl amine and the hydrogenated tallow alkyl amine, are solids leading to dust exposure, and they are not corrosive, but skin-irritating substances. Only for these two substances, according to TGD, quantitative inhalation and dermal exposure assessments were performed.

Table 2.1.A: Occupational exposure levels and internal body burden for octadecyl amine and hydrogenated tallow alkyl amine

Exposure scenario		Inhalation shift average	Dermal contact shift average		Internal body burden of workers after repeated exposure[1]		
					Inhalation[1]	Dermal[2]	Combined
		mg/m^3	mg/pers/d	mg/kg/d	mg/kg/d		
1.	Production	0.6	42	0.6	0.09	0.36	0.45
2.	Further processing	1	42	0.6	0.14	0.36	0.5
3.	Use of primary alkyl amines in flotation process	0.625	420	6	0.09	3.6	3.7
4.	Formulation of products containing primary alkyl amines	0.625	420	6	0.09	3.6	3.7

(1) based on the assumption of 100% inhalative absorption; breathing volume of 10 m^3 per shift

(2) based on the assumption of 60 % systemic availability after dermal contact

MOS Approach

The MOS approach for human risk characterisation is described in detail in the TGD (Human Health Risk Characterisation, Final Draft). The following paragraphs contain a short introduction to aspects relevant in case of primary alkyl amines. The basic principle of the MOS approach is a comparison of scenario-specific MOS values (the relationship between the experimental NOAEL respectively the adjusted starting point and the exposure level) with a reference MOS (product of various assessment factors).

MOS calculation and the adequate starting point

Basically, MOS values are calculated as quotient of a relevant NOAEL from experimental animal testing or human studies and actual workplace exposure levels. In specific situations, the MOS approach requires converting the original NOAEL into an adequate starting point or corrected NOAEL previously to MOS calculation in order to be directly comparable to the exposure assessment. If the route of application in animal or human studies is different from the actual occupational exposure, the dose units of the experimental data are converted to the dose unit of the exposure data. Additionally, possible differences in bioavailability between routes, as well as possible differences in bioavailability between animals and humans are accounted for in the calculation of the corrected NOAEL. If necessary in occupational risk assessment, the starting point for inhalation risk assessment also includes a correction for the

difference between the standard respiratory volume of a person at rest (6.7 m³) and the respiratory volume of workers under light activity (10 m³).

MOS values are calculated for different routes of exposure and for different toxicological endpoints. In occupational risk assessment inhalation and dermal contact generally resemble the relevant exposure routes. In addition, for assessment of combined risks the simultaneous exposure by inhalation and dermal contact needs to be considered. To this end the internal body burdens obtained by dermal and inhalation exposure are determined and summed up and compared to the internal equivalent of the respective NOAEL for the endpoint in question. Inhalation exposure and dermal exposure to primary alkyl amines may contribute differently to the internal body burden. With respect to the possible outcome of an assessment for combined risks, interest focuses on scenarios with conclusion ii at both exposure routes. Based on theoretical considerations, combined exposure will not increase the most critical route-specific risk component more than twice.

Reference MOS

The MOS values calculated have to be compared with a reference MOS. The reference MOS results as an overall assessment factor from the multiplication of the different specific factors for a certain risk situation. The Technical Guidance Document emphasis the different aspects which are involved in these considerations, especially the extrapolation of experimental data to the human situation. For several aspects default assessment factors are recommended. It is important to point out that any relevant substance-specific data and information may overrule the defined default values.

Interspecies extrapolation as one central element is based on allometric scaling (factor 4 for rats, factor 7 for mice, and factor 2.4 for rabbits). For remaining interspecies differences the TGD proposes an additional factor of 2.5. Another element is adjustment for intraspecies differences. For workers, a default factor of 5 is recommended, based on an evaluation of empirical data by Schneider et al. (2004). It is anticipated that a default factor of 5 will be sufficient to protect the major part of the worker population (about 95%).

It is usually expected that the experimental NOAEL will decrease with increasing duration of application. Furthermore, other and more serious adverse effects may appear with prolonged exposure duration. For duration adjustment, a default factor of 6 is proposed for extrapolation from a subacute to chronic exposure. The duration adjustment factor could be lower for the transition from subchronic studies. However, for the primary alkyl amines the relevant data come from subacute studies.

The TGD describes two further adjustment factors (uncertainty in route-to-route extrapolation and dose-response relationship including severity of effect) which in specific cases may be different from one. For primary alkyl amines route-to-route extrapolation is associated with a high degree of uncertainty because the local effects and their secondary consequences probably depend on the site of contact. However, in this report the few data available on this aspect are specifically evaluated to avoid using an additional default factor.

Comparison of MOS and reference MOS

The different scenario- and endpoint-specific MOS values are compared with the respective reference MOS. MOS values clearly above the reference MOS do not lead to concern, whereas MOS values that are clearly below the reference MOS give reason for concern. There are also risk-related aspects which cannot be covered quantitatively by assessment factors.

These additional aspects are considered qualitatively when performing the risk assessment and have adequate influence on the finding of the conclusions. Especially in case of borderline scenarios these aspects might be decisive.

Critical Exposure Levels

In a parallel procedure, which gives identical but more direct results, the adjusted toxicological starting point is directly divided by the reference MOS. As a result, an exposure level (in mg/m³ or mg/kg/d) is identified, which may serve as a direct trigger for decisions when compared with the occupational exposure levels. In the context of this risk assessment report this trigger value is called "critical exposure level". Concern will be expressed for scenarios with occupational exposure levels higher than the relevant "critical exposure level".

Acute toxicity

Rats were exposed to a coco alkyl vapour in the mean analytical concentrations of 0.063 and 0.099 mg/l for one hour. All animals showed signs of irritation but there were no other relevant clinical symptoms or necropsy findings.

The dermal studies with coco alkyl amines demonstrated no mortality. Dose levels of 500 and 2000 mg/kg/day were tested on rats, a single dose of 1600 mg/kg/day was used on rabbits. At all doses severe skin reactions were observed, clinical signs were noted at 2000 mg/kg/day in the rat study.

Several oral studies are available for the different primary alkyl amines. For each substance at least one acute study has been performed so that these data can be used for comparison: for some of the substances the LD50 is in a range between 1000 and 2000 mg/kg/day, for others it exceeds 2000 mg/kg/day. In some cases there was mortality also below 1000 mg/kg/day.

Based on the data available it is preferred to perform a semi-quantitative risk characterisation for workers using the acute inhalation and dermal toxicity data.

Inhalation exposure

The only inhalation study available did show signs of respiratory tract irritation in rats following a 1-hour exposure to about 100 mg/m³. These experimental conditions did not result in clinical symptoms.

For the three corrosive primary alkyl amines there is no dust exposure; the vapour pressure is less than 1 Pa. Exposure to vapour is considered very small; under these conditions acute systemic effects are not anticipated to occur.

For the two irritating primary alkyl amines dust exposure is estimated to be up to 1 mg/m³. The margin of safety between 100 mg/m³ without clinical effects in experimental animals and the occupational exposure up to 1 mg/m³ is considered high enough to recognize no concern.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Dermal contact

Human data on acute dermal toxicity of primary alkyl amines are not available. For coco alkyl amine, acute dermal exposure to 2,000 mg/kg bw caused clinical effects, but did not result in mortality. The highest dermal occupational exposure is estimated to be 6 mg/kg bw (based on the exposure assessment for the two irritating primary alkyl amines). For systemic effects following acute dermal exposure the margin of safety is judged to be sufficient.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Combined exposure

Based on the available data on occupational exposure, on route-specific acute systemic toxicity and on the semi-quantitative route-specific acute risk assessments there is no indication of a corresponding risk following combined exposure to the primary alkyl amines in the different exposure scenarios.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Irritation and corrosivity

Skin

Based on classification and labelling, the primary alkyl amines to be assessed can formally be differentiated in three corrosive and two skin irritating primary alkyl amines (see introduction of occupational risk assessment).

For the corrosive substance octadecenylamine a 14-day dermal study is available. The lowest tested concentration of 0.3% still caused moderate irritation.

It is not considered necessary to define a LOAEL-to-NOAEL extrapolation factor for local effects, because all occupational dermal exposure scenarios only refer to the undiluted primary alkyl amines. Without personal protective equipment, dermal exposure to the corrosive primary alkyl amines will result in skin erosion, and dermal exposure to the irritating amines in skin irritation.

For all primary alkyl amines for acute dermal irritation and for corrosivity conclusion ii is proposed on the grounds that control measures exist which can minimise exposure thereby reducing the risk of irritation and corrosivity adequately. However, these controls must be implemented and complied with for all primary alkyl amines to make sure that skin damage is prevented and that there is no reason for concern.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Eyes

For some primary alkyl amines corrosive properties have been identified in skin irritation studies, for others, eye irritation tests have been performed. In summary primary alkyl amines homogeniously demonstrated a potential to induce severe ocular lesions. This is expressed in the according proposals for classification and labelling.

Conclusion ii is proposed on the grounds that control measures exist which can minimise exposure thereby reducing the risk of irritation/corrosivity adequately. However, these controls must be implemented and complied with to make sure that eye damage is prevented and that there is no reason for concern.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Respiratory tract

In the only inhalation study available, exposure to coco alkyl amine vapour for 1 hour showed signs of respiratory tract irritation at concentrations of 63 and 99 mg/m^3.

The highest inhalation exposure) estimated for the primary alkyl amines is 1 mg/m³ (8-hour shift average). The margin of safety is considered sufficient to assume that acute inhalation exposure to primary alkyl amines does not result in acute respiratory tract irritation.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Sensitisation

Skin

Available data on the skin sensitisation potential of the different primary alkyl amines are not sufficiently conclusive. Due to the limited hazard data, the occupational risk of skin sensitisation following dermal exposure to the different primary alkyl amines cannot be sufficiently assessed. As to the substance-specific skin sensitisation data and the specific considerations on the need for further information and testing reference is made to the corresponding chapter on hazard assessment of the Risk Assessment Report.

Conclusion (i) There is a need for further information and/or testing.

Respiratory tract

No information on the sensitising potential of the substance at the respiratory tract is available. For the time being a valid study to investigate respiratory sensitisation in experimental animals cannot be recommended. However, primary alkyl amines are not suspected to be potent respiratory sensitisers in humans according to the fact that during all the years of use no notice of specific case reports has been given. There is no concern with respect to respiratory sensitisation at the workplace.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Repeated dose toxicity

Local effects

For skin irritation following repeated dermal exposure full reference is made to the RAR-chapter 4.1.3.2.2. The considerations and conclusions in the RAR-chapter 4.1.3.2.2 are considered valid for local effects following repeated exposure as well.

For respiratory tract irritation following repeated exposure reference is made to RAR-chapter 4.1.3.2.2 as well. In the only inhalation study available, exposure to coco alkyl amine vapour for 1 hour showed signs of respiratory tract irritation at concentrations of 63 and 99 mg/m^3. The highest inhalation exposure estimated for the primary alkyl amines is 1 mg/m³ (8-hour shift average). The margin of safety was considered sufficient to assume that acute inhalation exposure to primary alkyl amines does not result in acute respiratory tract irritation. There is no information of the influence of repeated inhalation exposure to primary alkyl amines on respiratory tract irritation. Additional reference is made to the reference exposure level of 0.15 mg/m³ which should be adhered to because of systemic effects (see below). Lowering the maximum inhalation exposure of 1 mg/m³ significantly will probably be sufficient to exclude local effects as well. Against that complex background there is no reason to indicate additional concern for respiratory tract irritation.

Inhalation exposure

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Dermal exposure

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Systemic effects

There is no inhalation study available with repeated exposure. The only dermal study with repeated application suffered the lack of histomorphology data. Therefore evaluation of systemic toxicity after repeated exposure has to rely on oral data.

The most relevant study which gave the most sensitive results was performed with octadecenylamine in an oral 28-day test on rats. Groups of five male and female SD-rats received octadecenylamine (Genamin OL 100 D) by oral gavage at dose levels of 0, 3.25, 12.5 or 50 mg/kg/day for a period of 28 days (Aventis, 2003). At a dose of 50 mg/kg/day clinical signs as gait abnormalities, reduction in body weight gain and clinical pathology findings indicating mild toxic effects on the liver and kidneys were found. Effects observed at the mid-dose level (12.5 mg/kg/day) were reduction in growth and increased urinary

concentration of urea nitrogen. At the low dose group of 3.25 mg/kg/day no effects were observed.

Inhalation exposure

Inhalation risk assessment will be based on the oral NOAEL for rats of 3.25 mg /kg/day. This value is taken forward to the inhalation exposure situation of workers, assuming similar absorption by oral and inhalation route and a bodyweight for workers of 70 kg (please be aware that the sequence of extrapolation steps in this report is not identical to the proposal in the actual Reach guidance documents; however, this different sequence does not lead to different results). As reference serves an 8 hours shift exposure with a respiratory volume of 10 m^3. The resulting air concentration is 23 mg/m^3 (3.25 mg/kg/day x 70 kg x / 10 m^3).

For the identification of the reference MOS the standard factor for duration adjustment is modified: For octadecyl amine a NOAEL of 10 mg/kg/day for a 2-year rat study is reported. It is clearly indicated in the hazard assessment, that this 2-year rat study is less valid than the 28-day study chosen as starting point for risk assessment. However, from the 2-year rat study there is at least no indication for a stringent necessity of applying the unchanged standard adjustment factor of 6. Based on the indicative results from the 2-year rat study with octadecyl amine it is considered proportionate to somewhat lower the standard factor for duration adjustment.

The following adjustment factors are applied for the identification of the reference MOS: (1) for duration adjustment a factor of 3 is used, (2) the allometric scaling factor for the rat is 4; (3) a default factor of 2.5 accounts for additional interspecies differences; (4) for intraspecies differences (workers) the default factor is 5. This gives a reference MOS of 150 (3 x 4 x 2.5 x 5). The respective critical inhalation exposure level at the workplace is identified as 0.15 mg/m^3 (23/150) representing a shift average value for long-term exposure.

This value leads to concern for all scenarios (for MOS values see table 2.1.B). This conclusion applies only to the two solid primary alkyl amines; for the other three primary alkyl amines there is conclusion ii for this toxicological endpoint (see introduction or summary to worker risk assessment).

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Dermal contact

Dermal risk assessment is based on the oral NOAEL of 3.25 mg/kg/day from the rat study as well. Taking into account the differences in oral (100%) and dermal (60%) absorption a value of 5.4 mg/kg/day (3.25 mg /kg/day /0.6), corresponding to 378 mg/person/day (bodyweight 70 kg), is obtained as corrected NOAEL for the dermal route which is used as starting point for the evaluation of dermal exposures.

The following adjustment factors are applied for the identification of the reference MOS: (1) for duration adjustment a factor of 3 is used, (2) the allometric scaling factor for the rat is 4; (3) a default factor of 2.5 accounts for additional interspecies differences; (4) for intraspecies differences (workers) the default factor is 5. This gives a reference MOS of 150

(3 x 4 x 2.5 x 5). The respective critical dermal exposure level at the workplace is identified as 0.04 mg /kg/day (5.4/150) or 2.8 mg/person/day (bodyweight 70 kg).

There is concern for all scenarios (for MOS values see table 2.1.B). This conclusion applies only to the two skin irritating primary alkyl amines; for the other three corrosive primary alkyl amines there is conclusion ii for this toxicological endpoint (see introduction or summary to worker risk assessment).

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Combined exposure

Taking into account 100% oral absorption the internal level of primary alkyl amines directly corresponds to the oral NOAEL of 3.25 mg/kg/day. This value is used as starting point for combined risk assessment concerning repeated dose toxicity, systemic effects.

The reference MOS is 150. The critical internal level of primary alkyl amines with respect to chronic toxicity results as 0.02 mg/kg/day.

For all exposure scenarios there is already concern for both routes of exposure and thus for combined exposure as well. For quantitative data see table 2.1.B. This conclusion applies only to the two solid primary alkyl amines; for the other three primary alkyl amines there is conclusion ii for this toxicological endpoint (see introduction or summary to worker risk assessment).

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Table 2.1.B: Repeated dose toxicity, systemic effects (octadecyl amine and hydrogenated tallow alkyl amine)

	Inhalation			Dermal			Combined		
Starting point for MOS calculation	23 mg/m^3			5.4 mg/kg/day (external value)			3.25 mg/kg/day (internal value)		
Reference MOS	150			150			150		
Critical exposure level	0.15 mg/m^3			0.04 mg/kg/day (external value)			0.02 mg/kg/day (internal value)		
	Exposure (mg/m^3)	MOS	Conclusion	Exposure (mg/kg/d)	MOS	Conclusion	Internal body burden (mg/kg/d)	MOS	Conclusion
1. Production	0.6	38	iii	0.6	9.5	iii	0.45	7.2	iii[(1)]
2. Further processing	1	23	iii	0.6	9.5	iii	0.5	6.5	iii[(1)]
3. Use of primary alkyl amines in flotation process	0.625	37	iii	6	0.95	iii	3.7	0.9	iii[(1)]
4. Formulation of products containing primary alkyl amines	0.625	37	iii	6	0.95	iii	3.7	0.9	iii[(1)]

[(1)]conclusion iii already results from dermal and inhalation exposure, therefore no specific concern for the combined exposure scenario is indicated

Mutagenicity

Several mutagenicity tests have been performed with the different substances of the primary alkyl amines. Only negative results were obtained. Although for some substances the data base is not complete, read across can be performed. Altogether the data are judged sufficient to exclude a mutagenic potential of primary alkyl amines. There is no reason for concern.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Carcinogenicity

Conventional carcinogenicity studies with primary alkyl amines are not available. Earlier studies on the chronic toxicity of octadecylamine provided no indication of a carcinogenic effect. There are no human data on the carcinogenicity of the primary alkyl amines. No potential for carcinogenicity was predicted for octadecylamines and octadecenylamines from the Danish QSAR database.

Due to the lack of reliable data no final conclusion can be drawn on the carcinogenic potential of any of the fatty alkylamines under consideration. Taking into account that all available mutagenicity tests gave negative results no indication may be seen for a carcinogenic potential of primary alkyl amines.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Toxicity for reproduction

Effects on fertility

From oral tests on tallow alkyl amines, octadecylamine and octadecenylamine information on fertility is available which is judged to be sufficient for the evaluation of the other primary alkyl amins.

Repeated oral studies with octadecylamine and octadecenylamine did not show any adverse effect on reproductive organs. The most relevant result concerning fertility has been observed in a rat screening test with tallow alkyl amines with doses of 12.5, 50, 150 mg/kg/day. At a dose of 50 mg/kg/day a lower fertility index and a lower conception rate compared to the control group was observed. Also maternal toxicity occurred at that dose. The NOAEL for fertility and for maternal toxicity likewise was 12.5 mg/kg/day. This value will be taken forward for quantitative worker risk assessment.

Inhalation exposure

Inhalation risk assessment will be based on the oral NOAEL for rats of 12.5 mg /kg/day. This value is taken forward to the inhalation exposure situation of workers, assuming similar absorption by oral and inhalation route and a bodyweight for workers of 70 kg. For an 8- hour shift exposure a respiratory volume of 10 m^3 is assumed. The resulting air concentration is 88 mg/m^3 (12.5 mg/kg/day x 70 kg x / 10 m^3).

The following adjustment factors are applied for the identification of the reference MOS: (1) the allometric scaling factor for the rat is 4; (2) a default factor of 2.5 accounts for additional interspecies differences; (3) for intraspecies differences (workers) the default factor is 5. A duration adjustment factor is not judged necessary. Overall the reference MOS is 50 (4 x 2.5 x 5). The respective critical inhalation exposure level at the workplace is identified as 1.8 mg/m^3 (88/50) representing a shift average value.

As can be seen from table 2.1.C there is no concern regarding fertility effects after inhalation.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Dermal contact

Dermal risk assessment is also based on the NOAEL of 12.5 mg/kg/day from the fertility study with tallow alkyl amines. Taking into account the differences in oral (100%) and dermal (60%) absorption a value of 21 mg/kg/day (12.5 mg /kg/day /0.6) is obtained as corrected NOAEL for the dermal route.

The following adjustment factors are applied for the identification of the reference MOS: (1) the allometric scaling factor for the rat is 4; (2) a default factor of 2.5 accounts for additional interspecies differences; (3) for intraspecies differences (workers) the default factor is 5. A duration adjustment factor is not judged necessary. Overall the reference MOS is 50 (4 x 2.5 x 5). The respective critical dermal exposure level at the workplace is identified as 0.4 mg /kg/day (21/50).

As can be seen from table 2.1.C there is concern for all three scenarios. It is realised, that exposure reduction is in any case necessary because of systemic toxicity. This will similarly and effectively reduce the assessed fertility risks too. This conclusion applies only to the two skin irritating primary alkyl amines; for the other three corrosive primary alkyl amines there is conclusion ii for this toxicological endpoint (see introduction or summary to worker risk assessment).

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Combined exposure

Taking into account 100% oral absorption the internal level of primary alkyl amines directly corresponds to the oral NOAEL of 12.5 mg/kg/day. This value is used as starting point for combined risk assessment concerning fertility.

The reference MOS is 50. The critical internal level of primary alkyl amines with respect to fertility results as 0.25 mg/kg/day (12.5 / 50).

For all exposure scenarios there is already concern for the dermal route of exposure and thus for combined exposure as well. This conclusion applies only to the two solid primary alkyl amines; for the other three primary alkyl amines there is conclusion ii for this toxicological endpoint (see introduction or summary to worker risk assessment).

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Table 2.1.C: Fertility effects (octadecyl amine and hydrogenated tallow alkyl amine)

	Inhalation			Dermal			Combined		
Starting point for MOS calculation	88 mg/m^3			21 mg/kg/day (external value)			12.5 mg/kg/day (internal value)		
Reference MOS	50			50			50		
Critical exposure level	1.8 mg/m^3			0.4 mg/kg/day (external value)			0.25 mg/kg/day (internal value)		
	Exposure (mg/m^3)	MOS	Conclusion	Exposure (mg/kg/d)	MOS	Conclusion	Internal body burden (mg/kg/d)	MOS	Conclusion
1. Production	0.6	147	ii	0.6	35	iii	0.45	28	iii[(1)]
2. Further processing	1	88	ii	0.6	35	iii	0.5	25	iii[(1)]
2. Use of primary alkyl amines in flotation process	0.625	141	ii	6	3.5	iii	3.7	3.4	iii[(1)]
3. Formulation of products containing primary alkyl amines	0.625	141	ii	6	3.5	iii	3.7	3.4	iii[(1)]

[(1)]conclusion iii already results from dermal exposure, therefore no specific concern for the combined exposure scenario is indicated

Developmental toxicity

Two guideline-conform studies on teratology in rats and rabbits are available for octadecenylamine. This is judged to be sufficient for the evaluation of the other primary alkyl amins. Up to oral doses of 80 mg/kg/day in the rat and 30 mg/kg/day in the rabbit, which clearly induced maternal toxicity, no indications for an embryotoxic, fetotoxic or teratogenic effect were observed.

On that background adverse effects on development by occupational exposure towards primary alkyl amines are not to be expected. A quantitative assessment is not deemed necessary. There is no concern for workers from this aspect.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Summary of risk characterisation for workers

There are five primary alkyl amines to assess, two liquids (coco alkyl amine and octadecenyl amine), a paste (tallow alkyl amine) and two solids (octadecyl amine and hydrogenated tallow

alkyl amine). The liquid and paste primary alkyl amines are corrosive (labelled with R 35). The solid amines are skin-irritating substances (R 38).

For the liquids and the paste inhalation exposure is only assumed via vapour, and because the vapour pressure is less than 1 Pa the inhalation exposure is considered to be low (no quantitative assessment). These three substances are also corrosive substances. For corrosive substances, it is the convention not to perform quantitative dermal exposure assessment.

The remaining two primary alkyl amines (octadecyl amine and the hydrogenated tallow alkyl amine) are solids leading to dust exposure, and they are not corrosive, but skin-irritating substances. Only for these two substances, according to TGD, quantitative inhalation and dermal exposure assessments were performed. It is implicitly assumed that there is a higher probability of repeated dermal exposure towards the skin irritating, but not to the corrosive primary alkyl amines. However, it is recognized that the clear-cut differentiation between corrosive and skin irritating primary alkyl amines is a formal simplification; in reality there seem to be gradual differences of skin irritation potency.

Based on the available data, the skin sensitising potential of the primary alkyl amines is difficult to assess; further testing is considered necessary.

Further risk management measures have to be implemented because of concern for repeated dose toxicity (systemic effects). It is the result and interpretation of the hazard data, that the oral NOAEL taken forward to risk characterisation should not be considered secondary to local effects. RDT risk assessment mainly relies on oral studies in combination with route-to-route extrapolation. 100% absorption is used as estimate for the oral and inhalation route. For dermal absorption a value of 60 % is taken.

Table 2.1.D summarizes the conclusions for the different toxicological endpoints.

Table 2.1.D: Endpoint-specific overall conclusions for the occupational risk assessment of primary alkyl amines

Toxicological endpoints		concern
Acute toxicity	inhalation	ii
	dermal	ii
	combined	ii
Irritation/ Corrosivity	dermal	ii
	eye	ii
	acute respiratory tract	ii
Sensitisation	skin	i
	respiratory	ii
Repeated dose toxicity	local, inhalation	ii
	local, dermal	ii
	systemic, inhalation	iii
	systemic, dermal	iii
	systemic, combined	iii(1)
Mutagenicity		ii

Toxicological endpoints		concern
Carcinogenicity	inhalation	ii
	dermal	ii
	combined	ii
Fertility impairment	inhalation	ii
	dermal	iii
	combined	iii[(1)]
Developmental toxicity	inhalation	ii
	dermal	ii
	combined	ii

(1) conclusion iii already results from dermal exposure and/or inhalation, therefore no specific concern for the combined exposure scenario is indicated

Tables 2.1.E (inhalation) and 2.1.F (dermal contact) intend to visualize the risk profile of the primary alkyl amines. According to the arrangement of the tables relatively high risks occur on the upper left side, relatively low risks on the lower right side of the table-matrix.

With respect to inhalation, exposure levels to primary alkyl amines should be controlled to values in the range of 0.15 mg/m^3 (critical exposure level for repeated dose toxicity). It is assumed, that adherence to this reference value prevents respiratory irritation as well.

Dermal contact to primary alkyl amines needs to be avoided because these substances are either skin irritating or corrosive. However, especially for the skin irritating primary alkyl amines, repeated dermal exposure cannot be ruled out. With respect to systemic effects, repeated dermal exposure at the workplace should be controlled to a level below 0.04 mg/kg/day.

Table 2.1.E: Ranking of health risks for workers (inhalation exposure to octadecyl amine and hydrogenated tallow alkyl amine)

Exposure scenario	Exposure level in mg/m³	Repeated dose toxicity, systemic effects	Fertility
		Critical exposure level in mg/m^3	
		0.15	1.8
2. Further processing	1	iii	ii
3. Use of primary alkyl amines in flotation process	0.625	iii	ii
4. Formulation of products containing primary alkyl amines	0.625	iii	ii
1. Production	0.6	iii	ii

Table 2.1.F: Ranking of health risks for workers (dermal contact to octadecyl amine and hydrogenated tallow alkyl amine)

Exposure scenario	Exposure level in mg/kg/day	Repeated dose toxicity, systemic effects	Fertility
		Critical exposure level in mg/kg/day	
		0.04	0.4
3. Use of primary alkyl amines in flotation process	6	iii	iii
4. Formulation of products containing primary alkyl amines	6	iii	iii
1. Production	0.6	iii	iii (borderline)
2. Further processing	0.6	iii	iii (borderline)

2.2 Consumers

Consumer Exposure

Exposure of consumers to primary alkyl amines occurs via the dermal route - through the application of lubricants and by metal (car) care products.

For acute toxicity, the dermal route from the use of lubricants was selected which may reach a value up to 3.5 mg/kg bw/day of primary tallow alkyl amines.

For chronic dermal toxicity the use of metal (car) care products is relevant which is 0.26 mg/kg bw/day.

The bioavailability is estimated as 60 % after skin contact.

Acute toxicity

Human data on the acute dermal toxicity of primary alkyl amines are not available. For coco alkyl amines, an available dermal acute toxicity test gives a LD50 value above 2000 mg/kg bw. The highest external dermal consumer exposure of 3.5 mg/kg bw/day corresponds to an internal exposure of 2.1 mg/kg bw/day. The margin of safety is judged to be sufficient. The substances seem of no concern for the consumer with regard to acute toxicity.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Irritation/Corrosivity

All considered alkyl amine mixtures were shown to have skin irritating properties in rabbit Draize tests. Coco alkyl amines, tallow alkyl amines and octadecenyl amine were classified as corrosive. Hydrogenated alkyl amines and octadecyl amine were classified as irritating to skin and as causing severe eye damage. Consumers may have dermal contact to products containing up to 5 % alkyl amines (metal (car) care products). Since adequate classification and labelling measures are in place there is no concern for consumers.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Sensitisation

Valid human data on the sensitising potential of primary alkyl amines are not available. Coco alkyl amines and hydrogenated tallow alkyl amines were studied in an animal test, that showed negative and inclusive results. These results may be further used for read-across to other alkyl amines in the category. However, read-across to the other primary alkyl amines considered in this report is limited by structural differences: Coco alkyl amines are of considerably shorter chain length, and tallow alkyl amines as well as octadecenyl amine have a higher degree of unsaturation, which significantly affects the overall molecular structure. Relevant skin contact of consumers with primary alkyl amines occurrs from the use of metal care products. Due to the lacking hazard data, the resulting risk of sensitisation cannot be assessed. The performance of a Local Lymph Node Assay (LLNA) is proposed with an appropriate substance of the category.

Conclusion (i) There is a need for further information and/or testing.

Repeated dose toxicity

Data on repeated dose toxicity are available for tallow alkyl amines and octadecenyl amine from valid oral 28 day studies in rats, for octadecyl amine from oral studies of limited reliability in rats and dogs, and for octadecyl amine and octadecenyl amine from dermal studies of limited reliability in rats and mice. From the best-conducted of these studies, NOAEL / LOAEL values are derived for the overall class of compounds.

In an oral 28 day study in rats, octadecenyl amine induced growth depression, increased enzyme activities, motoric and haematologic abnormalities. The NOAEL is 3.25 mg/kg bw/d. For the dermal route, no NOAELsys could be derived. Repeated dermal application of octadecenyl amine caused concentration-dependent irritative skin effects. The lowest tested concentration was 0.3%, which is converted to a dermal LOAELlocal of 12.5 mg/kg bw/d.

For the dermal route, the exposure via the use of metal (car) care products is calculated as 0.26 mg/ kg bw/day.

For the decision on the appropriateness of MOS, the following aspects have been considered and taken into account.

- overall confidence in the database:
The data taken into account for performing the risk characterisation have been evaluated with regard to their reliability, relevance and completeness according to section 3.2 of the TGD. Only two of the five alkyl amine mixtures under consideration were investigated in toxicity tests consistent with internationally recognized guidelines. For one further substance mixture, supportive data are available from studies of limited reliability. As the overall information derived from all studies is not contradictory, an overall risk characterisation for the primary alkyl amines based on this database seems justified. However, data gaps remain and the chosen category approach is associated with a special extent of uncertainty.

- uncertainty arising from the variability in the experimental data:
The data on toxicity after dermal exposure is limited to allow a firm identification of an effect level for risk characterisation. For oral exposure, even though the experimental data is also limited, the available information appears to be in good consistency, in both qualitative and quantitative terms, with regard to observed adverse effects. There are no reasons to assume a special extent of uncertainty which has to be taken into account.

- intra- and interspecies variation:
Available data do not allow a conclusion on the intraspecies or interspecies variability of the toxicokinetic or toxicodynamic characteristics of the substances under consideration.

- the nature and severity of the effect:
The observed adverse effects in animals are regarded as serious. The systemic health effects are the basis for a proposed classification as R48/22.

- dose-response relationship:
There is no reason to assume a special concern.

- differences in exposure (route, duration, frequency and pattern):
The estimated year-average daily dermal exposure is compared with a dermal LOAELlocal derived from a 12 day study in rats. This procedure is consistent with established risk assessment methodology.

- the human population to which the information on exposure applies:

Following the exposure pattern there is no reason to assume a special risk for children, elderly, or pregnant women.

- other factors:
There are no other factors known that might require a particular margin of safety.

MOS for the dermal exposure scenario, local effects:

The external dermal exposure to primary alkyl amines is calculated as 260 µg/kg bw/d. The margin of safety between the

external dermal exposure estimate of	0.260 mg/kg bw/d

and the

dermal LOAELlocal of	12.5 mg/kg bw/d

is judged to be not sufficient additionally taken also into account that a LOAEL value was selected.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

MOS for the dermal exposure scenario, systemic effects:

Assuming a bioavailability of 60 %, the external dermal exposure of 260 µg/kg bw/d corresponds to an internal exposure of 156 µg//kg bw/d. The margin of safety between the

internal dermal exposure estimate of	0.156 mg/kg bw/d

and the

oral NOAELsys of	3.25 mg/kg bw/d

is judged to be not sufficient.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Mutagenicity

Mutagenicity tests with the alkyl amine mixtures under consideration gave only negative results. For the longer chain compound mixtures (C16/C18), results are available from tests with bacteria and with mammalian cells *in vitro* and *in vivo*. For the shorter chain coco alkyl amines (C12/C14), only data from bacterial mutagenicity tests are available. However, taken together and in view of the consistency of the results the data base on mutagenicity is judged to be sufficient to exclude a concern for the consumer with regard to this endpoint.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Carcinogenicity

Data on the carcinogenic potential of primary alkyl amines from human experience or from valid animal carcinogenicity studies are not available. Limited data from older chronic toxicity studies, negative data from a variety of mutagenicity tests and negative predictions from the Danish QSAR database indicate no specific concern regarding the carcinogenic potential of these substances.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Toxicity for reproduction

Fertility impairment

Concerning effects on fertility, valid data are only available for tallow alkyl amines from a study according to OECD TG 421 (oral exposure). Additionally, data of limited reliability can be derived from oral chronic studies with octadecylamine. Based on the findings of a lower fertility index and a lower conception rate at daily dosages of 50 mg/kg bw/d a NOEL/fertility of 12.5 mg/kg bw/d is derived from the guideline-compliant test with tallow alkylamines.

For the dermal route, the exposure via the use of metal (car) care products is calculated as 0.26 mg/ kg bw/day.

For the decision on the appropriateness of MOS, the following aspects have been considered and taken into account.

- overall confidence in the database:
The data taken into account for performing the risk characterisation have been evaluated with regard to their reliability, relevance and completeness according to section 3.2 of the TGD. Only one of the five alkyl amine mixtures under consideration was investigated in a screening test for reproductive toxicity, which complied with an internationally recognized guideline. For one further substance mixture, supportive data of limited reliability are available. As the available information does not indicate a specific toxic potential adverse to fertility, an overall risk characterisation for the primary alkyl amines for this endpoint can be based on this database. However, the uncertainty associated with the present data gaps and the chosen category approach needs to be taken into account.

- uncertainty arising from the variability in the experimental data:
There are no reasons to assume a special extent of uncertainty.

- intra- and interspecies variation:
Available data do not allow a conclusion on the intraspecies or interspecies variability of the toxicokinetic or toxicodynamic characteristics of the substances under consideration.

- the nature and severity of the effect:
The observed adverse effects on fertility occur at dose levels which also produced non-specific signs of toxicity. There is no reason to assume a special potential for toxicity on fertility.

- dose-response relationship:
There is no reason to assume a special concern.

- differences in exposure (route, duration, frequency and pattern):

The estimated year-average daily dermal exposures was compared with an oral NOAEL. This procedure is consistent with established risk assessment methodology.

- the human population to which the information on exposure applies:
Following the exposure pattern there is no reason to assume a special risk.

- other factors:
There are no other factors known that might require a particular margin of safety.

MOS for the dermal exposure scenario:

The external dermal exposure to primary alkyl amines is calculated as 260 µg/kg bw/d. Assuming a bioavailability of 60%, this corresponds to an internal exposure of 156 µg//kg bw/d. The margin of safety between the

internal dermal exposure estimate of 0.156 mg/kg bw/d

and the

oral $NOAEL_{fertility}$ of 12.5 mg/kg bw/d

is judged to be not sufficient.

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Developmental toxicity

Concerning developmental toxicity, valid data are only available for octadecenylamine from oral studies in two species (rat and rabbit). These studies did not provide an indication of any embryo-/fetotoxic or teratogenic potential even at maternally toxic dose levels. From the study in rabbits, the $NOAEL_{dev.tox.}$ is derived to be above 30 mg/kg bw/d.

For the dermal route, the exposure via the use of metal (car) care products is calculated as 0.26 mg/ kg bw/day.

For the decision on the appropriateness of MOS, the following aspects have been considered and taken into account.

- overall confidence in the database:
The data taken into account for performing the risk characterisation have been evaluated with regard to their reliability, relevance and completeness according to section 3.2 of the TGD. Only one of the five alkyl amine mixtures under consideration was investigated in animal studies for developmental toxicity. As the available information does not indicate a specific toxic potential adverse to the development, an overall risk characterisation for the primary alkyl amines for this endpoint can be based on this database. However, the uncertainty associated with the present data gaps and the chosen category approach needs to be taken into account.

- uncertainty arising from the variability in the experimental data:
There are no reasons to assume a special extent of uncertainty.

- intra- and interspecies variation:
Available data do not allow a conclusion on the intraspecies or interspecies variability of the toxicokinetic or toxicodynamic characteristics of the substances under consideration.

- the nature and severity of the effect:
No adverse effect on development was observed in the tested dose range.

- dose-response relationship:
There is no reason to assume a special concern.

- differences in exposure (route, duration, frequency and pattern):
The estimated year-average daily dermal and oral exposures are compared with an oral NOAEL. This procedure is consistent with established risk assessment methodology.

- the human population to which the information on exposure applies:
Following the exposure pattern there is no reason to assume a special risk.

- other factors:
There are no other factors known that might require a particular margin of safety.

MOS for the dermal exposure scenario:

The external dermal exposure to primary alkyl amines is calculated as 260 µg/kg bw/d. Assuming a bioavailability of 60%, this corresponds to an internal exposure of 156 µg//kg bw/d. The margin of safety between the

internal dermal exposure estimate of	0.156 mg/kg bw/d

and the

oral $NOAEL_{dev.tox.}$ of	>30 mg/kg bw/d

is judged to be sufficient.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Summary of risk characterisation for consumers

Concern is expressed and risk reduction measures should be initiated for consumer by chronic exposure by handling metal (car) care products. Dermal intake in repeated dose toxicity and fertility induced conclusion (iii). Other toxicological endpoints are not covered with the exception of sensitisation. Further studies are proposed.

3 Current Risk Reduction Measures

Classification and labelling

The substances Amines, tallow alkyl, (Z)-Octadec-9-enylamine, Octadecylamine, Amines, hydrogenated tallow alkyl and Amines, coco alkyl are currently not classified in the Annex I of Directive 67/548/EEC.

Industry labels some of them currently as follows (GESTIS, 2008):
(Z)-Octadec-9-enylamine: C,N; R22-35-50; S26-28-36/37/39-45-61
Octadecylamine: Xi,N; R38- 41-51/53; S26-39-61
Amines, hydrogenated tallow alkyl: Xi,N; R38-41-50; S26-28-37/39-61.

The primary alky amines have not been discussed in the TC C&L, but directly in the TC NES (Technical Committee of New and Existing Chemical Substances). In the year 2007 the following proposal for a harmonised classification and labelling with respect to the Human Health classification was laid down in an Annex XV –Dossier.

Proposed classification based on Directive 67/548/EEC:

Amines, coco alkyl (CAS 61788-46-3)
Xn; R22
C; R35
Xi; R37
Xn; R48/22

Amines, tallow alkyl (CAS 61790-33-8)
Xn; R22
C; R35
Xn; R48/22

Amines, hydrogenated tallow alkyl (CAS 61788-45-2)

Xi, R38
Xi; R 41
Xn; R48/22

Octadecylamine (CAS 124-30-1)

Xi; R38
Xi; R41
Xn; R48/22

(Z)-Octadec-9-enylamine (112-90-3)

Xn; R22
C; R34
Xn; R48/22

Furthermore, it was proposed in the RAR to classify primary alkyl amines as: N, R 50/R53.

The Annex XV-Dossier will probably not be sent to the ECHA, because the endpoints are not of priority according to REACH (no CMR or sens. properties). It will only be for internal use in the TC NES.

Abbreviations:

C	Corrosive
N	Dangerous for the environment
Xi	Irritant
Xn	Harmful
R22	Harmful if swallowed
R34	Causes burns
R35	Causes severe burns
R37	Irritating to respiratory system
R38	Irritating to skin
R41	Risk of serious damage to the eyes
R48/22	Danger of serious damage to health by prolonged exposure if swallowed
R50	Very toxic to aquatic organisms
R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
R51/53	Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S26	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
S28	After contact with skin, wash immediately with plenty of . . .(to be specified by the manufacturer)
S36/37/39	Wear suitable protective clothing, gloves and eye/face protection
S37/39	Wear suitable gloves and eye/face protection
S39	Wear eye/face protection
S45	In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)
S61	Avoid release to the environment. Refer to special instructions/ Safety data sheets

3.1 Workers

As a result of their classification as hazardous substances primary alkyl amines are subject to general regulations concerning its supply and handling.

Safety data sheets

In accordance with Regulation (EC) No 1907/2006 of the European Parliament and of the council of 18 December 2006, corrected in May 07 and amended in November 07 (Regulation (EG) Nr. 1354/2007) anyone placing primary alkyl amines on the market has to provide safety data sheets to the professional user, if they meet the criteria for classification as dangerous in accordance with Directives 67/548/EEC or 1999/45/EC.

The information system for hazardous substances and preparations in the form of labelling and the safety data sheets is considered sufficient in principle to provide the user with appropriate information for the selection of suitable occupational safety measures.

Occupational safety and health regulations

Regarding the production and use of primary alkyl amines the following directives are primarily applicable as general regulations for occupational safety and health at the European level:

- 98/24/EC on the protection of workers from the risks related to exposure to chemical agents at work, if they fall under the definition of Hazardous chemical agent according Article 2(b)

- 89/656/EEC on the use of personal protective equipment

Only limited knowledge is available about the extent to which the EU Member States have in each case transposed these basic requirements into national law.

Occupational exposure Limits

OELs (Occupational exposure limits) are not established for primary alkyl amines in the EU (ARIEL, 2008).

Personal Protection Equipment (PPE) against dermal and eye exposure

According to community legislation workers have to be provided with suitable PPE if their health is at risk due to exposure against chemicals. PPE that protects against the risks of primary alkyl amines is available. The type of filter and the material of gloves, material thickness and breakthrough time have to be specified in the Safety Data Sheet.

Are existing controls sufficient to limit occupational risks?

It has been concluded from the risk assessment that there is a need for limiting the risks. The primary alkyl amines have been and are proposed to be classified and labelled as skin irritants or corrosives. Skin irritation and corrosive lesions need to be avoided by adequate skin-related risk management measures which – in the framework of workplace legislation - are considered to be effective and sufficient.

As a result of the Risk Assessment additional measures have to be implemented to reduce inhalative exposure to dust. Inhalative exposures have caused concern for repeated dose toxicity (systemic effects) because they exceeded the critical exposure limit (CEL) of 0.15 mg/m^3.

By convention, dermal exposure to corrosive substances is not assessed. For those primary alkyl amines (octadecyl amine and hydrogenated tallow alkyl amine) that will not be classified as corrosive (only as irritant) dermal exposures were assessed to be high and resulted in concern for repeated dose toxicity (systemic effects) (CEL 0.04 mg/kg/day) and also in concern for fertility impairment (CEL 0.4 mg/kg/day).

3.2 Consumers

The chemicals in the category are not currently regulated under Council Directive 76/769/EEC (Restrictions on the marketing and use of dangerous substances). Only the CAS No 124-30-1 and CAS No. 61790-33-8 are covered due to the selection in the dermal car scenario.

Both chemicals are listed in International Nomenclature of Cosmetic Ingredients (INCI), 2006.

Commission Decision 96/335/EC establishing an inventory and a common nomenclature of ingredients employed in cosmetic products (INCI), as amended by Decision 2006/257/EC (OJ (L 97) 1, 5 Apr 2006)
(Source: Ariel WebInsight 5.1, 2008)

4 Possible Further Risk Reduction Measures

4.1 Workers

The following further Risk Reduction Measure are considered to be probably effective :

- Occupational Exposure Limit
- Specific training, organisational measures and occupational hygiene in the framework of Directive 98/24

The options are assessed in section 5.

4.2 Consumers

The following Risk Reduction Measures are considered to be probably effective.

The risk reduction measures will cover the chemicals in the category amines, tallow alkyl (CAS No 61790-33-8) and octadecylamine (CAS No 124-30-1) by chronic exposure in handling metal (car) care products.

National regulations are effective to protect consumers for adverse effects.

5 Assessment of Possible Further Risk Reduction Measures

The TGD requires that possible further risk reduction options be examined against the following criteria

- effectiveness
- practicality
- economic impact
- monitorability.

5.1 Workers

Occupational Exposure Limit

Exposure reduction by technical and organisational measures and personal protection are accepted strategies in workplace legislation.

In order to put these instruments into action on company level and to make them enforceable in the framework of worker protection legislation it is recommended to establish an occupational exposure limit for the primary alkyl amines assessed in this strategy.

The OEL should take into account the risk assessment (critical exposure level CEL 0.15 mg/m^3 for the most critical effect). The OEL will also trigger that personal protective equipment is provided if workplace concentrations exceed the OEL.

Within the framework of workplace legislation an occupational exposure limit is an enforceable and effective means to make exposure control obligatory. If this OEL takes into account the risk assessment, it can also be considered to be an effective means for health protection in the workplace. It can be monitored by existing techniques of workplace measurement. The reduction of inhalative exposure is considered practical for the scenarios assessed in the RAR:

Scenario 1: Production (Drumming, 8 h/day daily)

The value used to derive concern was 0.6 mg/m^3. It is a worst-case value from workplace measurements that is taken forward for risk characterisation. Typical exposures ranged rather from 0.1-0.01 mg/m^3. Scenario 1 is in chemical industry and workplaces are stationary and well defined. It is considered to be practical that companies, which should fail to achieve the typical values can apply further state-of-the-art improvements of containment and ventilation to reduce exposure to a level in the range of an envisaged OEL of about 0.15 mg/m^3

Scenario 2: Further processing, (charging, dosing 8 h/day daily)

The value 1 mg/m^3 is the upper end of a range from 0-1 mg/m^3 assessed with the EASE model (supposing a low-dust technique and LEV). As the scenario is in chemical industry and workplaces are stationary and well defined, effective ventilation and, if necessary, containment are practical to control exposure. It is probable that on company level the lower end of the EASE assessment can be achieved. This will comply with the level to reduce of about 0.15 mg/m^3 required by an OEL.

Scenario 3: Floatation (charging, dosing, 1h/daily) and
Scenario 4: Formulation of products (charging, dosing, 1h/daily)

The value of 0.625 mg/m^3 results from the upper end of a range from 0 - 5 mg/m^3 assessed with the EASE model (supposing a low-dust technique but no LEV and only 1 h/day). The processes described by scenario 3 and 4 should undergo a risk assessment on company level and risk reduction measures according to the STOP-principle should be introduced as appropriate. The scenarios 3 and 4 are located in industry or in Downstream User chemical industry. Workplaces are stationary and well defined. If necessary, improvements of ventilation and containment are practical to reduce exposure. It is probable, that on company level the lower range of the EASE assessment can be achieved.

The economic impact of an OEL can not be assessed for any of the scenarios. However, taking into account the measured data and the ranges resulting from by the models applied for assessment, an OEL in theorder of magnitude of the CEL is considered to be achievable with current state-of-the-art- technology.

Specific training, organisational measures and occupational hygiene in the framework of Directive 98/24

The risk assessment has resulted in concern because of dermal exposure. The risks from dermal exposure cannot be reduced by establishing and complying with an OEL. Dermal exposure can in principle be reduced by technical measures (e.g.closing systems) and organisational measures that reduce the frequency, duration and area of exposure, by training to work cleanly, by personal hygiene and by appropriate use of PPE. Training, information and hygienic measures are foreseen in the framework of workplace legislation.

Especially it is supposed that the efficacy of gloves can be improved beyond the 90% that is assumed in risk assessment. Training is supposed to

- reduce unintended contamination during the handling of used gloves,
- rise awareness for limited performance of suitable gloves under real working conditions (e.g. mechanical tress),
- rise awareness that gloves must be changed if breakthrough time is reached.

Organisational measures and training are practical and of low or moderate economic impact. Documentation on company level makes them monitorable, but enforcement is on behalf of the Member States. The proof of efficiency of measures to control dermal exposure is generally difficult. The corrosive and irritant properties of the substances might work as an "early warning" mechanism.

Taking into account, that the exposures that were taken forward for risk assessment were worst case values from a generic model, it seems appropriate and sufficient, to apply the full range of technical and organisational measures foreseen in the framework of workplace legislation, with special attention to training, organisational measures and occupational hygiene.

Scenario 1: Production (Drumming, 8 h/day daily) and Scenario 2: Further processing, (charging, dosing, 8 h/day daily)

The value of 42 mg/p/day = 0.6 mg/kg/day is derived from the upper end of a range from 0 – 1 mg/p/day, assessed by the EASE model (Parameters: contamination of 1 hand (420cm"), use of gloves with 90% efficacy and 70kg body weight). This is much higher than the critical level for the most critical effect: repeated dose toxicity (systemic effects) (CEL 0.04 mg/kg/day). Gloves are supposed to be worn, and processes in these scenarios are supposed to use fairly closed systems. Therefore further reduction of dermal exposure is necessary and will require the full range of organisational measures foreseen in workplace legislation and described in general terms above.

Scenario 3: Floatation (charging, dosing, 1h/daily) and Scenario 4: Formulation of products (charging, dosing, 1h/daily)

The value of 420 = 6 mg/kg/day is derived from the upper end of a range from 0 – 1 mg/p/day, assessd by the EASE modell (Parameters: contamination of 1 hand (420cm"), no gloves and 70kg body weight). This is very much higher than the critical level for the most critical effect: repeated dose toxicity (systemic effects) (CEL 0.04 mg/kg/day). The processes described by scenario 3 and 4 shall already undergo a risk assessment on company level and risk reduction measures according to the STOP-principle because of the high inhalative exposure to dust. As the scenarios 3 and 4 are in industry or in Downstream User chemical industry, workplaces are stationary and well defined and improvements of ventilation and containment are practical to reduce exposure. Though these measures will also reduce dermal exposure to a certain extent, it is indispensable that gloves are used (90% efficacy assumed). However, gloves with a supposed reduction–factor of 90% are not sufficient to reduce dermal exposure to the extent that is required. Therefore further reduction of dermal exposure is necessary and will require the full range of organisational measures foreseen in workplace legislation and described in general terms above.

5.2 Consumers

For the dermal scenario in the use of metal (car) care products decisions for the protection of consumers should be initiated and performed. Since the chemicals in the category are not classified or proposed for classification in respect with CMR properties of Cat 1 or Cat 2 a DNEL for fertility should be derived to establish whether an insertion in the REACH regulation is promising.

6 Further Risk Reduction Measures Recommended

6.1 Workers

The risk reduction strategy recommends the following measures:

- to establish at community level an occupational exposure limit value according to Directive 98/24/EEC for :

  Amines, coco alkyl (CAS 61788-46-3),
  Amines, tallow alkyl (CAS 61790-33-8),
  Amines, hydrogenated tallow alkyl (CAS 61788-45-2),
  Octadecylamine (CAS 124-30-1),
  (Z)-Octadec-9-enylamine (112-90-3)

- to apply the following revised classifications and labelling in the forefront of a future Adaption to Technical Progress of Directive 67/548/EEC:

  Amines, coco alkyl (CAS 61788-46-3)
  Xn; R22
  C; R35
  Xi; R37
  Xn; R48/22

  Amines, tallow alkyl (CAS 61790-33-8)
  Xn; R22
  C; R35
  Xn; R48/22

  Amines, hydrogenated tallow alkyl (CAS 61788-45-2)
  Xi, R38
  Xi; R 41
  Xn; R48/22

  Octadecylamine (CAS 124-30-1)
  Xi; R38
  Xi; R41
  Xn; R48/22

  (Z)-Octadec-9-enylamine (112-90-3)
  Xn; R22
  C; R34
  Xn; R48/22

- to transfer the classification into the Inventory according to Article 114 of Regulation (EC) 1907/2006

- information on the need of specific training, organisational measures and occupational hygiene in the framework of Directive 98/24 in order to reduce dermal exposure in scenario 1 and 3.

6.2 Consumers

The future risk reduction strategy recommends the following measure for amines, tallow alkyl (CAS No 61790-33-8) and: Octadecylamine (CAS No 124-30-1):

To develop a derived no effect level (DNEL) for the dermal fertility scenario to evaluate whether an insertion in the REACH regulation is useful.

7 Marketing And Use Restrictions

Not applicable to:

Amines, coco alkyl (CAS 61788-46-3),
Amines, tallow alkyl (CAS 61790-33-8),
Amines, hydrogenated tallow alkyl (CAS 61788-45-2),
Octadecylamine (CAS 124-30-1),
(Z)-Octadec-9-enylamine (112-90-3)

8 Possible Monitoring Arrangements

9 Organisations consulted