European Committee of
Organic Surfactants and
their Intermediates

A Sector Group of **Cefic**

Classification and Labelling of Surfactants for human health hazards according to the Dangerous Substances Directive

CESIO recommendations for Anionic and Non-ionic surfactants

Update of the recommendation issued on January 2000

(May 2006, Version 3)

cefic sector group

Chemistry making a world of difference

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This Cesio Recommendation Guidance document includes the 1990 recommendations on Quaternary Ammonium Compounds and Fatty Amines and Derivatives (version 1).

The paragraph on "Risk Phrase R66 '*Repeated Exposure May Cause skin dryness or cracking'* to surfactants" has been added in December 2005 to the Cesio Recommendation Guidance document issued in January 2000 (version 2).

1. Introduction

On two separate occasions during the 1980's, CESIO[1] reviewed company reports of toxicology studies on marketed surfactants to provide guidance for classification and labelling in line with the requirements of Annex VI of the Dangerous Substances Directive [DSD] (1). By reviewing all available experimental results, CESIO believed that "weight of evidence" enabled them to provide the most accurate guidance. The first of these reviews was reported in 1984 (2). At this time many of the studies had not been conducted strictly according to developing OECD/EC guidelines (3, 4-*Annex V*) and for that reason, a second review was undertaken several years later. This was completed in 1990 (5).

For both reviews, surfactants were grouped into 4 categories (anionics [for convenience this group also contained 3 amphoteric categories], non-ionics, quaternary ammonium compounds and fatty amines and their derivatives) and several sub-categories on the basis of their chemical and physical properties. Acute oral toxicity, skin and eye irritation and skin sensitisation studies were reviewed by an expert task force (TF) and recommendations for classification and labelling were made.

In 1993, the European Union revised their criteria for classification and labelling of substances and preparations based on their potential to cause ocular lesions (6). Two of these new criteria are very specific for the use of risk phrase R41 (Risk of serious damage to eyes). Additionally, in 1995 new experimental data on the irritation potential of several surfactant raw materials became available, which were considered to be of value for a further refinement of the classification and labelling recommendations given in 1990. Consequently, CESIO established a new TF to review their guidance on the classification and labelling of anionic and non-ionic surfactants. This report describes the objectives of this exercise, the composition of the TF, the process followed, it presents results and updates recommendations for classification and labelling. Only studies conducted according to DSD Annex V methodology were taken account of in this exercise and interpretation was strictly according to the 18th ATP (6).

As a result, several classification and labelling recommendations are increased from those currently in place. The implications of these changes are discussed later in this document.

For completeness, the tables on quaternary ammonium compounds and fatty amines and derivatives from the 1990 TF report are appended.

2. Objectives

The following terms of references formed the basis of this task:

1. Review all available studies for acute oral toxicity and skin and eye irritation on anionic and non-ionic surfactants that conform to DSD (4) Annex V.
2. Determine whether existing CESIO classification and labelling recommendations for these endpoints are appropriate. Where not, revise recommendations. Classification for eye irritation was a particular issue since the previous TF had recommended a risk phrase of R 36* for surfactants that cause persistent effects on the eye. R 36* is not an official EC phrase.

3. The Task Force

The following toxicologists and classification and labelling specialists participated.

D Calcinai	Condea Augusta	ChB Jassogne	Cesio
H Certa	Condea Chemie	W Kohl	Henkel
W M Clous	Akzo Nobel	R Kreiling	Hoechst, now Clariant
S Dechert	Hüls, now Degussa Hüls	P A Martin	Albright & Wilson
O-J Grundler	BASF	B Molinier	Elf-Atochem

[1] CESIO = Comité Européen des Agents de Surface et leurs Intermédiaires Organiques

B Hendrickx	Rhone-Poulenc, now Rhodia	RAJ Priston	Shell Chemicals **[chairman]**
G Holland	Unilever	J-F Regnier	Elf-Atochem
L Hughes	ICI Performance Chemicals, now Uniqema	C Verge	Petresa

4. The process

The intent of this TF was to re-assess existing animal studies and to review as many new ones as possible whilst maintaining confidentiality of privileged information. To achieve this, questionnaires, developed for each of the end-points, were completed by participating companies and returned to CESIO secretariat. Confidential information (e.g. product name, company name) was then obscured and the questionnaires were coded before being passed to the TF for review. Questionnaires for each of the end points are shown in appendices 1-3 (skin irritation, eye irritation and acute oral toxicity, respectively). For inclusion in the final assessment, questionnaires were judged on the details provided on the test material and on compliance with current OECD/EC methodology. Adherence to Good Laboratory Practice was not a requisite if the test was otherwise well conducted.

The assessment was conducted during 2 meetings of the TF. Questionnaires were evaluated and classifications derived using EC criteria (6). Additionally, for some sub-categories and particularly for eye irritation, the TF ensured that its conclusions were in line with the ECETOC[2] report on eye irritancy (7) and took account of the findings of previous CESIO reviews.

5. Results and Discussion

Existing and proposed classification and labelling recommendations for anionic and non-ionic surfactants are summarised in tables 4 and 5, respectively. Supplementary information is provided in the following paragraphs:

5.1 Questionnaires

A total of 421 questionnaires (see table 1) were returned from the following companies:

Akzo Nobel	Goldschmidt	Muenzing Chemie
Albright and Wilson	Henkel	Rhodia
BASF	Hoechst	Shell Chemicals
Dr Th.Bohme	Huels	Unger Fabrikker
Condea	ICI Surfactants	Union Carbide
Elf-Atochem	Kao Corporation	Zschimmer & Schwarz

Table 1. Breakdown of questionnaires by study

Surfactant	Datasets			Totals
Category	Acute oral	Skin irritation	Eye irritation	
Non-ionics	109	94	102	305
Anionics	45	31	40	116
Totals	154	125	142	421

From chemical descriptions provided, several new anionic surfactant classes were identified, extending the coverage of sub-categories 4, 5 and 11. Data were not available for sub-categories 10 and 16 (anionics), 2.1 or 4.2 (non-ionics) in this or the previous review so the TF has deleted from the tables and renumbered categories as appropriate.

[2] ECETOC = European Centre for Ecotoxicology and Toxicology of Chemicals

5.2 Acute oral LD50

5.2.1 Anionics

No changes to current recommendations are proposed. alkylnaphthalene sulphonates (sub-category 16) and certain of the alkyl sulphates (sub-category 2), alkylaryl sulphonate salts (sub-category 6) and fluorine surfactants (sub-category 14) are correctly classified as "harmful if swallowed" (R 22). New animal study data on alkyl sulphates and alkylaryl sulphonate salts are consistent with this recommendation. New data were not available on alkylnaphthalene sulphonates or fluorine surfactants.

5.2.2 Non-ionics

No changes to current recommendations are proposed. fluorine surfactants (sub-category 11) and certain of the ethoxylated fatty alcohols (sub-category 1) and ethoxylated alkylphenols (sub-category 3) are correctly classified as "harmful if swallowed" (R 22). New animal data on ethoxylated fatty alcohols and ethoxylated alkylphenols are consistent with this recommendation. New data were not available for sub-category 11.

5.3 Skin Irritation

5.3.1 Anionics

In the absence of new data, the TF recommends no change to existing recommendations. This applies to the majority of the anionic surfactants.

New experimental data generally support existing classification and labelling guidance. For sub-category 5 (olefin sulphonates), new skin irritation data were available on materials with an active matter concentration >80 %, at which concentration they were irritant (Xi, R 38). New data were not available on olefin sulphonates at 40-80 %, but, because in the previous review they were also found to be irritant (Xi, R 38) at 40 %, this TF recommends the same classification. Based on new data, the cocoamphodiacetates (amphoterics, sub-category 16) need not be considered irritant.

5.3.2 Non-ionics

In general, classification and labelling recommendations derived from the new animal data are consistent with existing ones.

For three sub-categories, however, new animal data (table 2) strongly support a change from "irritating to skin" (R 38) to "not classified", due mainly to the increasing availability of studies using a 4 hour skin exposure period, as in the OECD/EC test protocol, rather than 24 hours used in the conventional "Draize" test.

Table 2. Non-ionics: Revised recommendations for skin irritation

Sub-category	EO	Carbon chain length	Conc. %	Classification Existing	Proposed
1. Fatty alcohol +EO	2-5	8-18	100	R 38	**NC**
	>5-15	8-18	100	R 38	**NC**
3. Alkylphenol+EO	>7-11	8-12	100	R 38	**NC**

5.4 Eye Irritation

5.4.1 Anionics

Except for a few anionics (see table 3), the animal findings reviewed by the previous TF are supported by new animal study data.

Table 3. Anionics: Recommended changes in classification due to new or expected findings

Sub-category	Cation	Carbon chain length	Conc. %	Classification - eye Existing	Proposed
1.1 Alkylpolyglycolether carboxylic acid, 4-11 EO, CM degree = 80 %	H	9-14	≥ 90	R 36	R 41
5. Olefin sulphonates	Na salt	14-16	40	R 36	NC
6. Alkylaryl sulphonate salts	Ca salt	10-13	95	R 36	R 41 #
8. Sulphosuccinates, di-alkyl	Na salt	i-10	65	R 36	R 41
Amphoteric surfactants					
- Cocoalkylamidobetaine	-	8-18	>15		R 41
		8-18	5-15		R 36
		8-18	<5		none
- Cocoamphodiactetate	-	10-18	30	R 36*	R 36 #

footnote: #: established by read-across rather than actual study data

In addition, the TF recommends that anionics that are currently assigned R 36* (possibility of persistent effects on the eye) should be re-classified with “risk of serious damage to eyes” (R 41) to be consistent with the updated classification and labelling legislation (6) and recent industry guidance (7). Except for two product sub-categories (see following paragraph) the degree of irritation recorded throughout the studies was less than severe but the low level of irritation persisted until the end of the observation period. This persistence of effect, according to the updated guidance criteria, equates to “irreversible changes of the cornea and/or iris” and so requires the R 41 phrase.

In contrast, for two anionic sub-categories (12.1, alkylphosphoric acid-mono/diester and 12.2, alkyl EO phosphate esters), the mean of the 24, 48 and 72 hour irritation scores was itself sufficiently severe enough to trigger a classification of “risk of serious damage to eyes” (R 41).

For two of the amphoteric sub-categories (cocalkylamidobetaine and cocoamphodiacetate), the recommendation is as follows:

Several new rabbit eye irritation studies indicate that, at 30 % active matter, cocoamphodiacetate is irritant (R 36) because the moderate level irritation seen shortly after application of the test material receded within 14 days.

Based on the review of data in March 2006 (?), it became evident that the classification of betaine solutions should be as follow:

For products containing more than 15% cocalkylamidobetaine (active material): R41

For products containing 5% to 15% cocalkylamidobetaine (active material): R36

For products containing less than 5% cocalkylamidobetaine (active material): no classification & labelling

5.4.2 Non-ionics

Except for a few non-ionics, the animal findings reviewed by the previous TF are supported by new animal study data. However, for others (categories 7 and some of categories 1 and 3), persistent effects (see previous section for more information) convinced the TF that a classification of R 41 rather than R 36* was correct.

6. Summary and recommendations

This document reports the findings of the third CESIO TF on the classification and labelling of major surfactants for human health effects according to EC legislation on dangerous substances. The database available to this TF consisted of animal studies covering acute oral toxicity and skin and eye irritation of the anionic and non-ionic surfactants. Only studies that met current OECD/EC test standards were taken into account. Human experience data were inadequately documented to use in this exercise and human test data were too limited to use as a basis for an industry recommendation on classification and labelling of surfactants.

For many of the surfactants, existing recommendations are unchanged, either because there were no additional data available or new data support these recommendations. For others, new data indicate that existing recommendations do not adequately reflect their acute oral toxicity or irritation potential when judged according to current legislation. For these, changes are recommended. New recommendations are shown in tables 4 and 5. For completeness, though not addressed by this TF, the existing recommendations for other surfactant categories are shown in Appendices 4 (quaternary ammonium compounds) and 5 (fatty amines and derivatives).

7. Comments on the application of this document

Within the surfactant industry there is an extensive safe history of the handling and use of surfactants during manufacture, supply and downstream applications and the purpose of this review, as with previous ones, is to provide guidance to underpin that for the future. The revised recommendations for classification and labelling in this report are derived from Annex V test methods (4), using current EC criteria for interpretation (6). As such, they are a basis for health and safety advice on individual surfactant substances and on preparations where no additional toxicity data are available.

EC Directives on dangerous substances and preparations, however, do allow other approaches to classification and labelling:

1. With regard to the use of alternative test methods using laboratory animals, the rabbit “Draize” test has been reported to over-predict eye irritancy of formulations containing surfactants for man (8-10). For many formulations, the rabbit low volume eye test may better reflect the eye irritancy hazard for man; it still may over-predict but less so than the “Draize” test (11-16).

2. The classification and labelling recommendations in this report apply only to individual surfactants. When applying these to formulations containing surfactants it should be noted that “antagonism” has been reported in the open literature i.e. the overall irritation profile of some preparations has been reported to be less than that expected on account of the effects of the individual components (17-19). Such situations must be handled on a case by case basis.

8. References

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Table 4. Anionics

Typical chemical ingredient	Typical specification			Recommended Symbol and R-phrases				
	Cation	Carbon Chain R-	Typical chemical conc (%)	**CURRENT**	Symbol	**PROPOSED** Oral	Skin	Eye
1. Fatty acid salts	K-salt	12-18	15	C, R34	C	NC	34	
	Morpholine	Oleyl	100	Xi, R36/38	Xi	NC	38	36
1.1..Ether carboxylic acids.								
-Alkylpolyglycolether carboxylic acid, 4-11 EO, (CM degree = 80 %)	H	9-14	≥ 90	Xi, R36/38	Xi	NC	38	**41**
-Alkylpolyglycolether carboxylic acid, ≤ 4.5 EO, (CM degree ≥ 90 %)	Na-salt	12-14	20	Xi, R36	Xi	NC	NC	36
-Alkylpolyglycolether carboxylic acid, ≥ 4.5 EO, (CM degree ≥ 90 %)	Na-salt	8-14	20	NC	-	NC	NC	NC
2. Alkyl sulphates	Na-salt	12	>90	Xn, R22, 36*/38	Xn	22	38	**41**
	salts of Na, Mg, NH4,TEA	12-18 and i-13-15	25-95	Xi, R36*/38	Xi	NC	38	**41**
3. Alkylether sulphate-salts-								
-2-3 EO	Na-salt	9-15	70-75	Xi, R36*/38	Xi	NC	38	**41**
-2-3 EO	Na-salt	9-15	25-28	Xi, R36/38	Xi	NC	38	36
- 7 EO	Na-salt	9-15	65	Xi, R36/38	Xi	NC	38	36
- 2 EO	Mg-salt	12-14	27	Xi, R36/38	Xi	NC	38	36
- 7 EO	Na/Mg-salt	12-18	27	Xi, R36	Xi	NC	NC	36
4. Alkane sulphonates								
NEW	Na-salt	13-18	≤ 70	-	**Xi**	**NC**	**38**	**41**
	Na-salt	13-18	30	Xi, R36*/38	**Xi**	**NC**	**38**	**41**
5. Olefin sulphonates NEW	Na-salt	14-16	>80	-	**Xi**	**NC**	**38**	**41**
NEW	Na-salt	14-16	40-80	-	**Xi**	**NC**	**38**	**36**
	Na-salt	14-16	40	Xi, R36/38	Xi	NC	38	NC
6. Alkylaryl sulphonate - salts	Ca-salt	10-13	95	Xi, R36/38	Xi	NC	38	**41**
	Ca-salt	12	70	Xi, R36*/38	Xi	NC	38	**41**
	Na-salt	9-14	≥ 65	Xi, R22, 36*/38	Xn	22	38	**41**
	Na-salt	9-14	50-65	Xi, R36*/38	Xi	NC	38	**41**
	TEA-salt	9-14	50	Xi, R36*/38	Xi	NC	38	**41**
7. Fatty acid methylester sulphonates	Na-salt	16-18	60	Xi, R36/38	Xi	NC	38	36
8. Sulphosuccinates								
di-alkyl-	Na-salt	iso 8-10	65	Xi, R36/38	Xi	NC	38	**41**
mono-alkyl-	Na-salt	12-14	32-40	Xi, R36*	Xi	NC	NC	**41**
9. Fatty acid sarcosides	-	12	30	Xi, R36*	Xi	NC	NC	**41**
	-	oleyl	60	Xi, R36*/38	Xi	NC	38	**41**
~~**10. Alkylisethionate salts**~~	~~**Na-salt**~~	~~**8-18**~~	~~**100**~~	**-**	**-**	**-**	**-**	**-**
10. Alkylmethyltaurides	-	16-18	63	Xi, R36*	Xi	NC	NC	41
	-	8-18	30	Xi, R36	Xi	NC	NC	**36**
11. Alkylphenol ethersulphates	Na-salt	9	50	Xi, R36*	Xi	NC	NC	**41**
NEW	NH4-salt	9	60	-	**Xi**	**NC**	**NC**	**41**

continued

Table 4. Anionics (continued)

Typical chemical ingredient	Typical specification			Recommended Symbol and R-phrases				
	Cation	Carbon Chain R-	Typical chemical conc (%)	**CURRENT**	Symbol	**PROPOSED** Oral	Skin	Eye
12. Fatty alcohol phosphoric acid esters,								
-Alkyl (4EO) phosphoric acid -di/triesters	-	12-14	100	Xi, R38	Xi	NC	38	NC
"	-	16-20	100	Xi, R38	Xi	NC	38	NC
-Alkyl (8EO) phosphoric acid -di/triesters	-	oleyl	100	Xi, R38	Xi	NC	38	NC
12.1. Alkylphosphoric acid-mono/diester	acid	iso-8	100	C, R34	C	NC	34	
-Octylphenol-7 EO mono/diester	acid	8	> 90	Xi, R36*/38	Xi	NC	38	**41**
-Alkylphenol-7 EO-mono/diester	Na-salt	8-9	100	Xi, R36/38	Xi	NC	38	36
-Phosphoric acid-mono/diester	K-Salt	12-14	75	Xi, R36*/38	Xi	NC	38	**41**
12.2. Alkyl EO phosphate esters **NEW**	H	13-18	100	-	**Xi**	**NC**	**38**	**41**
13. Fatty alkanolamide -ether sulphates	Mg-salt	8-18	30	Xi, R36*	Xi	NC	NC	**41**
	TEA-salt	8-18	40	NC	-	NC	NC	NC
14. Fluorine surfactants	-	6-12	80	Xn, R22	Xn	22	NC	NC
"	Na-salt	8-14	30	NC *	-	NC	NC	NC
15. Fatty ester sulphates	Na-salt	castor oil	45-80	Xi, R36*/38	Xi	NC	38	**41**
"	~~**Na-salt**~~	**-**	~~**<40**~~	**-**	**-**	**-**	**-**	**-**
16. Alkylnaphthalene sulphonate	Na-salt	dibutyl	77	Xn, R22, 36	Xn	22	NC	36

Amphoterics								
-Cocoalkylamidobetaine	-	8-18	30	Xi, R36*	Xi	NC	NC	36
-Cocoamphodiacetate	-	8-18	30	Xi, R36*/38	Xi	NC	NC	36
-Cocoaminobetaine	-	10-18	30	Xi, R36*/38	Xi	NC	38	41

Footnotes: **-** shading indicates that no new data were available for review.
- recommended changes are **highlighted**
*: Xi, R37 - irritant by inhalation.

Table 5: Non-ionics

Typical chemical ingredient	Typical specification				Recommended Symbol and R-phrases				
	Carbon chain R-R-	Mole - EO	Mole-PO	Typical chemical conc (%)	**CURRENT**	**PROPOSED** Symbol	Oral	Skin	Eye
1. Fatty alcohol +EO	8-18	2-5	-	100	Xi, R36*/38	Xi	NC	**NC**	**41**
	8-18	>5-15	-	100	Xn, R22, 36*/38	Xn	22	**NC**	**41**
	8-18	>15-20	-	100	Xn, R22, 36*	Xn	22	NC	**41**
	8-18	>20	-	100	NC	-	NC	NC	NC
2. Fatty alcohol +EO+PO	10-15	3-9	4-6	100	NC	-	NC	NC	NC
~~**2.1. Fatty alcohol +PO+EO**~~	~~**10-14**~~	~~**6-6.4**~~	~~**1.2-8**~~	~~**100**~~	**-**	**-**	**-**	**-**	**-**
3. Alkylphenol+EO	8-12	1-7	-	100	Xi, R36/38	Xi	NC	38	36
	8-12	>7-11	-	100	Xn, R22, 36*/38	Xn	22	**NC**	**41**
	8-12	>11-14	-	100	Xi, R36*	Xi	NC	NC	**41**
	8-12	>14	-	100	NC	-	NC	NC	NC
4. Fatty acid+EO	12-18	2-30	-	100	NC	-	NC	NC	NC
4.1. Di-ester	PEG	10-18	-	100	NC	-	NC	NC	NC
~~**4.2 Fatty acid+PO**~~	~~**14-18**~~	**-**	~~**1**~~	~~**100**~~	**-**	**-**	**-**	**-**	**-**
5. Fatty acid+EO+PO		44	2	100	NC	-	NC	NC	NC
6. Fatty acid glycerol ester+EO	12-18	2-30	-	100	NC	-	NC	NC	NC
7. Alkylamide									
- monoethanolamide	8-18	-	-	100	Xi R36*	Xi	NC	NC	**41**
- Diethanolamide	-	-	-	100	Xi, R36*/38	Xi	NC	38	**41**
7.1. Fatty acid amide+EO	8-18	5	-	100	Xi, R36*	Xi	NC	NC	**41**
8. EO-PO block polymers	-	10-50	10-50	100	NC	-	NC	NC	NC
9. Sorbitan fatty acid ester	12	20	-	100	NC	-	NC	NC	NC
10. Others									
-Fatty alcohol ethoxylated-n-butylether	12-18	5-7.3	-	100	Xi, R38	Xi	NC	38	NC
11. Fluorine surfactants									
-Ethoxylated perfluoroalkyl ethanol	12-14	**-**	-	≥ 90	Xn, R22	Xn	22	NC	NC

Footnotes: **-** shading indicates that no new data were available for review.
- recommended changes are **highlighted**

Appendix 1. Skin Irritation Questionnaire.

Please complete as much as possible. For assistance see "Guidance on completion"

Company name: | Report number and date

INFORMATION ON TEST PRODUCT

Chemical type		Anionic / Non-ionic	% active matter
C.chain distribution	No.mols EO	If a salt, what was the cation?	
Was tested material neutralised before testing y / n		Certificate of analysis y / n	
Other relevant information			

TEST VARIABLES

Physical form of material, as tested solid / liquid *(delete as appropriate)*	Was the product diluted for testing? y / n If so, give diluent and %	
pH of test sample (as tested)	Dose volume ml / g	
Animal species	Number of animals per group	
Exposure time (hours)	Observation period	
Occluded / semi-occl / non-occl *	OECD / EC method y / n	GLP y / n

**: occl = occluded*

INDIVIDUAL SKIN IRRITATION SCORES *

Animal →	1		2		3		4		5		6	
Observation at: ↓	Eryth	Oed	Eryth	Oed	Eryth	Oed	Eryth	Oed	Eryth	Oed	Eryth	Oed
1 hour												
4 hours												
24 hours												
48 hours												
72 hours												
96 hours												
7 days												
end ( )												

Group mean of scores at 24+ 48+ 72 hours	erythema :	oedema :
Mean of scores at end of study	erythema :	oedema :

** (Eryth = Erythema; Oed = Oedema).*

ADDITIONAL FINDINGS

Was corrosion reported? If so was it present after exposure of 3 minutes / 1 hour / 4 hours	
Were effects at termination considered to be permanent? If so, describe	
Other comments	

CLASSIFICATION (R-PHRASE):

Appendix 2. Eye Irritation Questionnaire.

Please complete as much as possible. For assistance see "Guidance on completion"

Company name: Report number and date:

INFORMATION ON TEST PRODUCT

Chemical type		Anionic / Non-ionic	% active matter
C.chain distribution	No.mols EO	If a salt, what was the cation?	
Was tested material neutralised before testing y / n		Certificate of analysis y / n	
Other relevant information			

TEST VARIABLES

Physical form of material, as tested solid / liquid *(delete as appropriate)*	Was the product diluted for testing? y / n If so, give diluent and %	
pH of test sample (as tested)	Dose volume ml / g	
Animal species	How many animals per group?	
Irrigation y / n and when (e.g. 10 sec / 1 hour)	Observation period	
	OECD / EC method y / n	GLP y / n

INDIVIDUAL EYE IRRITATION SCORES

Animal →	**1**				**2**				**3**			
Observation at:. ↓	Corn.	Iris	Chem	Redn	Corn.	Iris	Chem	Redn	Corn.	Iris	Chem	Redn
1 hour												
24 hours												
48 hours												
72 hours												
7 days												
14 days												
end ( )												

Animal →	**4**				**5**				**6**			
Time post exp. ↓	Corn.	Iris	Chem	Redn	Corn.	Iris	Chem	Redn	Corn.	Iris	Chem	Redn
1 hour												
24 hours												
48 hours												
72 hours												
7 days												
14 days												
end ( )												
Group mean of scores at 24+ 48+ 72 hours												
Mean of scores at end of study												

** (Corn. = corneal effects; Iris = iritis; Chem. = chemosis; Redn = redness)*

ADDITIONAL FINDINGS

Was initial pain reported? If so, at what score?	
Were effects at termination considered to be permanent? If so, describe	
Other comments	

CLASSIFICATION (R-PHRASE):

Appendix 3. Acute Oral Toxicity Questionnaire.

Please complete as much as possible. For assistance see "Guidance on completion"

Company name: | | Report number and date | |

INFORMATION ON TEST PRODUCT

Chemical type		Anionic / Non-ionic	% active matter
C.chain distribution	No.mols EO	If a salt, what was the cation?	
Was tested material neutralised before testing y / n		Certificate of analysis y / n	
Other relevant information			

TEST VARIABLES

Physical form of material, as tested solid / liquid *(delete as appropriate)*	Was the product diluted for testing? y / n If so, give diluent and %	
pH of test sample (as tested)	Dose volume ml / g	
Animal species	Number of animals per group	sex
Test concentration (e.g. 50 %, 10 % etc)	Observation period	
Dose levels:	OECD / EC method y / n	GLP y / n

CALCULATED ORAL LD 50:

ADDITIONAL FINDINGS

What were the clinical signs of treatment?	
Were effects dose-related?	
Other comments	

CLASSIFICATION (R-PHRASE):

Appendix 4. Quaternary Ammonium Compounds (Based on CESIO report, October 1990 (reference 5)

Typical chemical ingredient	Typical specification			Recommended Symbol and R- phrases	
	Carbon chain R-	Typical Chemical conc. (%)	Solvent consistence	Label-Symbol	R-phrases
1. Alkyl-trimethyl-ammonium-chloride					
1.1. Alkyl = Lauryl					
C12/14-Alkyl-trimethyl-ammonium chloride	12-14	35		C	22-34
1.2. Alkyl = Coco					
Cocoalkyl-trimethyl-ammonium-chloride	8-18	50	37 % IPA*	C	22-34
Cocoalkyl-trimethyl-ammonium-chloride	8-18	35		Xn	22-38-41
1.3. Alkyl = Soya					
Soyaalkyl-trimethyl-ammonium-chloride	16-18	50	30 % IPA	C	22-34
1.4. Alkyl = Tallow					
Tallowalkyl-trimethyl-ammonium-chloride	16-18	50	30 % IPA	C	22-34
1.5. Alkyl = Behenyl					
Behenyl-trimethyl-ammonium-chloride	20-22	80	17 % IPA	Xi	36/38
1.6. Alkyl = C16					
Cetyl-trimethyl-ammonium-chloride	16	29		Xn	22-38-41
1.7. Anion-variations					
Tetradecyl-trimethyl-ammonium-bromide	14	100	Powder	Xn	20/22-37/38-41
Hexadecyl-trimethyl-ammonium-methosulphate	16	29		Xn	22-38-41
1.8. Others					
Alkyl-trimethyl-ammonium-chloride	13-15	35		Xn	22-38-41
Alkyl-trimethyl-ammonium-methosulphate	13-15	80	1,4-Butanediol	C	22-34
2. Alkyl-dimethyl-benzyl-ammonium-chloride					
2.1. Alkyl = Coco					
Cocoalkyl-dimethylbenzyl-ammonium-chloride	8-18	50		C	22-34
2.2. Alkyl = Lauryl / Myristyl					
Alkyl-dimethylbenzyl-ammonium-chloride	12-14	7,5		Xi	38-41
Alkyl-dimethylbenzyl-ammonium-chloride	12-14	10		C	34
Alkyl-dimethylbenzyl-ammonium-chloride	12-14	35		C	22-34
2.3. Alkyl = Hydrogenated tallow					
Hydr. Tallowalkyl-dimethylbenzyl-ammonium-chloride	16-18	80	20 % IPA	Xn	22-38-41
2. 4. Others					
Alkyl-dimethylbenzyl-ammonium-chloride	13-15	50		C	22-34
3. Dialkyl-dimethyl-ammonium-chloride					
3.1. Alkyl = C8					
Dioctyl-dimethyl-ammonium-chloride	8	50	10 % Ethanol	C	22-34
3.2. Alkyl = C8/10					
3.3. Alkyl = C10					
Didecyl-dimethyl-ammonium-chloride	10	50	20 % IPA	C	22-34
3.4. Alkyl = Coco					
Dicocoalkyl-dimethyl-ammonium-chloride	8-18	75	15 % IPA	C	22-34
3.5. Alkyl = Hydrogenated tallow/Stearyl					
Bis(hydr.tallowalkyl)dimethyl-ammonium-chloride	16-18	>95	Powder	Xi	41
Bis(hydr.tallowalkyl)dimethyl-ammonium-chloride	16-18	75	15 % IPA	Xi	38-41

continued

Appendix 4. Quaternary Ammonium Compounds (continued)

Typical chemical ingredient	Typical specification			Recommended Symbol and R-phrases	
	Carbon chain R-	Typical chemical conc. (%)	Solvent consistence	Label-Symbol	R-phrases
3.6. Others					
Ditallowalkyl-dimethyl-ammonium-chloride	16-18	70	20 % IPA	C	34
3.7a. Anion – variations					
Didecyl-methyloxyethyl-ammonium-propionate	10	70	25 % Glycol	C	22-34
4. Ethoxylated Quaternay Ammonium Compounds					
4.1. Alkylamine-EO-methyl-ammonium-chloride					
Alkylamine-1 EO-methyl-ammonium-chloride	13-15	35		C	22-34
Alkylamine-15 EO-methyl-ammonium-chloride	12-18	>95		Xi	36/38
4.2. Anion-variations					
Alkylamine-2 EO-methyl-ammonium-methosulphate	13-15	90	10 %IPA	C	22-34-43
Alkylamine-5 EO-methyl-ammonium-methosulphate	13-15	100		Xn	22-38-41
Alkylamine-10 EO-methyl-ammonium-methosulphate	13-15	100		Xn	22-36-38
Alkylamine-15 EO-methyl-ammonium-methosulphate	13-15	100		Xi	36-43
Alkylamine-20 EO-methyl-ammonium-methosulphate	13-15	100		Xi	36
Alkyl-5 EO-ammonium-lactate	16-18	30		Xi	38-41
4.3. Tallowamine-10 EO-benzyl-ammonium-phosphate	-	-	-	-	-
4.4. Cocoamine-EO-benzyl-ammonium chloride	-	-	-	-	-
Cocodietyleneglycol-benzyl-ammonium-chloride	8-18	50	C		22-34
5. Bis-quaternary ammonium salts	-	-	-	-	-
6. Imidazoline – derivates					
Imidazoline derivate $MeOSO_3$	16-18	90	IPA	Xi	38-41
7. Others					
7.1. Lauryl-pyridinium-chloride	12	90	Powder	C	22-34
7.2. N-2(hydroxy-hexadecyl)-N,N-dimethyl-N-(2-hydroxyethyl)-ammonium-chloride	16	28		C	34
7.3. Coco-guanidinium-chloride	8-18	50	20 % IPA	C	22-34
7.4. N-alkyl-N(beta-stearoylethyl-N,N-dimethyl-ammonium-methosulphate	13-15	80	15 %IPA	C	34-43

Footnotes. * IPA: isopropyl alcohol. NLN: No labelling necessary

Appendix 5. Fatty Amines and Derivatives (Based on CESIO report, October 1990 (reference 5)

Typical chemical ingredient	Typical specification			Recommended Symbol and R-phrases	
	Carbon chain R -	Typical chemical conc. (%)	Solvent consistence	Label-Symbol	R-phrases
1. Primary alkylamines					
1-Octanamine	8			C	22-35
1-Dodecanamine	12			C	22-35
1-Octadecanamine	18			Xi	38-41
Amines, cocoalkyl	8-18			C	22-35
Amines, (hydrogenated tallowalkyl)	16-18			Xi	38-41
Amines, tallowalkyl	16-18			C	22-35
Amines, (C13-C15 alkyl)	13-15			C	22-35
2. Secondary amines					
Amines, dicocoalkyl	8-18			Xi	38-41
Amines, (C13-C15) alkylmethyl	13-15			C	22-35
Amines, bis (cocoalkylpentaoxyethyl)	8-18			C	22-35
3. Tertiary amines					
3.1. Alkyldimethylamines					
1-Decanamine, N,N-dimethyl	10			C	22-34
1-Dodecanamine, N, N-dimethyl	12			C	22-35
1-Tetradecamine, N, N-dimethyl	14			C	22-34
1-Hexadecanamine, N, N-dimethyl	16			C	22-34
Amines, cocoalkyldimethyl	8-18			C	22-34
Amines, (middle cut coco alkyl) dimethyl	12-14			C	22-34
Amines, (hydrogenated tallowalkyl) dimethyl	16-18			C	22-34
Amines, (C13-C15 alkyl) dimethyl	13-15			C	22-34
3.2. Dialkylmethylamines					
Amines, didecylmethyl	10			Xi	38-41
Amines, bis (hydrogenated tallowalkyl) methyl	16-18			Xi	38
3.3. Trialkylamines					
Amines, tri (C8-C10 alkyl)	8-10			NLN	
4. Alkylamine Salts					
Amines, tallowalkyl, acetates	16-18			C	22-34
Amines, oleylakyl, acetates	14-18			C	22-34
Amines, (C13-C15 alkyl), acetates	13-15			C	22-34
Amines, cocoalkyl, acetates	8-18			C	22-34
Amines, (C13-C15 alkyl), dimethyl, acetates	13-15			C	22-35
Amines, hydrogenated tallowalkyl), acetates	16-18			Xi	38-41
5. Alkylamine ethoxylates					
Amines, (C13-C15 alkyl) ethoxylated 2 EO	13-15			C	22-35
5 EO				Xn	22-38-41
10 EO				Xn	22-38-41
15 EO				Xn	22-38-41
Amines, cocoalkyl, ethoxylated 2 EO	8-18			C	22-34
5 EO				Xn	22-38-41
10 EO				Xn	22-36
20 EO				Xi	36

continued

Appendix 5. Fatty Amines and Derivatives (Continued)

Typical chemical ingredient		Typical specification			Recommended Symbol and R-phrases	
		Carbon chain R -	Typical chemical conc. (%)	Solvent consistence	Label-Symbol	R-phrases
Amines, tallowalkyl, ethoxylated	2 EO	16-18			C	22-34
	5 EO				Xn	22-38-41
	40 EO				Xi	36
Amines, (hydrogenated tallowalkyl), ethoxylated	2 EO	16-18			Xi	38-41
	50 EO				NLN	
Amines, oleylalkyl, ethoxylated	2 EO	14-18			C	22-34
6. Alkyldiamines						
Amines, N-tallow alkyltrimethylenedi-		16-18			C	22-34
Amines, N-coco alkyltrimethylenedi-		8-18			C	22-35
Amines, N-(C13-C15 alkyl) trimethylenedi-		13-15			C	22-35
Amines, N-(hydrogenated tallowalkyl) trimethylendi-		16-18			Xi	38-41
Amines, N-cyclohexyl-trimethylenedi-		6			C	22-35
7. Alkyldiamine ethoxylates						
Amines, N-tallow alkyltrimethylenedi-, ethoxylated	10 EO	16-18			Xn	22-38-41
	15 EO				Xn	22-38-41
Amines, N(C13-C15 alkyl) trimethylenedi-, ethoxylated	3 EO	13-15			C	22-35
	10 EO				Xn	22
Amines, N-(hydrogenated tallowalkyl) trimethylenedi-, ethoxylated	3 EO	16-18			C	22-34
8. Alkyldiamine salts						
Amines,N-cocoalkyltrimthylenedi-, acetates		8-18			Xi	38-41
9. Alkylamineoxides						
Amines, cocoalkyldimethyloxide		8-18	30	Water	Xi	38-41
Amines, middles cut cocoalkyl) dimethyloxide		12-14	30	Water	Xi	38-41
Amines, cocoalkyl bis (2-hydroxyethyl) oxide		8-18	30	Water	Xi	38-41
Amines, (C13-C15 alkyl) dimethyloxide		13-15	30	Water	Xi	38-41

Footnotes: NLN: No labelling necessary.