former European Chemicals Bureau

European Union Risk Assessment Report
dimethyldioctadecylammonium chloride

CAS: 107-64-2
EC: 203-508-2

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Institute for Health and Consumer Protection

former
European Chemicals Bureau

Existing Substances

1st Priority List

Volume: 14

European Union Risk Assessment Report

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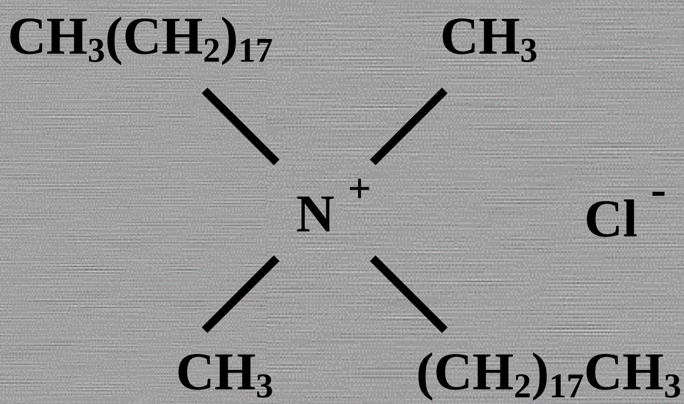
dimethyldioctadecylammonium chloride (DODMAC)



EUROPEAN COMMISSION

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with addendum 2009

The mission of the IHCP is to provide scientific support to the development and implementation of EU polices related to health and consumer protection. The IHCP carries out research to improve the understanding of potential health risks posed by chemical, physical and biological agents from various sources to which consumers are exposed.

The former Toxicology and Chemical Substances Unit (TCS), commonly known as the European Chemicals Bureau (ECB), provided scientific and technical input and know-how to the conception, development, implementation and monitoring of EU policies on dangerous chemicals including the co-ordination of EU Risk Assessments. The aim of the legislative activity of the ECB was to ensure a high level of protection for workers, consumers and the environment against dangerous chemicals and to ensure the efficient functioning of the internal market on chemicals under the current Community legislation. It played a major role in the implementation of REACH through development of technical guidance for industry and new chemicals agency and tools for chemical dossier registration (IUCLID5). The TCS Unit ensured the development of methodologies and software tools to support a systematic and harmonised assessment of chemicals addressed in a number of European directives and regulation on chemicals. The research and support activities of the TCS were executed in close co-operation with the relevant authorities of the EU Member States, Commission services (such as DG Environment and DG Enterprise), the chemical industry, the OECD and other international organisations.

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European Union Risk Assessment Report

DIMETHYLDIOCTADECYLAMMONIUM CHLORIDE

(DODMAC)

Addendum – 2009

(followed by the comprehensive risk assessment report)

CAS No: 107-64-2

EINECS No: 203-508-2

RISK ASSESSMENT

EXPLANATORY NOTE

This report is an addendum to the European Risk Assessment Report (RAR) on dimethyldioctadecylammonium chloride (DODMAC), that has been prepared by Germany in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances and published in 2002 on the European Chemicals Bureau website (European Risk Assessment Report Vol. 14, EUR 20397 EN) [1].

For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references the reader is referred to the comprehensive Final Risk Assessment Report (Final RAR).

[1] Former European Chemicals Bureau – Existing Chemicals –http://ecb.jrc.ec.europa.eu/

Data requirement according to Regulation (EC) 1217/2002

DHTDMAC (Cas-No. 61789-80-8)

Evaluation of provided information

According to Art. 12 (2) of Regulation EEC 793/93 industry had to provide information on the yearly consumption volumes of the substance DHTDMAC (quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chlorides) (Cas-No. 61789-80-8) for the year 2000 to 2002. The reason for this requirement was the concern for a significant increase in consumption volumes of the substance which would pose a potential risk for the environment.

Within the frame of an EU risk assessment for the substance DODMAC, which is contained in the technical mixture DHTDMAC with a percentage of 42%, consumption figures for the years 1998 and 1999 have already been available.

Therefore, an evaluation of the consumption figures for DHTDMAC for the years 1998 to 2002 can be performed.

The following data have been provided by industry:

Year	Organo field bentonites [t/a]	Fabric softener [t/a]	Other uses [t/a]	Σ softener and other uses [t/a]	Total consumption [t/a]
1998	4,986	408	276	684	5,670
1999	3,656	333	642	975	4,631
2000	3,116	526	669	1,195	4,311
2001	3,594	101	684	785	4,379
2002	4,278	73	603	676	4,954

No clear trend in the consumption of DHTDMAC over these 5 years can be observed. A potential risk for the environment (surface waters and sediment) may occur from the direct use of the substance as fabric softener or in other uses (hair conditioner, car washing…). The amount of DHTDMAC used in these applications (wide dispersive use) increased from 1998 to 2000 from 684 tonnes/annum to 1,195 tonnes/annum but decreased afterwards to 785 and 676 tonnes/annum in 2001 and 2002. It cannot be excluded that the consumption of DODMAC for these applications will increase again in the following years.

The highest consumption volume of DHTDMAC in direct applications in 2000 was by a factor of 1.75 higher than the volume used in the risk assessment of DODMAC for the year 1998. Considering the fact, that the PEC/PNEC ratio for DHTDMAC is by a factor of 2.4 higher than the ratio for DODMAC, as DODMAC is contained in the technical product DHTDMAC with a fraction of 42% gives the following PEC/PNEC ratios for DHTDMAC for the year 2000 (based on the PEC and PNEC derivation in the EU RAR DODMAC):

	PEC/PNEC ratio
Surface water	0.37
Sediment	0.53

Conclusion

The consumption of DHTDMAC for the years 1998 to 2002 will not result in a risk for the aquatic environment (surface water and sediment). However, an increase by a factor of about 2 compared to the figures for 2000 may result in a risk for the sediment compartment

European Union Risk Assessment Report

DIMETHYLDIOCTADECYLAMMONIUM CHLORIDE

(DODMAC)

CAS No: 107-64-2

EINECS No: 203-508-2

RISK ASSESSMENT

A great deal of additional information on the European Union
is available on the Internet.
It can be accessed through
the Europa Server
(http://europa.eu).

Cataloguing data can be found at the end of this publication

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DIMETHYLDIOCTADECYLAMMONIUM CHLORIDE

(DODMAC)

CAS No: 107-64-2

EINECS No: 203-508-2

RISK ASSESSMENT

Final Report, 2002

Germany

The Rapporteur for the risk assessment of dimethyldioctadecylammonium chloride is the Federal Institute for Occupational Safety and Health.

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Date of Last Literature Search :	**1995**
Review of report by MS Technical Experts finalised:	**December 1998**
Final report:	**2002**

Foreword

We are pleased to present this Risk Assessment Report which is the result of in-depth work carried out by experts in one Member State, working in co-operation with their counterparts in the other Member States, the Commission Services, Industry and public interest groups.

The Risk Assessment was carried out in accordance with Council Regulation (EEC) 793/93[2] on the evaluation and control of the risks of “existing” substances. “Existing” substances are chemical substances in use within the European Community before September 1981 and listed in the European Inventory of Existing Commercial Chemical Substances. Regulation 793/93 provides a systematic framework for the evaluation of the risks to human health and the environment of these substances if they are produced or imported into the Community in volumes above 10 tonnes per year.

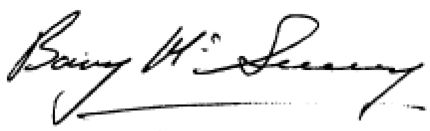
There are four overall stages in the Regulation for reducing the risks: data collection, priority setting, risk assessment and risk reduction. Data provided by Industry are used by Member States and the Commission services to determine the priority of the substances which need to be assessed. For each substance on a priority list, a Member State volunteers to act as “Rapporteur”, undertaking the in-depth Risk Assessment and recommending a strategy to limit the risks of exposure to the substance, if necessary.

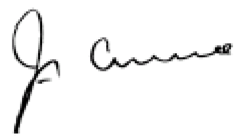
The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94[3], which is supported by a technical guidance document[4]. Normally, the “Rapporteur” and individual companies producing, importing and/or using the chemicals work closely together to develop a draft Risk Assessment Report, which is then presented at a Meeting of Member State technical experts for endorsement. The Risk Assessment Report is then peer-reviewed by the Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) which gives its opinion to the European Commission on the quality of the risk assessment.

If a Risk Assessment Report concludes that measures to reduce the risks of exposure to the substances are needed, beyond any measures which may already be in place, the next step in the process is for the “Rapporteur” to develop a proposal for a strategy to limit those risks.

The Risk Assessment Report is also presented to the Organisation for Economic Co-operation and Development as a contribution to the Chapter 19, Agenda 21 goals for evaluating chemicals, agreed at the United Nations Conference on Environment and Development, held in Rio de Janeiro in 1992.

This Risk Assessment improves our knowledge about the risks to human health and the environment from exposure to chemicals. We hope you will agree that the results of this in-depth study and intensive co-operation will make a worthwhile contribution to the Community objective of reducing the overall risks from exposure to chemicals.





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Environment, Nuclear Safety and Civil Protection

[2] O.J. No L 084, 05/04/199 p.0001 – 0075

[3] O.J. No L 161, 29/06/1994 p. 0003 – 0011

[4] Technical Guidance Document, Part I – V, ISBN 92-827-801 [1234]

0 OVERALL CONCLUSIONS/RESULTS OF THE RISK ASSESSMENT

CAS Number: 107-64-2
EINECS Number: 203-508-2
IUPAC Name: Dimethyldioctadecylammonium chloride

Overall results of the risk assessment

( )	Conclusion (i)	There is need for further information and/or testing.
(X)	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.
( )	Conclusion (iii)	There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Summary of conclusions

Environment

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.

Human Health (toxicity)

Workers

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.

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.

Humans exposed via the environment

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

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.

Human Health (risks from physico-chemical properties)

DODMAC has no explosive or oxidising properties due to structural reasons and is not flammable. Therefore with regard to physico-chemical properties and with regard to the occupational exposure and consumer exposure, DODMAC is not expected to cause specific concern relevant to human health.

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.

CONTENTS

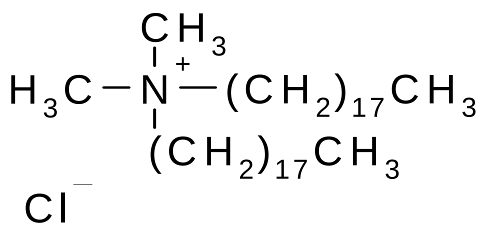
EUSES Calculations can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.jrc.it

TABLES

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

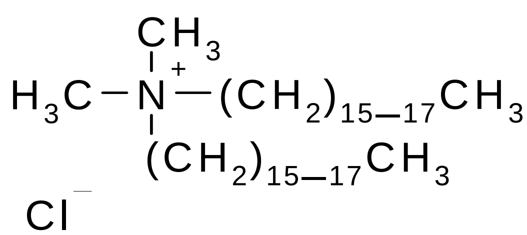
CAS Number: 107-64-2
EINECS Number: 203-508-2
IUPAC Name: Dimethyldioctadecylammonium chloride
Synonyms: DODMAC
Distearyldimethylammonium chloride (DSDMAC)
CA-Index name: 1-Octadecanaminium, N,N-dimethyl-N-octadecyl-, chloride
Empirical formula: $C_{38}H_{80}NCl$
Structural formula:



Molecular weight: 586.52 g/mol

Dimethyldioctadecylammonium chloride (DODMAC) as an isolated substance is not produced or used in a commercial range. But it is one of the active component of the technical product ditallowdimethylammonium chloride (DHTDMAC) which is of commercial interest:

CAS Number: 61789-80-8
EINECS Number: 263-090-2
IUPAC Name: N,N-Dimethyl-N,N-di-n-alkyl(C16-18)-ammoniumchloride
Synonyms: Di(hydrogenated tallow alkyl) dimethylammoniumchlorides (DHTDMAC)
Empirical formula: approx. $C_{36,4}H_{76,8}NCl$
(related to approx. 65 % $C_{38}H_{80}NCl$, 30 % $C_{34}H_{72}NCl$, 5 % $C_{30}H_{64}NCl$)
Structural formula:



Molecular weight: approx. 567 - 573 g/mol (ECETOC, 1993)

Dimethyldialkyl(C_{16-18})ammoniumchloride (DHTDMAC) is a mixture of quaternary ammonium compounds, with DODMAC as the main component, which is produced from hardened, i.e. hydrogenated natural fats. The alkyl chain length distribution related to the total molecule in standard European products with bovine tallow as the most important raw fat (e.g. Praepagen WK, Genamin DSAC) is:

C_{12}	max. 2 %	
C_{14}	1 - 5 %	
C_{16}	25 - 35 %	
C_{18}	about 65 %	
C_{20}	max. 2 %	(Hoechst AG, 1980)

According to these distributions, DHTDMAC consists of about 65 % of C_{18}-chains. Since each molecule contains two alkyl chains, the proportion of DODMAC related to the total content of dimethyldialkylammonium compounds can be estimated as 42 % DODMAC contained in DHTDMAC.

1.2 PURITY/IMPURITIES, ADDITIVES

The active content of technical pure DHTDMAC amounts to a w/w ≥ 95 %, of which free amines and hydrochlorides amount to a w/w ≤ 3 % (the active content is defined as the sum of quaternary ammonium compounds inclusively the free amines and hydrochlorides).

Impurities are:

Monoalkyl(C_{16-18})trimethylammoniumchloride	< 4 %
Dialkyl(C_{16-18})methylamine, Trialkyl(C_{16-18})amine and their hydrochlorides	< 2 %
Isopropanol	< 2 %
Water	< 4 %
Sodium chloride	< 1 %

Technical pure DHTDMAC is not used as such but as paste-like preparations with an active content of a w/w approx. 77 %, approx. 13 % isopropanol, < 2 % free amines and hydrochlorides and approx. 10 % water (Hoechst AG, 1980).

Concerning DODMAC the exact composition regarding the impurities is not known. Therefore an active content of 100 % for DODMAC is assumed in the following risk assessment.

1.3 PHYSICO-CHEMICAL PROPERTIES

DODMAC and DHTDMAC belong to the group of the quaternary ammonium compounds (“quats”) and are cationic tensides.

Table 1.1 Physico-chemical properties

	DODMAC (active content 100 %)	**DHTDMAC (active content ≥ 95 %)**
Physical state	solid	solid
Melting point	72-122 °C (ECETOC, 1993) [149.4 - 151 °C (Swain, 1955) 1)]	60 - 65 °C (Hoechst AG, 1993)
Boiling point	decomposition at 135 °C (ECETOC, 1993)	decomposition at 120 °C (Hoechst AG, 1993)
Density	0.84 g/cm^3 at 88 °C (ECETOC, 1993)	0.86 g/cm^3 at 50 °C (ECETOC, 1993)
Vapour pressure	negligible because of the salt character 2)	negligible because of the salt character
Surface tension	11 mN/m at 20 °C (saturated solution; method: film balance) (Bonosi & Gabrielli, 1991)	no data available
Water solubility	not soluble, dispersible 2.7 mg/l (Kuneida & Shinoda, 1982) [< 1 pg/l (Laughlin, 1990) 3)]	not soluble, dispersible 3)
Partition coefficient log Kow	3.80 (measured) (Sánchez-Leal et al., 1994)	no data available 4)
Flash point	not applicable because substance is solid	not applicable because substance is solid
Flammability	not highly flammable; no data available, but the behaviour is assumed to be comparable to DHTDMAC	not highly flammable; A.12 not conducted because of structural reasons (Hoechst AG, 1996a)
Explosive properties	not explosive because of structural reasons	not explosive because of structural reasons
Oxidising properties	no oxidizing properties because of structural reasons	no oxidizing properties because of structural reasons

Note: The ECETOC values are considered to be reliable.

1) Melting point / boiling point

Swain (1955, cited in Beilstein) determined a melting point for DODMAC of 149.4 - 151 °C. Taking into account this value, the decomposition starts at 150 °C. The melting point was determined at a not pure substance. No information about the testing method was given. Therefore this value was not accepted.

2) Vapour pressure

According to the EPI program an estimated vapour pressure of 10^{-15} Pa was given from EPA, which confirms that the vapour pressure for DODMAC is negligible (EPA, 1996).

3) Water solubility

The estimate by Kuneida and Shinoda was based on the measurement of surface tension as a function of composition. This is a classical method for measuring critical micelle concentrations, not solubilities. The authors point out that the establishment of equilibrium was very slow. In the literature there are no data on water solubility which have been proven by measurements. The system DODMAC/water was examined thoroughly by Laughlin et al. (1990), both mechanically and kinetically. Once the solubility limit has been exceeded, at first a lamellar liquid-crystal phase forms. It transforms into a very stable dispersion of liquid crystal in water if the water content is increased further (w/w 96 %). According to Laughlin it is highly probable that the estimate of the solubility by Kuneida and Shinoda is far too high, perhaps by as much as ten orders of magnitude (10^{10}). Conventional means of determining solubilities are invalid for determining the solubility of this class of compounds (surface active substance at low concentration).

In sewage or surface waters, DODMAC is not really dissolved but always adsorbed onto particles or included in vesicles together with other organics (cf. 3.1.1.3). The water solubility is not a limiting factor for emissions into the wastewater or for environmental pollution. The only endpoint for the environmental distribution models is the Henry's law constant: for this parameter a fictitious low value is used as the substance is regarded to be not volatile.

4) log Kow (Sánchez-Leal et al., 1994)

Because DODMAC is a surface-active substance, the log Kow value can not be used to derive the environmental distribution constants. Instead of this, experimentally determined figures are used (cf. Section 3.1.1.3).

1.4 CLASSIFICATION

Classification of pure DODMAC according to Annex I of Directive 67/548/EC; 28th ATP:

Xi	*Irritant*	R 41	*Risk of serious damage to eyes*
N	*Dangerous for the environment*	R 50/53	*Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment*

Technical grade DODMAC (77% dimethyldioctadecylammonium chloride, 11.3% isopropanol and 11.7% water) causes corrosion after a 4-hour contact with the skin of rabbits: A test with 6 rabbits (semi-occlusive application of 0.5 ml for 4 hours) resulted in moderate irritation, the effects increased after the day of application till exhibition of severe necrosis after a 14-day observation time. According to these data and the criteria of Directive 93/21/EEC, technical grade “DODMAC” (containing approximately 12% isopropanol) is to be classified “C, corrosive” and labelled “R 34, causes burns”.

2 GENERAL INFORMATION ON EXPOSURE

Dimethyldioctadecylammonium chloride (DODMAC) as an isolated substance is not produced or used in a commercial range. DODMAC occurs as a major component of the technical product dihydrogenated tallow dimethyl ammonium chloride (DHTDMAC). For production methods cf. Section 3.1.1.1. The alkyl chains of this compound consist of 60-70% C18-chains, so the proportion of DODMAC is about 42% related to the total content of dialkyldimethylammonium compounds. The following exposure assessment is performed for DODMAC in particular. If appropriate, data for DHTDMAC are considered. All figures for DHTDMAC (if not other more stated) are related to the active compound and do not include the solvent content of the technical product.

Six European DHTDMAC producers submitted an IUCLID dataset:

- Akzo Nobel (SWE and UK),
- Atochem-Ceca (FRA),
- Fina (BELG),
- Hoechst AG, (GER),
- Kao Corp. (SPA).

The actual production volume was estimated at 5,004 t in 1996 and 5,651 t in 1997 (CEFIC APAG, 1998).

The use pattern of DHTDMAC in the EU is:

- Fabric softeners. The consumption amount in the EU decreased from about 65,000 t/a in 1990 to 24,000 t/a in 1993 (BUA, 1995). The consumption dropped to 591 t in 1996, 677 t in 1997 (CEFIC APAG, 1998) and 408 t in 1998 (CEFIC APAG, 1999). Data about the spatial distribution of the current use are not available.

- Synthesis of organic clays, which are used as drilling muds in oil industry and rheological additives in paints and lacquers (Hoechst, 1995; ECETOC, 1993). In Europe, 4,113 t of the DHTDMAC production were used for organofield bentonites in 1996, 4,605 t in 1997 (CEFIC APAG, 1998) and 4,986 t in 1998 (CEFIC APAG, 1999). In 1997, 4,137 t DHTDMAC were used in solvent-based paints (CEFIC APAG & CEPE, 1998). The total DHTDMAC amount processed by 5 organofield bentonite producers is 5,221 t (year unclear, cf. Section 3.1.2.2.2).

- Other uses. In 1997, 369 t (1998: 276 t) DHTDMAC were used especially for car washing agents and hair conditioners (CEFIC APAG, 1998, 1999).

Further uses are mentioned in the literature:

- Conditioning agent in personal care products: shampoos, hair conditioners, emulsifier in lotions (Hoechst, 1995; ECETOC, 1993).

- Car washing agents, sugar refining (ECETOC, 1993).

- Antistatic agents, corrosion inhibitors, foam depressants, flotation chemicals, asphalt and petroleum additives (Topping & Waters, 1982).

For European countries, the consumption figures for DHTDMAC are presented in **Table 2.1**.

Table 2.1 Consumption figures for DHTDMAC

Country	Year	Volume [t/a]	Uses	Reference
Denmark	1995	17	rinsing aids, polishing and cleaning agents	Danish Product Register; 1995
France	1989/90	9,400	softener	ECETOC, 1993
Germany	1980	18,000	softener	Hellmann, 1982
	1989/90	12,000	softener	ECETOC, 1993
	1993	110	softener, cosmetics	Hoechst, 1995
	1993	990	activated bentonites	Hoechst, 1995
	1995	605	softener, car washing, others	UBA, 1995
Italy	1989/90	4,300	softener	ECETOC, 1993
Netherlands	1989/90	2,000	softener	ECETOC, 1993
	1991	2,540	softener	Versteeg et al., 1992
Sweden	1992	385	softener, rinsing agents, antistatic agents	Swedish Product Register, 1995
UK	1989/90	8,600	softener	ECETOC, 1993

In Germany, 1,520 t DHTDMAC were produced in 1994. The use pattern in Germany was:

- Fabric softeners. There are inconsistent information about the volume: While 60 t/a (1993) are declared by the producer (Hoechst, 1995), 507 t/a (state 1/1995; later data are not available) are notified in the tenside database of the German Federal Environmental Agency (UBA). The difference may be due to imports.
- Car washing agents: 84 t/a are notified in the UBA tenside database.
- Cosmetics: 50 t/a (1993) resp. 26.4 t/a (1995) (Hoechst, 1995, 1996).
- 990 t/a are processed to activated bentonites, from which 330 t/a were used in laquers (especially for automobile industry) for the home market, and 660 t/a for drilling muds in oil industry (the last is exported) (Hoechst, 1995).
- Others: 14 t/a (UBA-tenside database).

The industry association AISE (Association International de la Savonnerie, de la Détergence et des Produits d’Entretien) stated that its member companies have no intention to reintroduce DHTDMAC in household liquid fabric softeners. In this context, AISE will check regularly the consumption of DHTDMAC in softeners (AISE, 1998).

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 General discussion

3.1.1.1 Release into the environment

DHTDMAC is produced from tallow acids by the following synthesis pathway:

tallow → tallowfatty acid → tallowfatty acid nitrile → dihydrogenated tallow amine → dihydrogenated tallow methyl amine → dihydrogenated tallow dimethyl ammonium chloride (DHTDMAC, containing about 42% DODMAC).

There are two different procedures for the last reaction step (BUA, 1995):

1. Dihydrogenated tallow amine is converted with an excess of chloromethane in the presence of NaOH or Na_2CO_3 at 80°C and 500 kPa in isopropanol to DHTDMAC, or

2. Dihydrogenated tallow amine is catalytically converted with formaldehyde and hydrogen to dihydrogenated tallow methyl amine, which subsequently reacts with chloromethane in isopropanol.

During cooling down the reaction product solidifies to a paste. Either it is sold in this form (the composition is given in Chapter 1), or it is dried before to a powder containing maximum 4% water and 3% isopropanol (BUA, 1995).

There is different information about releases into the wastewater during production. While some producers state that under regular conditions no emission occurs, another company submitted analytical data. In the literature, high DHTDMAC concentrations in the wastewater of a producer are reported (cf. Section 3.1.2).

During the use of fabric softeners, DHTDMAC is adsorbed nearly quantitatively onto the fibre, but will be removed completely during the next wash. As the substance is chemically stable under washing conditions, the total volume used for softeners will be emitted into the household sewage (Berenbold, 1990). The same release path has to be expected for additives in cosmetics and car washing products.

To activate bentonites, the natural cations are replaced by DHTDMAC to improve the swelling properties. The activated bentonites are used for the formulation of laquers (which are especially applied in the automobile industry), as drilling muds in oil production, in plastics and greases. The application purpose in paints and laquers is to stabilize the colloidal system by preventing pigment settling, reducing separation of liquid components, enhancing application properties and controlling absorption into porous substrates. Due to the thixotropic properties, the paint is enabled to form readily a thin film, which must regain viscosity sufficiently rapid to minimize sagging (Jones, 1983). With analytical measurements in the sewage no DODMAC could be detected. Therefore the release factor must be below 1.1% (cf. Section 3.1.2.2.3).

3.1.1.2 Degradation

As there are only few tests on the biological degradation of pure DODMAC and degradation of the technical DHTDMAC seems to be similar also test results with the technical product are referred to in the following. Not every published result for DODMAC/DHTDMAC is cited but they are in a similar range, for a detailed documentation see ECETOC (1993). When the test substance was named DSDMAC in a reference it was not always obvious whether DODMAC or DHTDMAC was meant as this is used as synonym for both.

Degradation in Wastewater treatment plant (WWTP) and surface water

In two low biomass tests with non-adapted inocula biodegradation of DSDMAC was insignificant (Schöberl et al., 1988). No CO_2-production could be observed after 28 days in a Sturm test and the biological oxygen demand was 5% after 30 days in a closed bottle test. The reference gives no information on the test substance concentrations.

Degradation of DODMAC by activated sludge of a domestic wastewater treatment plant was investigated in a closed bottle test (OECD 301D, Van Ginkel & Kolvenbach, 1991). At a substance concentration of 10 mg/l, degradation was < 20% after 180 days and > 65% after 280 days (related to theoretical BOD). The inoculum was preincubated with hexadecyltrimethylammoniumbromide.

A modified closed bottle test was used to compare the biodegradability of DODMAC and DHTDMAC by a mixture of preadapted soil bacteria (Clancy & Tanner, 1991). The degradation of DODMAC was approx. 36% and that of DHTDMAC was approx. 19% of the theoretical BOD after 20 days (1 mg/l test substance, 15 mg/l O_2-content). When the inoculum was not adapted degradation was only 8% at 1 mg/l DHTDMAC and 35% at 0.4 mg/l.

In a Zahn-Wellens-test (OECD 302B) with industrial activated sewage sludge, DHTDMAC was eliminated to more than 70% after 3 hours. Elimination reached 92 % after 15 days, measured as DOC reduction. A rate of biological degradation could not be determined (Hoechst, 1993a).

An OECD-confirmatory test was conducted with DHTDMAC and activated sludge from a domestic wastewater treatment plant (Hoechst, 1989d). The system was dosed with increasing concentrations of 0.5 -5 mg/l. Based on the concentration of disulfineblue active substance in the effluent of the test system the elimination was higher than 95% after 10 days.

The results of a continuous activated sludge test and a SCAS test are reported in ECETOC (1993). In the SCAS test 80 to 98% of 0.5 mg/l DSDMAC and DHTDMAC were adsorbed to the sludge after 7 days (Hopping, 1975). Production of $^{14}CO_2$ could not be observed. In the CAS test 71.2% of 0.01 mg/l DSDMAC were adsorbed after 5 days (Shimp, 1992). Production of CO_2 was not monitored.

Results for DODMAC and DHTDMAC degradation in batch activated sludge tests measuring $^{14}CO_2$ production are cited in ECETOC 1993 (Brown, 1975). 0.5 mg/l DODMAC alone and addition of two different concentrations of LAS were tested over 240 days (120 days at low LAS conc.) with activated sludge as inoculum. DODMAC alone was degraded to 31.7%, preadaptation resulted in 60.2% degradation. Addition of 5 mg/l LAS showed the best degradation of 67.7% (240 days) and with 0.29 mg/l LAS it was only 10.8% (after 120 days, non adapted inoculum). Degradation of DHTDMAC was better under the respective comparable conditions in every case (up to 89.8%, non-adapted, without LAS). Adaptation had no influence and increasing LAS concentrations had a slightly decreasing tendency.

Biological degradation of DODMAC in a standard CO_2-screening test with adapted activated sludge and laboratory test medium was compared with a river water die-away test (flow-through shake flask system) with natural river water and added sediment (Larson, 1983). DODMAC was radiolabeled only in the natural water tests. Unlabeled DODMAC used in the other test system was a commercial mixture with an average alkyl chain length of 17.7. The screening test inoculum had been acclimated before in a SCAS system for a few days. Natural test medium was collected 0.5-1 mile below the discharge of a municipal wastewater treatment plant (Rapid Creek, Ohio, ca. 50 mg/l suspended solids) so that adaptation has to be expected also. Degradation in laboratory water was 3.8% after 32 days at a DODMAC concentration of 20 mg/l. In river water alone 48.4% of 0.5 mg/l DODMAC were degraded after 80 days ($^{14}CO_2$ measurement). Addition of 5 g/l river sediment increased the degradation to 66% after 80 days.

With the same test methods as cited above similar results were obtained for different concentrations of DODMAC (Larson & Vashon, 1983). In laboratory water less than 5% of 10 and 20 mg/l DODMAC were degraded after 28 days by acclimated activated sludge. In river water alone (50 mg/l suspended solids, < 25 mg/l sediment) 8% of 0.05 mg/l DODMAC were degraded to $^{14}CO_2$ and 19% of 0.5 mg/l in 28 days. After 63 days the degradation results are not much higher (11% and 22% respectively), and the degradation curve ends in a plateau, suggesting that degradation will not continue. When 5 g/l adapted sediment were added to the river water 43% of 0.05 mg/l were degraded after 28 days and 65% after 63 days. The reason for insignificant degradation in the tests with laboratory water could possibly be that too high concentrations of DODMAC were toxic or the adaptation phase was too short.

In another river water die-away test primary degradation of DHTDMAC was assessed (Schneider & Levson, 1987). With an initial concentration of 8.25 mg/l 70% degradation were observed after 40 and 70 days. With a substance concentration of 0.5 mg/l primary degradation was almost the same with 75% after 40 and 55 days. Degradation started after 15 resp. 20 days.

It is shown in several tests that DODMAC/DHTDMAC are not readily biodegradable and there is no standard guideline test from which inherent biodegradability could be concluded. Adaptation seems to be necessary for significant degradation but even then mineralisation is very slow. In river water tests with adapted inocula degradation is occurring with a half-life in the range of several weeks. In two cases degradation discontinued after 63 days reaching approx. 10% at a lower and 20% at a higher DODMAC concentration. In another study a degradation half-life of approx. 80 days could be derived. Based on these results a degradation constant **$kbio_{water}$ = 0.0047 d^{-1}** can be extrapolated for surface water, which would correspond to inherently biodegradable substances (DT_{50} = 150 days). With this value it is taken into account that the lower DODMAC concentrations in surface waters are degraded slower than in the cited tests probably. DT_{50}-values of <80 days from river water tests with added adapted sediment reveal situations where the concentration of biodegrading microorganisms is increased over the normal level. Therefore these results can not be used for the derivation of the degradation rate constant in surface waters.

Most of the data referring to the elimination in wastewater treatment plants do not distinguish between biodegradation and adsorption. Therefore no degradation constant can be derived but an elimination of 95% is used in the following calculations based on the monitoring data. It can be estimated that about 55% of the elimination are attributable to adsorption (cf. Section 3.1.2.1).

Degradation in soil

Degradation of ^{14}C-DSDMAC in sandy loam and loam mixed with digested sewage sludge was measured with a batch incubated flask method (Fieler, 1975a, cited in ECETOC 1993). The $^{14}CO_2$-production was approximately 48% after 55 weeks in both soils, when 50 mg DSDMAC per kg dry soil were applied. Addition of 30 mg/l LAS reduced the result to 38%. Degradation of 0.5 mg DSDMAC/kg dry soil was measured in a loam amended with or without digested sewage sludge and two other soils. The $^{14}CO_2$-production after 62 weeks was as follows: ca. 27% in sandy loam and loam with sludge; ca. 18% in loam without sludge and silt loam. At concentrations of 5 and 50 mg/kg DSDMAC degradation increased in all soils with highest results of 50 and 63% in sludge amended soils.

Degradation of DSDMAC in soils over a long period of 116 days was reported also from other tests (Weston, 1987, cited in ECETOC 1993). 0.1 mg DSDMAC/kg dry soil were degraded to 18-27% based on $^{14}CO_2$-production and at 1.0 mg/kg degradation was 34-38%.

A comparable degradation test with DHTDMAC lasted 120 days (Weston, 1989, cited in ECETOC 1993). In sandy loam with sludge 0.1 mg DHTDMAC/kg dry soil showed 36 and 52% $^{14}CO_2$-production. Corresponding values of 38 and 41% were derived with 1.0 mg/kg under the same conditions.

Procter & Gamble (1992, cited in ECETOC, 1993) performed various studies on the biological degradation of DSDMAC in soils using several types of dispersion of the substance. Aqueous dispersion resulted in about 35% $^{14}CO_2$-production after a mean test period of 118 days. The mean degradation of a solution with a solvent was below 15% after a mean test period of 184 days. In these cases the majority of the test results was obtained between 130 and 169 days test duration where the $^{14}CO_2$-production was less than 10%. Results with lecithin emulsions were in between.

In a 72-day study no degradation of ^{14}C-DHTDMAC could be observed under anaerobic conditions (Fieler, 1975b, cited in ECETOC 1993). About 90-95% of the test substance (20, 200 and 1500 mg/l) were adsorbed to particles. Solids concentration in the digester was 30 g/l. No other study could find any evidence that DHTDMAC undergoes anaerobic degradation.

Biodegradation studies performed in soil indicated that 18-60% mineralisation was observed within 120-430 days. As a first approach, a half-life of 500 days is used for the terrestrial exposure assessment (**$kbio_{soil} = 1.4 \cdot 10^{-3}\ d^{-1}$**).

Degradation in sediment

For degradation in sediments simulation tests are lacking. Two tests on degradation in river water spiked with sediment (Larson, 1983; Larson & Vashon; cited above) suggest degradation half-lifes in sediment of 80 days or lower. Some experimental details did presumably not represent regular environmental conditions, e.g. sediments were possibly pre-adapted and the concentration of biodegrading microorganisms is regarded to be increased above the normal level.

The available monitoring data reveal that biodegradation in environmental sediments is lower. In Section 3.1.6, it is elaborated that a rapid degradation is not compatible with measured concentrations in sediments. Hellmann (1995; cited in Section 3.1.2.1) found an increase of the DHTDMAC concentration at high river flows. As the causes whirling of sediments and rinsing of agricultural soil during strong rainfalls are stated. These results indicate that DHTDMAC adsorbed onto sediments is not or very slowly degraded. A degradation rate cannot be derived from the monitoring data. Therefore, analogously to the degradation in soil, a half-life of 500 d ($k = 1.4 \cdot 10^{-3}\ d^{-1}$) for the aerobic sediment layer is used in the exposure assessment.

There is no hint that DODMAC/DHTDMAC can be degraded under anaerobic conditions. According to the TGD biodegradation in total sediments is assumed to be a factor of 10 lower than in soil: **$kbio_{sed} = 1.4 \cdot 10^{-4}\ d^{-1}$**.

Abiotic degradation

Based on the molecular structure, no abiotic degradation (e.g. hydrolysis, photolysis) under environmental conditions is expected.

3.1.1.3 Distribution

No data for the vapour pressure are available. Based on the molecular structure, no volatility is expected.

Both DODMAC and DHTDMAC have to be considered as nearly insoluble in water (cf. Section 1). However, the compounds form stable dispersions in water containing unilamellar or multilamellar particles such as vesicles. The size of the dispersed particles depends on temperature and the sheer forces applied when making the dispersion (e.g. by stirring or ultrasonication). Both substances can also form mixed aggregates with other substances, e.g. anionic tensides or humic substances (ECETOC, 1993).

All relevant concentrations in environment, wastewater or toxicity test solutions are far above the water solubility. It is evident that in the hydrosphere DODMAC resp. DHTDMAC is not really dissolved but always adsorbed onto suspended matter or included in vesicles together with other lipophilic organics (e.g. humic acids, tensides). The water solubility is not a limiting factor for emissions into wastewater or pollution of the hydrosphere.

The determination of a Koc from log Pow is not opportune, because the common Koc derivations are not valid for surface active substances like DODMAC. As revealed by the following investigations, DODMAC adsorbs onto both the mineral and the organic fraction of soil and sediments.

In a test with ^{14}C-DODMAC and 3 different sediments, sediment-water partitioning coefficients from 3,833 to 12,489 l/kg dw were analytically determined. The results indicate that the coefficient is more dependent on the nature of the mineral phase than on the organic carbon content. Kinetic studies indicated that adsorption was rapid, reaching equilibrium values within a few hours (Larson & Vashon, 1983).

During a test on toxic effects on sediment organisms, the ^{14}C-DODMAC concentrations were measured in sediment (organic carbon 4.2%) and in interstitial water. From these results, a distribution coefficient can be calculated. The $K_{sed\text{-}water}$ values are in the range of 2,150 to 15,000 (related to dry weight and dimensionless). The $K_{sed\text{-}water}$ values are increasing with rising DODMAC concentrations (Pittinger et al., 1989).

The partitioning of 14C-DODMAC between porewater and the whole sediment (collected from a gravel pit) was studied by Conrad et al. (1999). The equilibrium was reached before the first sampling time (2 days). Sediment and porewater concentrations were measured applying different DODMAC amounts, and from the regression slope the partitioning coefficient was determined to 3018 l/kg.

ECETOC (1993) cites a Kp_{susp} value of 85,000 l/kg, however it is not clear how it was derived.

Kappeler (1982; cited in Section 3.1.2.1) found that on average 27% of the DHTDMAC in river water is adsorbed onto suspended matter (mean 22 mg/l suspended solids). Assuming that the DODMAC distribution can be set equal to DHTDMAC, the Kp_{susp} is calculated to 16,800 l/kg from these values.

Hellmann (1984) examined the remobilisation of DODMAC adsorbed onto bentonite. Activated bentonite (loaded with 34% DODMAC) was treated with water. The substance could not be detected in the water phase. With the detection limit, a distribution coefficient above 10^5 l/kg was calculated.

The distribution of DODMAC in a clay-mineral/water-methanol system was determined by Hellmann (1987). Different mixtures between 100% methanol and methanol : water 60 : 40 were used for the adsorption experiment. After equilibrium was reached, DODMAC was measured in the solutions and the distribution coefficients were calculated. The higher the water content, the higher the K value was. Extrapolated to pure water, the value was estimated to $30 \cdot 10^6$ l/kg.

McAvoy et al. (1994) examined the mobility of DHTDMAC in an aquifer containing 78% sand, 5.8% clay, 16.1% silt, and 0.26% organic carbon. The estimated sorption coefficients were relatively low, varying from 25 to 62 l/kg.

These investigations demonstrate that DODMAC can be bound very strongly by some minerals, while in others relatively small distribution constants were estimated. Under environmental conditions, the sorption properties of DODMAC resp. DHTDMAC probably vary in a wide range depending on the nature of the adsorbant. We assume that the sorption properties of DODMAC and DHTDMAC are nearly identical.

In the following exposure assessment, a value of **10,000 l/kg dw** is chosen for both $\mathbf{Kp_{sed}}$ and $\mathbf{Kp_{soil}}$.

With an assumed Kp_{susp} of 10,000 l/kg and a concentration of 15 mg suspended matter per litre river water, about 87% of the DHTDMAC would remain in the water phase. Kappeler (1982; cited in Section 3.1.2.1) found that in river water on average 27% of the DHTDMAC is adsorbed onto suspended matter (average concentration 22 mg/l). From these values, the Kp_{susp} is calculated to **16,800 l/kg**. As the latter value has a better empirical basis, it is used in the exposure calculation.

3.1.1.4 Accumulation

Lepomis macrochirus was exposed to ^{14}C-DHTDMAC for 49 days in a continuous flow-through system in river water and laboratory water with mean concentrations in the test period of 18 µg/l and 16 µg/l respectively (no solvent carrier, Lewis & Wee, 1983). The river water was sampled at Town River, Massachusetts, and contained 2-84 mg/l suspended solids, 0.04-0.59 mg/l methylene blue active substances - MBAS and 10-15 mg/l disulfine blue active substances - DBAS (pH = 6.4-7.7, total hardness = 14-38 mg/l $CaCO_3$). In river water BCFs of 13 l/kg in the whole body and 94 in the inedible tissue (viscera) were estimated based on measured concentrations. When laboratory water was used the respective BCFs were 32 and 256 l/kg. In both waters DHTDMAC did not concentrate to a significant degree in edible tissue (BCF of the fillets < 5 l/kg). In a depuration phase in well water 93% of the accumulated radioactivity was eliminated from the inedible tissues after 14 days.

The short-term uptake (24h) of DODMAC by juvenile *Pimephales promelas* was assessed in a flow-through system with laboratory water and two different concentrations of humic acids (Versteeg & Shorter, 1992). A depuration phase of 72 hours followed. Compared with the laboratory water controls 6.8 mg/l humic acids decreased the uptake rate by a factor of 20 and increased the depuration rate twofold.

These values indicate the dependence of the BCF-values on the surrounding medium which is also obvious in ecotoxicological testing (see below). Based on test results with laboratory water, a bioaccumulation is indicated, but it is assumed that it is low under environmental conditions. A **BCF** of **13 l/kg** is used in the risk assessment (related to PEC_{bulk}), assuming fish to be representative for all aquatic organisms. It should be pointed out, that for the diversity of organisms and environmental conditions the bioaccumulation potential (bioconcentration and biomagnification) is not known. A relatively simple microcosm study might clarify these uncertainties.

Bioaccumulation of ^{14}C-labelled DODMAC by *Lumbriculus variegatus* from a natural sediment was measured over a period of 28 days. The total organic carbon content of the sediment was 1.73 %. Worms were exposed to DODMAC concentrations in the sediment in the range of 150 -5,800 mg/kg dw. After 28 days the DODMAC tissue concentration in the worms was measured by liquid scintillation counting. A biota sediment accumulation factor (BSAF) of 0.28 was derived from the experimental data. As the concentration in the worms was only measured at the end of the 28-day test period it is not clear whether equilibrium was reached (Conrad et al., 1999).

The aim of a second experiment was the identification of the main uptake routes of DODMAC by *Lumbriculus variegatus* from the sediment. For this test feeding and non-feeding worms were exposed to a sediment containing 8.7 mg/kg of DODMAC. A viable non-feeding worm was generated by removing the head of an intact feeding worm. The new worm is unable to ingest sediment for up to 6 - 8 days. The use of non-feeding worms allows the contribution of ingestion as an uptake route to be assessed. A 13-day bioaccumulation study with feeding and non-feeding *Lumbriculus variegatus* showed that the main route of uptake for DODMAC was via sediment ingestion. At day 5, a comparison of tissue concentrations between the feeding and non-feeding worms showed that around 86 % of the body burden in the feeding worms could be attributed to ingestion (Conrad et al., 1999).

Bioaccumulation of ^{14}C-labelled DODMAC by *Tubifex tubifex* from a natural sediment was measured over a period of 28 days. The total organic carbon content of the sediment was 1.73 %. Worms were exposed to DODMAC concentrations in the sediment in the range of 300 – 5,000 mg/kg dw. After 28 days, the DODMAC tissue concentration in the worms was measured by liquid scintillation counting. A biota sediment accumulation factor (BSAF) of 0.78 was derived from the experimental data. As the concentration in the worms was only measured at the end of the 28-day test period it is not clear whether equilibrium was reached (Comber/Conrad, 2000).

To evaluate the uptake of DSDMAC (purity > 98%) by plants, soil experiments were conducted with tomato, bean, cucumber and radish seedlings. DSDMAC was applied to soil adsorbed to activated sludge (2 g/kg) and a concentration of 2 mg DSDMAC/kg soil was achieved. Concentrations of 0.02 to 0.05 mg/kg were found in the shoots of the plant seedlings and the radish roots after 28 to 36 days exposure (Lötzsch et al., 1984).

3.1.2 Aquatic compartment

3.1.2.1 Monitoring

For the interpretation of the following monitoring data, it has to be considered that (if not otherwise noted) the figures stand for total concentrations, i.e. no distinction has been made between the “dissolved” (in reality: included in vesicles) and the adsorbed fractions.

Wastewater treatment plants (WWTPs)

In 1979 DHTDMAC was analysed in a wwtp in Dülmen (Germany), which receives a high proportion (> 95%) of domestic sewage. An overall removal rate of about 94% was found during primary settlement, aerobic treatment and secondary settlement. The average concentrations were 1.57 mg/l in raw sewage and 0.09 mg/l in the effluent. In activated sludge 8.3 g DHTDMAC/kg dry solid was detected. The river below outfall contained 0.03-0.12 mg/l (0.07 mg/l) (Topping & Waters, 1982).

In a WWTP in Alderly Edge (UK) which also receives mainly municipal sewage, a total removal rate of >95% was found (average concentrations: 1.38 mg/l in raw sewage, 0.04 mg/l in secondary effluent). In activated sludge, 3 g DHTDMAC/kg dry solid was detected. The concentrations are lower than in Dülmen because of the lower use of softeners in UK (Topping & Waters, 1982).

DHTDMAC was measured in the biological treatment plant of Lüdinghausen (Germany) by 5 laboratories in 1987. Generally, the results were in good agreement. The average values are 830 µg/l in the raw sewage, 30 µg/l in the final effluent (corresponding to 96% removal), and 3.3 g/kg in the wasted sludge. The fraction of municipal and industrial wastewaters are not reported (Gerike et al., 1994).

During several monitoring studies in the USA, the WWTP elimination was calculated from measured influent and effluent concentrations. The removal rates were 19-32% (mean 26%) for 4 primary treatment plants, 44-94% (mean 72%) for 5 trickling filter plants, and 89-98% (mean 94%) for 5 activated sludge plants (Versteeg et al., 1992).

In 1984 and 1985, ditallow dimethyl ammonium chloride (DTDMAC) and its impurity monotallow trimethyl ammonium chloride (MTTMAC) were measured in the production site effluent and in influent and effluent of the public owned treatment work in Lima (Ohio, USA) which receives the producer's sewage (Hopping, 1987). We assume that the detected substance is DHTDMAC in reality. The results are presented in **Table 3.1**.

Table 3.1 Measurements of DTDMAC and MTTMAC concentration [µg/l]

Year	Sample point	DTDMAC	MTTMAC
1984	Plant waste	mean 552,000	mean 51,900
	POTW influent	mean 3,650	mean 410
	POTW effluent	mean 63	mean <10
	Removal	98%	>98%
1985	Plant waste	280,000-520,000 (mean 353,000)	13,000-33,000 (mean 24,000)
	POTW influent	3,000-7,300 (mean 4,430)	270-590 (mean 370)
	POTW effluent	62-120 (mean 91)	<10-33 (mean 20)
	Removal	98%	95%

In 1988, DHTDMAC was measured in wasted activated sludge from the treatment plant in Koblenz (Germany). With 14 measurements, concentrations of 8.8-9.2 g/kg were detected (Hellmann, 1989).

From 1991 to 1994, DHTDMAC was repeatedly measured in digested sewage sludge of 5 Swiss municipal treatment plants. In 1991, the concentrations were in the range of 2.57 to 5.87 g/kg dry sludge. Until 1994, they dropped to 0.15 to 0.30 g/kg because of the widely replacement of the substance (Fernandez et al., 1996).

Based on the monitoring studies cited above, an elimination rate of 95% in biological treatment plants is used for the following exposure calculations.

Based on measurements at different sites of treatment plants, ECETOC (1993) estimated the DHTDMAC fractions being adsorbed onto primary sludge to 31% and onto wasted activated sludge to 24%. In the regional exposure assessment, it is assumed that in all 55% of the used substance is adsorbed and reaches agricultural soils during use of sludge as fertilizer.

Rivers, suspended matter and sediments

In 1981, DHTDMAC was measured at 30 locations at the Rhine and its tributaries. At every location, 2 grab samples were taken: in the first the bulk concentration was measured, while in the second the suspended matter was allowed to settle down during 2 weeks and afterwards the DHTDMAC concentration in the overlying water was measured. The bulk concentrations were found to be in the range between 4-92 µg/l with an average of 19 µg/l, the average fraction adsorbed onto suspended matter was found to be 27%. The concentration of suspended solids was in the range of 9 to 72 mg/l with an average of 22 mg/l (Kappeler, 1982).

In the river Rhine near Bonn, DHTDMAC was detected in concentrations of 6-12 µg/l (no further data available) (Schneider & Levsen, 1986).

The pollution of suspended particles in the river Rhine was examined by Hellmann, 1995. The DHTDMAC concentrations decreased from about 200 mg/kg in 1982 to 25-50 mg/kg in 1994. In the same period the German DHTDMAC consumption for softeners had dropped by more than 90% (cf. Section 2). It was found that the DHTDMAC concentrations in 1993/94 were not reciprocal to the river flow as it would be expected. Detailed hydrological studies showed that the DHTDMAC loads rise strongly with increasing river flows. As the reason raising of sediments and rinsing of agricultural soil during strong rainfalls are stated. These soils and sediments are loaded with historical DHTDMAC emissions. The results reveal that DHTDMAC adsorbed onto soil and sediments is not or very slowly degraded.

In a sediment sample from the German river Saar, 220 mg DHTDMAC per kg (unknown if dry or wet weight) were detected in 1988 (Hellmann, 1989).

DHTDMAC was detected in the Spain river Llobregat being highly polluted with wastewater from surfactants and pesticide industries. No concentration is reported (Rivera, 1987).

From March 1990 to June 1991, DTDMAC concentrations between 2 and 34 µg/l were measured in 6 different rivers in the Netherlands (van Leeuwen et al., 1992). We assume that the detected substance is DHTDMAC in reality.

In 1990, the following DHTDMAC concentrations were measured in Dutch rivers: 15-25 (mean 20) µg/l in large rivers, 22-52 (mean 30) µg/l in rivers, 11-48 (mean 27) µg/l in tributaries, 15-116 (mean 43) µg/l in canals and 17-114 (mean 56) µg/l in polders (ECETOC, 1993).

Furthermore the monitoring data (DHTDMAC) without further information are presented in **Table 3.2**.

Table 3.2 Monitoring data (DHTDMAC)

Medium	Country	Concentration	Year	Reference
Main - suspended solids	Germany	11 - 201 (mean 85) mg/kg	1989 - 90	Klotz, 1990
Elbe - suspended solids	Germany	mean 20 mg/kg	1990	Hellmann, 1990
Weser - suspended solids	Germany	80-100 mg/kg	1990	Hellmann, 1990
Niederrhein - suspended solids	Germany	50-150 mg/kg	1990	Hellmann, 1990
3 rivers (sediments)	Belgium	11-67 mg/kg	1987	ECETOC, 1993
Rhein at Iffezheim (sediments)	Germany	78 mg/kg	1987	Klotz, 1990

3.1.2.2 Model Calculations

The substance-specific parameters for DODMAC used in the exposure calculations are listed in **Table 3.3**.

Table 3.3 Substance-specific parameters for DODMAC

Parameter	Value
Fraction of DHTDMAC in the technical product	75%
Fraction of DODMAC in DHTDMAC	42%
$Fstp_{water}$	5%
$kbio_{water}$	$4.7 \cdot 10^{-3}\ d^{-1}$
$kbio_{sediment}$	$1.4 \cdot 10^{-4}\ d^{-1}$
$Kp_{sediment}$	10,000 l/kg dw
Kp_{susp}	16,800 l/kg

It has to be kept in mind that in aqueous phases DODMAC is not really dissolved but always occurs in vesicles together with other lipophilic organics (cf. Section 3.1.1.3). The values for C_{water} and PEC_{water} calculated below will include the fraction incorporated in vesicles.

The ecological effects of the substance are strongly dependent on the test medium, differences are caused by adsorption onto suspended matter and complexation with anionics. Therefore the relevant ecotoxicity values are derived from tests in river water (cf. Section 3.2). For the aquatic risk assessment, the PEC_{bulk} (which includes the fraction adsorbed onto suspended matter) has to be calculated as the PEC being adequate to the river water tests.

3.1.2.2.1 Local exposure / Production

Generic model

In the Technical Guidance Document (TGD), a generic exposure scenario for the release during production is proposed. The largest known production volume at one site is yearly 15,000 t of the technical DHTDMAC (1994). With an average content of 75% quarternary amine compounds in the technical product, and from this 42% are DODMAC, yearly 4,725 t DODMAC are produced. Using the TGD defaults, the following concentrations are calculated:

Release factor 0.3%: ⇒	14 t/a into the sewage
Production during 300 d/a: ⇒	47 kg/d into the sewage
Sewage flow 2,000 m^3/d: ⇒	24 mg/l in the raw sewage
Elimination in wwtp 95%: ⇒	**C_{eff} = 1.2 mg/l**
Dilution 1:10: ⇒	**$C_{bulk,local}$ = 120 µg/l**
Considering adsorption onto suspended matter: ⇒	**$C_{water,local}$ = 96 µg/l**
Adsorption onto sediment: ⇒	**$C_{sed,local}$ = 1,600 mg/kg dw**

In the last years, the production volumes have decreased. However, DHTDMAC is produced in a batch process, and the duration of the production period has decreased simultaneously. Thus the environmental concentrations remain unchanged, although the exposure time is shortened.

The generic scenario is not used in the risk characterisation, as it does not reflect the recent European situation. The risk characterisation is performed on the basis of site-specific information.

Site A

The maximum daily capacity of this plant is 28.8 t. As a by-product, 2.4 t/d NaCl is formed containing 2.6% DHTDMAC (i.e. 62.4 kg/d) which is discharged into the sewer. The local exposure is calculated as follows:

Amount DHTDMAC in sewage	62.4 kg/d
Amount DODMAC in sewage (42%)	26.2 kg/d
Elimination by precipitation with anionics	98.7%
Amount DODMAC in WWTP influent	341 g/d
Elimination in wwtp	95%
Amount DODMAC in WWTP effluent	17 g/d

Sewage flow	7270 m^3/d
C_{eff}	2.3 µg/l
River flow (90%ile)	2.45 m^3/s
$C_{bulk,local}$	0.080 µg/l
$C_{water,local}$	0.064 µg/l
$C_{sed,local}$	1.1 mg/kg dw
$PEC_{bulk,local}$	0.22 µg/l
$PEC_{water,local}$	0.17 µg/l
$PEC_{sed,local}$	2.9 mg/kg dw

Sites B, C, D and E

These companies state that generally there are no emissions into the sewage during production, because the equipment is separated from the sewer system.

Site F

At this plant, the content of quartenary amino compounds is measured in the sewage. The local exposure is calculated as follows:

Concentration of quartenary amines in raw sewage	3.2 g/l
Fraction of DHTDMAC (based on production volumes)	0.38
Concentration of DHTDMAC in sewage	1.2 g/l
Concentration of DODMAC in sewage (42%)	511 mg/l
Removal in precipitation step	98%
Concentration of DODMAC after precipitation	10.2 mg/l
Dilution in WWTP	1:10,250
Concentration of DODMAC in WWTP influent	1.0 µg/l
Elimination in WWTP	95%
C_{eff}	**0.05 µg/l**
Dilution in the river	6.3
$C_{bulk,local}$	**0.0079 µg/l**
$C_{water,local}$	**0.0063 µg/l**
$C_{sed,local}$	**0.11 mg/kg dw**
$PEC_{bulk,local}$	**0.15 µg/l**
$PEC_{water,local}$	**0.12 µg/l**
$PEC_{sed,local}$	**2.0 mg/kg dw**

Literature:

High DHTDMAC concentrations (552 and 353 mg/l as yearly averaged values) were measured in the sewage of a producer plant in the USA, the flow is not reported (Hopping, 1987; cited in Section 3.1.2.1). These measurements reveal that high emissions of DODMAC during DHTDMAC production are possible. In this scope the exposure calculations based on default values seem to be not unrealistic.

3.1.2.2.2 Local exposure / Processing to activated bentonites

In Europe, 5,221 t DHTDMAC (including 2,193 t DODMAC) were used for the production of activated bentonites in 1997 (CEFIC APAG & CEPE, 1998).

Site 1

This site uses yearly 990 t DHTDMAC (i.e. 416 t DODMAC). At this plant, regular monitoring in the wastewater is performed. DHTDMAC is normally not detected (dl = 50 µg/l) in the sewage. The sewage (flow = 150 m^3/d) is released into the receiving stream (1/3 of the mean flow = 47 m^3/s).

Detection limit related to DODMAC	42% of 50 µg/l = 21 µg/l
Mechanical sewage treatment (elim. 50%)	10.5 µg/l
Dilution factor150 m^3/d	47 m^3/s = 1 : 27,000
$C_{bulk,local}$	**0.39 ng/l**
$C_{water,local}$	**0.31 ng/l**
$C_{sed,local}$	**5.2 µg/kg dw**
$PEC_{bulk,local}$	**0.14 µg/l**
$PEC_{water,local}$	**0.11 µg/l**
$PEC_{sed,local}$	**1.7 mg/kg dw**

The sludge is dumped into a landfill and not used onto farmland.

Site 2

Processing volume: yearly 750 t DHTDMAC in a “wet process”.
Analysed content of DHTDMAC in the wastewater: < 2 mg/l (i.e. 840 µg DODMAC/l).

Wastewater from organoclay production 113 m^3/d	840 µg/l
Flow into wwtp 80,000 m^3/d	1.2 µg/l
95% elimination (cf. Section 3.1.1.2)	59 ng/l
Dilution in surface water 1:1.1	
$C_{bulk,local}$	**54 ng/l**
$C_{water,local}$	**43 ng/l**
$C_{sed,local}$	**720 µg/kg dw**
$PEC_{bulk,local}$	**0.19 µg/l**
$PEC_{water,local}$	**0.15 µg/l**
$PEC_{sed,local}$	**2.5 mg/kg dw**

The sludge is dumped into a hazardous waste disposal and not used onto farmland.

The same site uses 399 t/a by a “dry process” for organoclay production. Emissions from this process into surface waters are zero.

Site 3

This site uses 354 t DHTDMAC/a for organoclay production. There is no wastewater, thus emissions into surface waters are considered to be zero.

Site 4

Processing volume: 600 t DHTDMAC/a.
Analysed content of DHTDMAC in the wastewater: < 0.05 mg/l (i.e. 21 µg DODMAC/l).

Dilution of wastewater 1:2	10.5 µg/l
Industrial treatment plant (95% elimination)	530 ng/l
Emission into sea (dil. 1:10)	
$C_{bulk,local}$	**53 ng/l**
$C_{water,local}$	**42 ng/l**
$C_{sed,local}$	**710 µg/kg dw**
$PEC_{bulk,local}$	**0.19 µg/l**
$PEC_{water,local}$	**0.15 µg/l**
$PEC_{sed,local}$	**2.5 mg/kg dw**

The sludge is dumped and not used onto farmland.

Site 5

Processing volume: 2,128 t DHTDMAC/a.
Analysed content of DHTDMAC in the wastewater: maximum 1 mg/l (i.e. 420 µg DODMAC/l).

Dilution factor in WWTP: 30	14 µg/l
Municipal treatment plant (95% elimination)	0.7 µg/l
Sewage flow	5,712 m^3/d
River flow (1/3 of mean flow)	8,000 m^3/d
Dilution factor in surface water	2.4
Emission into sea (dil. 1:10)	
$C_{bulk,local}$	**0.29 µg/l**
$C_{water,local}$	**0.23 µg/l**
$C_{sed,local}$	**3.9 mg/kg dw**
$PEC_{bulk,local}$	**0.43 µg/l**
$PEC_{water,local}$	**0.34 µg/l**
$PEC_{sed,local}$	**5.7 mg/kg dw**

The sludge is dumped and not used onto farmland.

3.1.2.2.3 Local exposure / Use of activated bentonites as additive in paint and lacquers

Laquers with activated bentonites always contain organic solvents. They are normally applied in spray cabins. In the air lacquer smog (overspray) is remaining which is scrubbed with water. The aqueous phase is decanted from the lacquer coagulate sludge and recirculated. There are no data available about the content of organic solvents in the washing water. It can not be excluded that a part of the DHTDMAC is resolved, especially as the washing water is recirculated and both organic solvent and the surfactant may accumulate during this process. After a certain time, the washing water has to be renewed and the wastewater is released into the sewer. For the exposure estimation, we propose the following scenario:

The annual European use volume of DHTDMAC in paints is 4,137 t. The total consumption of solvent borne paints in 1996 was 2,490,000 t. Typical levels of organoclays in solvent-borne paints are in the range from 0.1 to 0.5% (CEFIC APAG & CEPE, 1998). The average content of DHTMAC is calculated to 0.17% (or 0.07% DODMAC).

In the scope of the draft VOC directive, there are 400,000 paint user installations (CEFIC APAG & CEPE, 1998). For the exposure scenario, a medium/large paint user site with a paint consumption of 10 t/month is chosen. The DODMAC content is 7 kg/month or (with 20 working days) 350 g/d.

The transfer efficiency in spray cabins is generally in the range of 50 to 99%. With a worst-case assumption of 50% overspray, daily 175 g DODMAC will reach the washing water.

With analytical measurements in the sewage no DODMAC could be detected. Therefore the release factor must be below 1.1%. Thus daily maximum 1.9 g DODMAC will be emitted into the sewer.

With an elimination of 95% in the treatment plant and a wastewater flow of 2,000 m^3/d, the effluent concentration is 0.048 µg/l.

$C_{bulk,local}$	**0.0048 µg/l**
$C_{water,local}$	**0.0039 µg/l**
$C_{sed,local}$	**0.065 mg/kg dw**
$PEC_{bulk,local}$	**0.41 µg/l**
$PEC_{water,local}$	**0.11 µg/l**
$PEC_{sed,local}$	**1.7 mg/kg dw**

3.1.2.2.4 Local exposure / Emissions via household sewage

Generally, only actual consumption figures have to be considered for the exposure assessment of a substance. In this special case, we deviate from this principle and calculate two scenarios:

Scenario 1

The first scenario is based on the DHTDMAC consumption figures in 1998 (CEFIC APAG, 1999): 408 t are used in fabric softeners and 276 t in others (hair conditioners, car washing etc.), totally 684 t DHTDMAC resp. 287 t DODMAC.

With a split of 90:10, 29 t DODMAC are taken as input for the regional and 258 t for the continental model.

According to the TGD, the fraction for the main source of 0.002 is used for the local scenario, leading to an emission of 58 kg/a or 157 g/d into a wwtp. This approach includes the assumption that the substance is not equally emitted within the region. In this case this is justified as the DHTDMAC consumption did not decrease simultaneously in the European countries. No figures about the current spatial consumption pattern are available. Thus the TGD default seems to be a reasonable conservative approach.

Scenario 2

Additionally, a scenario based on the fabric softener consumption from 1989/90 is calculated, with the following rationale:

The majority of the monitoring investigations were conducted before 1990. A comparison between estimated and measured concentrations (cf. Section 3.1.6), which is necessary to support the parameters of the exposure models resp. model validation, can only be based on the historical figures.

The comparison between the results of both scenarios reflect the decrease of environmental pollution in the last years.

This scenario is not used for the risk characterisation.

An adequate basis for this scenario are country-specific consumption volumes published by ECETOC (1993). In **Table 3.4**, the consumption related to a population of 20 million people is calculated to estimate the releases for both the local and regional exposure model.

Table 3.4 Presentation of the consumption related to the population

Country	Tonnage DHTDMAC	Population [Mio.]	Cons. per 20 Mio. p [t]
Germany	12,000	61	3,930
Netherlands	2,000	15	2,670
France	9,400	56	3,360
U.K.	8,600	57	3,020
Italy	4,300	58	1,480
Total	**36,300**	**247**	**mean 2,940**

The annual regional use is estimated to 2,940 t DHTDMAC (i.e. 1,235 t DODMAC). It is assumed that the consumption of the substance is equally distributed in the region, so the releases into a standard stp (10,000 inhabitants) are 618 kg DODMAC/a (i.e. 1.69 kg/d).

For the continental consumption, the figures from BUA (1990) are used (65,000 t DHTDMAC = 27,300 t DODMAC). Considering the regional use of 1,235 t, for the continental model a release 26,065 t DODMAC/a of is taken.

The local DODMAC concentrations are as shown in **Table 3.5**.

Table 3.5 Local concentrations of DODMAC

Year	1989/90	1998
Consumption	1.69 kg/d	0.16 kg/d
Wastewater flow	200 l/d/person = $2 \cdot 10^6$ l/d /10,000 inhabitants	
Influent concentration	850 µg/l	79 µg/l
C_{eff} (WWTP elimination 95%)	42 µg/l	3.9 µg/l
$C_{bulk,local}$ (dilution 1:10)	4.2 µg/l	0.39 µg/l
$C_{water,local}$ (Kp_{susp} = 16,800 l/kg)	3.4 µg/l	0.31 µg/l
$C_{sed,local}$ (Kp_{susp} = 16,800 l/kg)	57 mg/kg dw	5.3 mg/kg dw
Direct release: $C_{bulk,local}$	85 µg/l	7.9 µg/l
Direct release: $C_{water,local}$	68 µg/l	6.3 µg/l

The scenario for direct releases is calculated to reflect the situation at sites without WWTP purification. The values are not used in the risk characterisation.

As DHTDMAC has been widely replaced since 1989/90, the DODMAC concentrations have substantially been decreased. It has to be mentioned, however, that the actual consumption does not lead to a homogeneous emission, as the remaining use is probably be limited to some countries or regions and not all over Europe. Moreover, remobilisation of the substance from sediments and agricultural soils during rainfalls occurs, as shown by Hellmann, 1995 (cited in Section 3.1.2.1).

The calculated DODMAC concentrations in wastewater for 1989/90 can be compared with the monitoring data cited in Section 3.1.2.1. As the measured values are related to DHTDMAC, they are converted to DODMAC concentrations (42% from DHTDMAC).

Table 3.6 Comparison of the calculated DODMAC concentration with monitoring data

Medium	Calculated [µg/l	Measured [µg/l	Location / Year	Source
Raw sewage	850	660	Duelmen / 1979	Topping & Waters, 1982
		580	Alderly Edge / 1979	Topping & Waters, 1982
		350	Lüdinghausen / 1987	Gerike et al., 1994
WWTP effluent	42	38	Duelmen / 1979	Topping & Waters, 1982
		17	Alderly Edge / 1979	Topping & Waters, 1982
		13	Lüdinghausen / 1987	Gerike et al., 1994

The calculated wastewater concentrations are somewhat higher than the monitoring data from Topping & Waters, the reason is not known. The measurements in Lüdinghausen should be regarded with care, as the fraction of household sewage in this plant is not known; possibly there is a significant fraction of industrial wastewaters.

The total release of DODMAC into the hydrosphere has to be estimated for the use in the regional models. In accordance to the TGD, a connection rate of 70% to biological wwtps is assumed. Based on the consumption figures for Western Europe (cf. Chapter 2) and the EU model region, the emission [t/a] is calculated as follows in **Table 3.7**:

Table 3.7 Calculation of the emission of DODMAC into the hydrosphere

	1989/ 90		1998	
	EU-region	EU-continent	EU-region	EU-continent
Consumption DHTDMAC	2,940	62,060	68	616
Fraction DODMAC	1,235	26,065	29	258
30% direct emission	371	7,820	8.6	77
70% in WWTP, elim. 95%	43	910	1.0	9.0
Total release into hydrosphere	414	8,730	9.6	86

3.1.3 Atmosphere

Because an extremely low volatility of DODMAC is to be expected, no significant exposure of the atmosphere is assumed.

3.1.4 Terrestrial compartment

The elimination of DHTDMAC resp. DODMAC in wwtps is dependent on adsorption onto sludge to a large extent. During application of sludge as fertilizer, the substance reaches agricultural soils.

3.1.4.1 Monitoring

DHTDMAC was measured in an agricultural soil which had received 9.4 t sludge·acre^{-1}·a^{-1} (i.e. 23 t·ha^{-1}·a^{-1}) during 7 years. In the sludge the DHTDMAC concentration was 2.8 g/kg dw. The soil was cultivated to a depth of about 6 to 8 inches (15-20 cm) during two years. Soil specifications are not reported. Three core samples were collected, sliced into sections and air-dried. The DHTDMAC concentrations [ppm] were as follows in **Table 3.8** (Rapaport, 1987):

Table 3.8 Measured concentrations of DHTDMAC in agricultural soil

Depth [cm]	Core 1	Core 2	Core 3	Mean Core 1-3
0-7.5	164	61	32	86
7.5-15	201	15	23	82
15-23	25	-	4	15
23-30	<1	8	-	4
53-61	<4	4	3	<4
81-91	<1	-	-	<1

The mean value in the upper layer of 86 mg DHTDMAC/kg corresponds to 36 mg DODMAC/kg. With a sludge application of 5 t/ha (instead of 23 t/ha), a DODMAC concentration of 7.8 mg/kg would be expected.

Further measurements are reported in ECETOC, 1993 (original literature not available): In 42 fields that received their last sludge application prior to 1987 (the year of sampling), DHTDMAC concentrations from <2 mg/kg to 37 mg/kg (mean 9.5 mg/kg) were detected. 95%

of the samples contained less than 20 mg/kg and 62% had less than 10 mg/kg. In 9 fields that received their last application of sludge in the year of sampling, concentrations ranged from 2 mg/kg to 33 mg/kg (mean 3.3 mg/kg). Sludge application rates are not stated.

3.1.4.2 Calculation of $PEClocal_{soil}$

The available monitoring data reveal that the elimination of DHTDMAC in treatment plants is primarily due to adsorption onto sewage sludge. Both biodegradation and partitioning properties of DODMAC are assumed to be equal to DHTDMAC. The concentration of DODMAC in sewage sludge is calculated from the emission into the local treatment plant, the sludge adsorption rate of 55% and the sewage sludge production rate of 710 kg/d.

Table 3.9 Calculated concentration of DODMAC in sewage sludge

Year	Influent [g/d]	Fraction adsorbed [g/d]	Csludge [mg/kg dw]
1989/90	1,690	930	1,300
1998	160	88	120

The value for 1989/90 (1.3 g DODMAC/kg dw) can be compared with the monitoring data. With a fraction of 42% DODMAC in DHTDMAC, it corresponds to 3.1 g DHTDMAC/kg sludge, which is within the range of measured concentrations (cf. Section 3.1.2.1).

The local concentration in soils is calculated according to the TGD model. The substance-specific input parameters and the resulting PECs are given in **Table 3.10.**

Table 3.10 Substance-specific input parameters and resulting PECs

Parameter	Value / 1989 / 90	1998	Remarks
Kp_{soil}	10,000 l/kg dw		cf. 3.1.1.3
$kbio_{soil}$	$1.4 \cdot 10^{-3}$ d^{-1}		$t_{½}$ = 500 d; cf. 3.1.1.2
C_{sludge}	1.3 g/kg dw	0.12 g/kg dw	
$PEClocal_{soil}$	5.3 mg/kg dw	0.49 mg/kg dw	endpoint: terrestrial ecosystem
$PEClocal_{agr.soil}$	4.8 mg/kg dw	0.44 mg/kg dw	endpoint: crops for human cons.
$PEClocal_{grassland}$	1.9 mg/kg dw	0.18 mg/kg dw	endpoint: grass for cattle
$PEClocal_{soil,porew}$	0.48 µg/l	0.044 µg/l	endpoint: drinking water

The calculated $PEClocal_{agr.soil}$ for DODMAC [mg/kg] for the period 1989/90 can be compared with the monitoring data:

Table 3.11 Comparison of $PEClocal_{agr.soil}$ with monitoring data

PEC DODMAC	measured DHTDMAC	fraction DODMAC	Reference
4.8	7.8 (related to 5 t sludge/a)	3.3	Rapaport, 1987
	up to 37 (mean 9.5)	up to 16 (mean 4.0)	ECETOC, 1993
	up to 33 (mean 3.3)	up to 14 (mean 1.4)	ECETOC, 1993

The calculated value for $PEClocal_{agr.soil}$ is within the range of the DODMAC concentrations based on DHTDMAC measurements. However, the sludge application rates are not reported by ECETOC, thus the PEC cannot be compared.

The total release of DODMAC into the terrestrial compartment has to be estimated for the use in the regional models. As a worst case approach, it is assumed that the sludge from all municipal wwtps is applied as fertilizer on agricultural soils. The emission amount [t/a] is calculated for both emission scenarios as follows (**Table 3.12**):

Table 3.12 Calculation of the emission amount into the soil

	1989 / 90		1998	
	EU-region	EU-continent	EU-region	EU-continent
Consumption DHTDMAC	2,940	62,065	68.4	616
Fraction DODMAC	1,235	26,070	29	258
70% in WWTP	865	18,200	20	181
Adsorption onto sludge 55% of influent (cf. 3.1.2.1)	475	10,000	11	99

3.1.5 Regional exposure

For the assessment of regional exposure only the emissions during use as fabric softeners, car washing agents and hair conditioners are considered. The releases during production, processing to activated bentonites and use of the bentonites by lacquers are relatively small and can be neglected. In **Table 3.13**, DODMAC release amounts, degradation rates, distribution constants and the resulting PEC's of EUSES calculations are presented.

Table 3.13 Presentation of DODMAC release amounts, degradation rates, distribution constants and the resulting PECs of EUSES calculations

	1989 / 90		1998	
Parameter	EU-region	EU-cont.	EU-region	EU-cont.
Emission hydrosphere [t/a]	414	8,730	9.6	86
Emission soil [t/a]	475	10,000	11	99
$kbio_{water}$ [d^{-1}]	$4.7 \cdot 10^{-3}$			
$kbio_{sediment}$ [d^{-1}]	$1.4 \cdot 10^{-4}$			
$kbio_{soil}$ [d^{-1}]	$1.4 \cdot 10^{-3}$			
$Kp_{susp-water}$ [l/kg]	16,800			
$Kp_{sed-water}$ [l/kg dw]	10,000			
$Kp_{soil-water}$ [l/kg dw]	10,000			
$PEC_{water,bulk}$ [µg/l]	6.3	2.4	0.14	0.023
$PEC_{waterphase}$ [µg/l]	5.1	1.7	0.11	0.016
$PEC_{sediment}$ [mg/kg dw]	80	27	1.7	0.27
$PEC_{agr.soil}$ [mg/kg dw]	0.29	0.07	0.0067	0.0007

3.1.6 Calculation of PEC_{local}

According to the TGD, the relevant PECs for the risk assessment are the sum of local and regional concentrations. The DODMAC PECs for the use as fabric softeners, hair conditioners and car washing products are given in **Table 3.14.**

Table 3.14 PECs for the use as fabric softeners, hair conditioners and car washing products

Sub-compartment	C_{local}	$PEC_{EU\text{-}region}$	PEC_{local}	Year
bulk (water+susp.) [µg/l]	4.2	6.3	10.5	1989/90
waterphase [µg/l]	3.4	5.1	8.4	
sediment [mg/kg dw]	57	80	137	
bulk (water+susp.) [µg/l]	0.40	0.14	0.54	1998
waterphase [µg/l]	0.31	0.11	0.42	
sediment [mg/kg dw]	5.3	1.7	7.0	

The calculated PEClocal from the use as fabric softener in the period 1989/90 can be compared with monitoring data cited in Section 3.1.2.1. It has to be kept in mind that the measured values in river water are generally related to the bulk concentration (which includes the fraction adsorbed onto suspended matter). An overview is given in **Table 3.15**.

Table 3.15 Comparison of the calculated PEClocal from use as fabric softener with monitoring data

Sub-compartment	PEC	Measured DHTDMAC	Fraction DODMAC	Location	Reference
PEC_{bulk} [µg/l]		4-92 (mean 19)	1.7-39 (mean 8)	Rhine and tributaries	Kappeler, 1982
local	10.5	6-12	2.5-5	Rhine	Schneider & Levsen, 1987
regional	6.3	2-34	1-14	6 rivers	van Leeuwen et al., 1992
continental	2.4	15-25 (mean 20)	6-11 (mean 8.4)	large rivers	ECETOC, 1993
		22-52 (mean 30)	9-22 (mean 13)	rivers	ECETOC, 1993
		11-48 (mean 27)	5-20 (mean 11)	tributaries	ECETOC, 1993
		15-116 (mean 43)	6-49 (mean 18)	canals	ECETOC, 1993
		17-114 (mean 56)	7-48 (mean 24)	polders	ECETOC, 1993
$PEC_{sediment}$ [mg/kg dw]		220	92	Saar (sed.)	Hellmann, 1989
local	137	11-67	4.6-28	3 Belg. rivers (sed.)	ECETOC, 1993
regional	80	78	33	Rhein (sed.)	Klotz, 1990
continental	27	11-201 (mean 85)	4.6-84 (mean 36)	Main (susp.)	Klotz, 1990
		20-150	8.4-63	Elbe, Weser, Niederrhein (susp.)	Hellmann, 1990

From this comparison the following conclusions can be drawn:

- In large rivers like the Rhine, the measured water concentrations are generally lower than the calculated because of the high dilution.
- In medium-sized rivers there is a good match between calculated and measured values for the water concentration.

- In small surface waters like creeks, canals or polders the calculated water concentrations underestimate the real pollution. A relatively high fraction of untreated wastewater or a small dilution causes the high loads.
- The measured values in sediments and in suspended matter (in which pollution should be in the same range) are lower than the calculated $PEC_{local,sed}$. The reason is that DHTDMAC was measured in large rivers where, because of the high dilution, the concentrations were relatively low.
- A rapid degradation in sediments can be excluded: A recalculation of the EU-regional model (figures from 1989/90) with half-lives of 1 year and 80 d results in sediment concentrations of 22 and 5.9 mg/kg (instead of 80 mg/kg with a half-life of 5,000 d). Many of the measured concentrations are above these values.

3.1.7 Secondary poisoning

Because bioconcentration of DODMAC in fish is only low (cf. Section 3.1.1.4), a biomagnification via this route is not expected. In addition, bioaccumulation tests with the endobenthic species *Lumbriculus variegatus* and *Tubifex tubifex* also show a low bioaccumulation potential. Therefore, bioaccumulation via the food chain is not to be expected for DODMAC.

3.2 EFFECTS ASSESSMENT: HAZARD IDENTIFICATION AND DOSE (CONCENTRATION) - RESPONSE (EFFECT) ASSESSMENT

The toxicity of DODMAC is influenced by adsorption onto surfaces, complexation, water quality, usage of solvents and concentration of by-products. Because the databasis for the pure DODMAC (> 95% purity, C_{18}-chain length) would be too small to reveal all these parameters, it is necessary to use ecotoxicological test results for the commercial product DHTDMAC (71-78% active ingredient = quarternary ammonia, different chain lengths) for the effects assessment as well. Another reason for this approach is that not in all references the identity of the test substance is quite obvious, as not all give a detailed characterization of the substance used and it is not clear whether DODMAC or DHTDMAC was used. This is also the case when the test substance was named DSDMAC which can be used as synonym for both. With the DHTDMAC tests it has to be born in mind that different concentrations of monoalkyl impurities (MTTMAC) may occur which possibly might contribute to the toxicity of DHTDMAC.

3.2.1 Aquatic compartment

Tests concerning the toxicity of DODMAC/DHTDMAC for aquatic organisms are listed in **Table 3.16**. For DHTDMAC only those are chosen which are relevant for the risk assessment but many more are cited in ECETOC, 1993. As an example for marine organisms only the most sensitive species is mentioned in the table as there are no great differences in the range of toxicity between marine/estuarine and limnic species.

Table 3.16 Toxicity of DODMAC/DHTDMAC to aquatic organisms

Species	Endpoint	Effect Conc.	Substance	Water quality	Reference
Lepomis macrochirus	96h LC_{50}	1.04 mg/l 0.62-3.0 mg/l 10.1 - >24 mg/l 9.4 mg/l 186 mg/l nominal conc.	DODMAC DHTDMAC DHTDMAC DHTDMAC/C_{12}LAS 2:1 DHTDMAC/C_{12}LAS 1:2	well water laboratory w. river water laboratory w. laboratory w.	Lewis & Wee, 1983
Pimephales promelas	96h LC_{50}	3.55 mg/l 6.3 - 13.8 mg/l 21.3/36.2 mg/l nominal conc.	DODMAC DODMAC DODMAC	well water well water + humic acids river water	Versteeg & Shorter, 1992
Pimephales promelas	96h LC_{50}	0.29-0.558 mg/l nominal conc.	DHTDMAC	laboratory water	Versteeg, 1989, cited in ECETOC, 1993
Pimephales promelas	34d NOEC 33d NOEC	0.053 mg/l 0.23 mg/l measured conc.	DHTDMAC DHTDMAC	well water river water	EG & G Bionomics, 1982
Pimephales promelas	7d NOEC	> 12.7 mg/l measured conc.	DODMAC	river water	Versteeg & Shorter, 1993
Gasterosteus aculeatus	96h LC_{50} 28d NOEC abnormal behaviour of larvae	3.5 mg/l 0.58 mg/l nominal conc.	DHTDMAC with 1.7% MTTMAC	lake water 1-4 mg/l suspended solids	Roghair et al., 1992
Daphnia magna	48h LC_{50} 48h LC_{50}	3.1 mg/l 0.16 mg/l measured conc.	DODMAC DODMAC	river water laboratory w.	Lewis & Wee, 1983
Daphnia magna	48h LC_{50} 48h LC_{50}	0.19/0.48 mg/l 1.06 mg/l nominal conc.	DHTDMAC DHTDMAC	laboratory w. well water	Lewis & Wee, 1983
Daphnia magna	21d NOEC	0.38 mg/l measured conc.	DODMAC	river water	Lewis & Wee, 1983
Daphnia magna	21d NOEC	0.18 mg/l nominal conc.	DHTDMAC	ground water	Akzo, 1991a
Daphnia magna	21d NOEC	0.18 mg/l 0.32 mg/l 0.32 mg/l 0.18 mg/l nominal conc.	DHTDMAC + 0%MTTMAC 1%MTTMAC 2%MTTMAC 3%MTTMAC	Laborat. water	Akzo, 1991b, cited in ECETOC 1993
Ceriodaphnia dubia	7d EC_{20} 7d EC_{50}	0.26 mg/l 0.70 mg/l measured conc.	DODMAC DODMAC	river water river water	Versteeg & Shorter, 1993
Ceriodaphnia dubia	7d EC_{20} 7d EC_{50}	0.20 mg/l 0.78 mg/l measured conc	DHTDMAC DHTDMAC	river water river water	Taylor, 1984,cited in ECETOC, 1993

Table 3.16 continued overleaf

Table 3.16 continued

Species	Endpoint	Effect Conc.	Substance	Water quality	Reference
Ceriodaphnia dubia	7d MATC	0.1-3.75 mg/l measured conc	DHTDMAC	river water + wwtp effluent	Versteeg 1987
Mysidopsis bahia	96h LC_{50} 28d NOEC life cycle, parent mortality	0.22/0.42 mg/l nominal conc. 0.075 mg/l measured conc.	DHTDMAC DHTDMAC	filtered nat. sea water filtered nat. sea water	EG & G Bionomics, 1981a EG & G Bionomics, 1983
Selenastrum capricornutum *Microcystis aeruginosa*	96h EC_{50} 96h EC_{50}	0.06 mg/l 0.05 mg/l nominal conc.	DODMAC DODMAC	laboratory water laboratory water	Lewis & Hamm 1986
Selenastrum capricornutum	96h EC_{50} 96h EC_{100}	1.12 mg/l > 16.4 mg/l measured conc.	DODMAC DODMAC	river water river water	Versteeg & Shorter, 1993
Selenastrum capricornutum	96h EC_{50} 96h NOEC 96h EC_{50} 96h NOEC	1.17 mg/l 0.6 mg/l 0.46 mg/l 0.16 mg/l nominal	DODMAC DODMAC	river water laboratory water	Akzo, 1990a,b, cited in ECETOC, 1993
Selenastrum capricornutum	96h E_bC_{50} 96h NOEC 96h EC_{50}	0.026 mg/l 0.006 mg/l 0.074 mg/l nominal conc.	DHTDMAC " "	laboratory water " "	Akzo, 1991c
Selenastrum capricornutum	 96h EC_{50} 96h EC_{50} 96h EC_{50} 96h EC_{50}	 0.014 mg/l 0.021 mg/l 0.017 mg/l 0.026 mg/l nominal conc.	DHTDMAC + 0%MTTMAC 1%MTTMAC 2%MTTMAC 4%MTTMAC	laboratory water	Akzo, 1990a,b, cited in ECETOC 1993
Selenastrum capricornutum	5d NOEC 5d EC_{100} 5d NOEC 5d EC_{100}	0.078 mg/l 0.228 mg/l 0.062 mg/l 0.708 mg/l nominal conc.	DHTDMAC " DHTDMAC "	laboratory water " river water "	EG & G Bionomics, 1981 b,c,d
Selenastrum capricornutum	5d NOEC 5d EC_{100}	0.075 mg/l 0.13 mg/l nominal conc.	DHTDMAC, 4.6% MTTMAC	laboratory water "	Procter & Gamble, 1974 - 1986, cited in ECETOC 1993
Selenastrum capricornutum	5d EC_{100}	2.58/35.7 mg/l nominal conc.	DHTDMAC	river water	EG & G Bionomics, 1981 b,c,d
Microcystis aeruginosa	5d NOEC 5d EC_{100} 5d NOEC 5d EC_{100}	0.13 mg/l 0.32 mg/l 0.078 mg/l 0.21mg/l nominal conc.	DHTDMAC DHTDMAC	laboratory water river water	EG & G Bionomics, 1981 b,c,d
Microcystis aeruginosa	5d NOEC 5d EC_{100}	0.075 mg/l 0.12 mg/l nominal conc.	DHTDMAC, 4.6% MTTMAC	laboratory water	Procter & Gamble, 1974 - 1986, cited in ECETOC 1993

Fish

The acute toxicity of DODMAC for fish was investigated in a study by Lewis & Wee (1983). A static 96h US EPA test was used with well water and *Lepomis macrochirus* (pH = 7.1 - 7.9, total hardness = 315 - 348 mg/l $CaCO_3$). A LC_{50} of 1.04 mg/l was derived (nominal concentration of active ingredient). When the same test method was used for DHTDMAC and reconstituted laboratory waters the LC_{50}-values ranged from 0.62 to 3.0 mg/l. In these cases it is not known whether different water qualities might have been used or which other test parameters were varied. These results demonstrate similar toxicities for DODMAC and DHTDMAC for *Lepomis macrochirus*.

Compared with the results described above the toxicity of DHTDMAC for *Lepomis macrochirus* was reduced in natural surface water which received municipal wastewater effluent (Town River, Massachusetts: pH = 6.4 - 7.7, total hardness = 14 -38 mg/l $CaCO_3$, 2-84 mg/l suspended solids, 0.04 - 0.59 mg/l methylene blue active substances - MBAS, 10-15 µg/l disulfine blue active substances - DBAS). 96h LC_{50}-values of 10.1 to > 24.0 mg/l were derived (Lewis & Wee, 1983). A combination with C_{12}LAS reduced the adverse effects of DHTDMAC in laboratory water tests. The 96h LC_{50}-values at molar ratios of DHTDMAC/ C_{12}LAS ranging from 2:1 to 1:2 varied from 9.4 to 186 mg/l (nominal concentrations of active ingredient). In these tests of Lewis & Wee (1983), no information is given on the purity of the test substance but isopropanol or methanol were added as carrier solvent.

In ECETOC (1993) for different molar ratios of DHTDMAC/C_{12}LAS the following 96h LC_{50}-values for *Lepomis macrochirus* are cited: 7.1 mg/l at 2:1; 17.6 mg/l at 1:2; 7.9-171 mg/l at 1:1 (no more details on test procedure, Procter & Gamble, 1974 - 1986).

The acute toxicity of DODMAC (97% purity, containing no MTTMAC) for *Pimephales promelas* was also investigated in different filtered natural river waters and well water enriched with different contents of humic acids (Versteeg & Shorter, 1992). Fish were exposed for 96 hours under static renewal conditions. In well water alone a LC_{50} of 3.55 mg/l (nominal) was derived (< 1 mg/l total organic carbon). In well water to which different amounts of dissolved humic acids extracted from natural rivers were added (1.6 - 2.2 mg/l total organic carbon) the corresponding LC_{50}-values were 6.3 to 13.8 mg/l. In river water with a total organic carbon content of 4.6 mg/l (Dry Fork Creek, Ohio; pH = 8.4 - 8.6, hardness = 173 mg/l $CaCO_3$) the LC_{50} was 21.3 mg/l. In another river with a total organic carbon content of 6.2 mg/l the LC_{50} was 36.2 mg/l (Little Miami River, Ohio; pH = 7.5 - 8.5, hardness = 175 mg/l $CaCO_3$). In these tests the toxicity of DODMAC was positively correlated with the humic acid concentration and the total organic carbon content.

To assess the long-term toxicity of DHTDMAC (71.4% active ingredient, 8% MTTMAC) embryo larval tests were conducted with *Pimephales promelas* in filtered well water and natural river water (EG & G Bionomics, 1982; Lewis & Wee, 1983). Exposure was initiated within 48 hours after fertilization and continued through 30 days post hatch in a flow-through system. In well water the most sensitive parameters were mean percent survival, length and weight of larvae. The NOEC was 0.053 mg/l (measured concentration) after 34 days test duration. In river water the NOEC for the most sensitive parameters hatchability and mean weight of larvae was 0.23 mg/l after 33 days test duration. The river water (Town River) had the following characteristics: pH = 6.4 - 6.9, total hardness = 62 mg/l $CaCO_3$, 9.4 mg/l suspended solids, 0.59 mg/l MBAS and triethyleneglycol was used as carrier solvent. The well water had a hardness of 28 -31 mg/l $CaCO_3$, pH = 6.8-7.6 and isopropanol was used as carrier solvent. In well water the measured concentrations were equal to the nominal concentrations whereas in river water measured concentrations averaged 45-67% of the nominal concentrations.

In a study with natural water from Little Miami River, Ohio, newly hatched larvae of *Pimephales promelas* were exposed to DODMAC for 7 days (Versteeg & Shorter 1993). Measured concentrations up to 12.7 mg/l did not cause toxicity. However, the carrier solvent acidic methanol reduced the dry weight of the larval fish in a dose-dependent manner relative to control fish so that the authors concluded that it would be better to test the substance in the absence of a carrier solvent. (river water quality, filtered: 5.4 mg/l total organic carbon, pH = 8.1 - 8.4, hardness = 171 mg/l $CaCO_3$.) That this NOEC is higher than that derived by EG & G Bionomics possibly is caused by exposure in different periods in the life cycle and does not necessarily show that DHTDMAC is more toxic than DODMAC. (DODMAC was synthesized by a special route which ensures no MTTMAC.)

Invertebrates

The influence of the test medium on the acute toxicity of DODMAC to *Daphnia magna* was investigated by Lewis & Wee, 1983. Surface water was collected from a North American river which received municipal wastewater effluent (White River, Indiana). The quality of the river water was: pH = 8.4 - 8.6, total hardness = 345 - 363 mg/l $CaCO_3$, 3-5 mg/l suspended solids, < 25 µg/l MBAS, 2 µg/l DBAS. As reference laboratory reconstituted water was used: pH = 6.6 - 7.9, total hardness = 131 -163 mg/l $CaCO_3$, no suspended solids, < 25 µg/l MBAS, < 1 µg/l DBAS. In semistatic tests the LC_{50}-values were 3.1 mg/l in river water and 0.16 mg/l in laboratory water after 48 hours (measured conc.).

Daphnia magna was also tested in a 21d-static renewal test with the same river water as qualified above (Lewis & Wee, 1983). Referring to the reproduction rate and mean length of the daphnids a NOEC of 0.38 mg/l DODMAC was derived (measured conc.). Parent mortality was not significantly affected up to 0.76 mg/l.

The acute toxicity of DHTDMAC (no information on purity) to *Daphnia magna* was assessed for different reconstituted waters and well water with the same US EPA test method as above (Lewis & Wee, 1983). After 48 hours, LC_{50}-values of 0.19 and 0.48 mg/l were derived for the reconstituted waters and the LC_{50} for well water was 1.06 mg/l (nominal levels of the active ingredient). From the available reference it is not possible to relate the LC_{50}-values to the different qualities of the reconstituted waters, which were given as follows. One water had a pH of 6.5 to 7.3 and a total hardness of 131 - 163 mg/l $CaCO_3$. The other water had a pH of 7.0 to 7.6 and a total hardness of 34 - 40 mg/l $CaCO_3$. (Well water: pH = 7.1 - 7.9, total hardness = 315 - 348 mg/l $CaCO_3$.) All waters contained no solids and the surfactants concentrations were below the detection limit.

In a semistatic 21d-study (OECD 202) with *Daphnia magna* DHTDMAC (76.6% active ingredient) was emulsified in reconstituted groundwater by treatment for 30 minutes in an ultrasonic vibration bath (Akzo, 1991a). All test vessels were conditioned with the test solutions 24 hours before the start of the test. The most sensitive endpoint was the reproduction rate with a NOEC of 0.18 mg/l (nominal concentration of active ingredient). The NOEC for adult mortality was 0.56 mg/l. Test substance was analyzed at the end of the test only for concentrations of 0.56 mg/l and higher showing that they had not decreased in the course of the test. Analytical determination of all test concentrations at the start of the test revealed higher measured concentrations than nominal concentrations in tests up to 0.10 mg/l.

The toxicity of DODMAC to *Ceriodaphnia dubia* was investigated in a 7-day static renewal test (Versteeg & Shorter, 1993). As test medium filtered water from the Little Miami River, Ohio, was used (5.4 mg/l total organic carbon, pH = 8.1 - 8.4, hardness = 171 mg/l $CaCO_3$). Based on reproduction the EC_{20} was 0.26 mg/l and the EC_{50} was 0.70 mg/l (measured concentrations). Survival was affected from 0.41 mg/l upwards. These results have to be treated with care as the reproduction was decreased by exposure to the carrier solvent acidic methanol alone. Results from Taylor, 1984 (cited in ECETOC, 1993) were similar for DHTDMAC tested in Ohio River water. A 7 d EC_{50} of 0.78 mg/l and an EC_{20} for reproduction of 0.20 mg/l were reported (nominal conc.). (DODMAC was synthesized by a special route which ensures no MTTMAC.)

In tests reported by Versteeg (1987) DTDMAC (this is assumed to be DHTDMAC) concentrations were produced by treatment of surfactant containing influents of two municipal wwtps in a laboratory scale continuous activated sludge system (CAS). The influent was supplemented with different amounts of 0, 1 and 3% untreated industrial plant wastewater. This resulted in different DTDMAC concentrations in the effluent matrix which were diluted with Little Miami River water. (The system was preacclimatized for 32 days.) Toxicity to *Ceriodaphnia dubia* was measured in a 7-day reproduction test with the effluents diluted with river water. MATC-values were lowest in the CAS effluents where no industrial wastewater was added additionally with 99 and 267 µg/l DTDMAC, which is similar to studies with river water. In the CAS effluents where industrial wastewater was added toxicity was reduced to between 1.0 and 3.75 mg/l, demonstrating the high influence of the effluent matrix. The concentrations of total suspended solids in the first case were 3.8 and 6.6 mg/l and in the second case 13 to 33 mg/l which might be one possibility of explanation for the different toxicities. The concentration of MTTMAC increased with decreasing toxicity.

The acute data for *Daphnia magna* show that the toxicity of DODMAC is very similar to that of DHTDMAC. This conclusion can be supported by the long-term data for *Ceriodaphnia dubia*.

Algae

The toxicity of DODMAC for *Selenastrum capricornutum* and *Microcystis aeruginosa* in laboratory water was investigated according to an ASTM method (Lewis & Hamm, 1986). For growth reduction after 96h the EC_{50} was 0.06 mg/l for *Selenastrum capricornutum* and 0.05 mg/l for *Microcystis aeruginosa* (nominal concentrations; pH = 6.8 - 7.2, hardness = 131 - 146 mg/l $CaCO_3$).

An algae study with DODMAC in filtered natural water of the Little Miami River, OH (5.4 mg/l total organic carbon, pH = 8.1 - 8.4, hardness = 171 mg/l $CaCO_3$) was conducted by Versteeg & Shorter, 1993. For *Selenastrum capricornutum* a 96h EC_{50} of 1.12 mg/l was derived for growth reduction (measured concentration) and the algistatic concentration was above 16.4 mg/l. In this study acidic methanol was used as carrier solvent, which had a growth stimulating effect on the algae. (DODMAC was synthesized by a special route which ensures no MTTMAC.)

Another study with DODMAC is cited in ECETOC, 1993, but no test protocol is available (Akzo, 1990a). *Selenastrum capricornutum* was tested in laboratory and river water but water qualities are not characterized. In laboratory water the EC_{50} was 1.17 mg/l, in river water an EC_{50} of 0.46 mg/l was measured after 96 hours (nominal conc.).

Selenastrum capricornutum was also tested with DHTDMAC (no information on purity) in laboratory water according to OECD guideline 201 (Akzo, 1991c). Although the study was initiated by the same sponsor as above it is not clear whether the same test method was used with DODMAC. DHTDMAC was emulsified in the stock solution by a 60-minute ultrasonic treatment. The test flasks were conditioned by incubation with the test solutions prior to the test. For biomass reduction a 96h NOEC of 0.006 mg/l, an EC_{10} of 0.013 mg/l and an EC_{50} of 0.026 mg/l were derived. For effects on the growth rate an EC_{50} of 0.074 mg/l resulted. The effect values were based on nominal concentrations of the active ingredient although in a preliminary range finding test DHTDMAC concentrations had decreased below the detection limit of 20 µg/l in flasks which were not incubated with algae. A shorter sonication of $\leq$ 10 minutes resulted in a higher 96h EC_{50}- and NOEC-value of 0.21 mg/l and 0.12 mg/l (no details on test conditions; Akzo, 1991d, cited in ECETOC, 1993).

The influence of different test media on the sensitivity of *Selenastrum capricornutum* towards DHTDMAC (71.4% active ingredient) was investigated by EG & G Bionomics, 1981 b,c,d. Laboratory water with a hardness of 20 mg/l $CaCO_3$ (no further characterization) and algae nutrient enriched White River water (Indiana) of the following quality prior to autoclaving were used: pH = 7.3, total hardness = 299 mg/l $CaCO_3$, 68 mg/l suspended solids, 0.2 µg/l MBAS). In laboratory water a NOEC of 0.078 mg/l and an algistatic concentration of 0.228 mg/l were derived for the reduction of cell number after 5 days (nominal concentrations of active ingredient). The corresponding values for the river water were: NOEC = 0.062 mg/l and algistatic concentration = 0.708 mg/l. The table above shows that results for *Microcystis aeruginosa* are similar (EG & G Bionomics, 1981 b,c,d).

In ECETOC (1993), also the toxicity of DHTDMAC containing 4.6% MTTMAC to *Selenastrum capricornutum* and *Microcystis aeruginosa* in laboratory water is cited (no details on test conditions, Procter & Gamble, 1974 - 1986). The 5 d EC_{50}-values were 0.13 and 0.12 mg/l and the NOECs for both species were 0.075 mg/l, which are a factor of 2-3 lower than the effect values for DHTDMAC containing 8% MTTMAC derived in EG & G Bionomics, 1981 b,c,d.

In tests with two other river waters, for which the water quality was not characterized in the test protocol, the 5-day algistatic concentrations were 2.58 mg/l and 35.7 mg/l (nominal concentrations of active ingredient, EG & G Bionomics, 1981 b,c). From the reference Lewis and Wee, 1983, it could be concluded possibly that it might be autoclaved Rapid Creek water in one case and in the other the same water enriched after filtration with 131 mg/l sediment. (Rapid Creek, South Dakota: pH = 6.6 - 7.3, total hardness = 388 - 442 mg/l $CaCO_3$, 131 mg/l suspended solids, < 20 µg/l DBAS). In the tests EG & G Bionomics, 1981 b,c,d isopropanol was used as carrier solvent and DHTDMAC contained 8% MTTMAC.

The toxicity of DTDMAC (this is assumed to be DHTDMAC) incorporated in wwtp effluent to *Selenastrum capricornutum* was reported by Versteeg (1987). Test solutions were prepared from laboratory scale CAS-units as described above for *Ceriodaphnia dubia.* After 96 hours the EC_{20}-values for growth reduction were in the range of 0.047 and 2.91 mg/l. The toxicity decreased with increasing amounts of added industrial wastewater. In a comparable study from Versteeg & Woltering (1990) DTDMAC concentrations in CAS-unit effluents up to 20.3 mg/l had no effect on *Selenastrum capricornutum*. The test concentrations were produced by treatment of surfactant containing influents of two municipal wwtps in a laboratory scale continuous activated sludge system (CAS). The influent was supplemented with different concentrations of untreated industrial plant wastewater. This resulted in different DTDMAC concentrations in the effluent matrix. The system was preacclimatized for 32 days. Toxicity to Ceriodaphnia dubia was measured in a 7-day reproduction test with the effluents diluted with river water. MATC-values were lowest in the CAS effluents where no industrial wastewater was added additionally with 99 and 267 µg/l DTDMAC, which is similar to studies with river water. In the CAS effluents where industrial wastewater was added toxicity was reduced to between 1.0 and 3.75 mg/l, demonstrating the high influence of the effluent matrix. The concentrations of total suspended solids in the first case were 19 and 21 mg/l and in the second case 38 to 111 mg/l might be one possibility of explanation for the different toxicities. The concentration of MTTMAC increased with decreasing toxicity.

PNEC derivation:

The algae data demonstrate that the difference in the EC_{50}-values of DODMAC and DHTDMAC for laboratory and river water is lower (factor 3 at maximum) than for fish and daphnids. Whereas the toxicity of DODMAC and DHTDMAC seems to be similar for fish and daphnids the sensitivity of algae might be higher for DHTDMAC. However the results for algae described above are not comparable directly as in no reference both substances were tested in parallel under the same conditions. Contradicting results are reported in ECETOC, 1993, for *Selenastrum capricornutum* in laboratory water, where MTTMAC concentrations increasing from 0% to 4% (added to DHTDMAC) resulted in very similar EC_{50}-values although MTTMAC is reported to be more toxic than DODMAC for algae (Akzo, 1990a,b). Also the chronic toxicity of DHTDMAC in laboratory water for *Daphnia magna* does not increase with increasing concentrations of the more toxic MTTMAC (Akzo, 1991b; cited in ECETOC, 1993). Another point is that MTTMAC adsorbs stronger onto solids than DODMAC[5] so that the bioavailability is relatively lower. Because of the discrepancy of the test results it can only be concluded that the data currently available do not allow firm conclusions to be drawn upon possible different toxicities of DODMAC and DHTDMAC but point to the extreme caution needed for the interpretation of toxicity test results on DHTDMAC. However, when all facts are considered the influence of the water quality seems to be more important than that of MTTMAC.

The above cited test results have a high variability and the interpretation is complicated as the test reports do not always provide all details which would be needed. The difference in different water qualities was most probably caused by adsorption losses and complexation with dissolved colloidal anionic surfactants and humic substances which may reduce bioavailability and thus the effective doses. Although the adsorption onto suspended matter can be modelized for the PEC-calculation (cf. Section 3.1.1.3), the complexation with anionics can not be calculated. The tests in river water probably reflect both properties (cf. Section 3.2.1), so that the substance should be assessed with these respective results, having in mind that these results may be due to the special local properties of the water and that it is not possible to simulate the most realistic exposure conditions. The water qualities of the river water tests reflect the range of variability in natural surface waters. Toxicity tests with effluent from a wwtp are not more useful because this matrix increases the complexicity of the problem. It is much more difficult to take such results which are dependent on a combination of two matrices as representative for other environmental situations.

Not the lowest aquatic NOEC in tests with laboratory water of 6 µg/l for *Selenastrum capricornutum*, but the lowest NOEC from river water tests (62 µg DHTDMAC/l, *Selenastrum capricornutum*) is taken into account in order to calculate the predicted no effect concentration (PNEC). This value is supported by other long-term test results with DHTDMAC with *Microcystis aeruginosa* and *Mysidopsis bahia* for which almost the same values are reported.

According to the EU TGD, the value of the assessment factor F is to be determined to 10 for the aquatic compartment, as data from long-term toxicity tests of 3 trophic levels are available and a PNEC is calculated as follows:

[5] Larson & Vashon (1983) estimated the adsorption coefficient for dodecyl trimethyl ammonium chloride onto sediments to 65,724 resp. 225,677 l/kg (DODMAC 3,833 - 12,489 l/kg).

$$\textbf{PNEC}_{\textbf{river water}} = 62\ \mu g/l / 10 = \mathbf{6.2\ \mu g/l}$$

Also other PNEC derivations are possible: In case it would be proven that toxicity of DODMAC for algae is lower than that of DHTDMAC the lowest river water NOEC would be 0.26 mg/l DODMAC for *Ceriodaphnia dubia* (PNEC = 26 µg/l). Relevant for the risk assessment are also DHTDMAC test results with wwpt effluent diluted with river water where the lowest EC_{20}-values were 0.047 and 2.91 mg/l for *Selenastrum capricornutum*. Similar MATC-values of 0.1 and 3.7 mg/l were obtained for *Ceriodaphnia dubia*. No comparable test was conducted with fish.

A statistical PNEC extrapolation is proposed by van Leeuwen et al., 1992, which gives a maximum tolerable risk level of 50 µg/l based on river water NOECs. However, it is questionable, whether the necessary assumptions for this approach are justified.

<u>Sediment organisms</u>

Concerning toxicity of DODMAC (> 96% pure) to sediment organisms there is one test with natural stream sediment (Pittinger et al., 1989). Sediment originated from Rapid Creek, South Dakota, with an organic carbon content of 4.2% prior to testing (71% clay, 19% fine silt, 4% medium and 6% fine sands). 72-h old larvae of *Chironomus riparius* were exposed for 24 days to prespiked sediment (stirred overnight) in a flow-through system. A single subchronic DODMAC concentration was replenished to the overlying laboratory water in all tests. A significant reduction in midge emergence was observed at 2.7 g/kg sed. dry weight (measured concentration), the NOEC was 876 mg/kg sed. dry weight. The concentration in the overlaying water was 0.29 mg/l and in the interstitial water 0.06 mg/l. In an experiment with water only a 24-day NOEC of 0.45 mg/l was derived related to midge emergence (measured conc.).

In the absence of sediments the effects of DODMAC on egg hatchability of *Chironomus riparius* were assessed in a static renewal test with laboratory water without sediment (Pittinger et al., 1989). The highest concentration of 21.5 mg/l had no effect on the egg hatching success. The survival of the hatched larvae was more sensitive and the LC_{50} after 72 hours was 11.3 mg/l (measured concentration).

The toxicity of DODMAC to the oligochaete Lumbriculus variegatus was examined in a 28d test using natural sediment (organic carbon content: 1.73 %). 10 intact worms per vessel were exposed to nominal DODMAC sediment concentrations between 150 and 5,800 mg/kg dw. for 28 days. A mixture of radio-labelled and non-labelled DODMAC was used for the experiment and the analytical determinations were made using the radio-labelled DODMAC. The endpoints of this test were survival, reproduction and growth. Survival and reproduction were treated as single endpoint, that is, the total number of worms per vessel at the end of the test.

At the highest tested concentration no significant decline in worm number or biomass compared to the control was found. Observations throughout the test period showed that the worms did not even avoid the sediment at this concentration. Analytical monitoring showed that the concentration of DODMAC in the sediment did not decline significantly. For the highest tested concentration an average value of 4,830 ± 550 mg/kg was measured after 28 days. Therefore, from this test a NOEC of about 5,000 mg/kg dw can be derived (Conrad et al., 1999).

The toxicity of DODMAC to the oligochaete *Tubifex tubifex* was assessed using a 28d sediment bioassay (Comber/Conrad, 2000). The same sediment as in the test with *Lumbriculus* was used. A mixture of radio-labelled and non-labelled DODMAC was used for the experiment and the analytical determinations were made using the radio-labelled DODMAC. 4 adult worms per test vessel (6 vessels per concentration) were exposed to the spiked sediment containing nominal DODMAC concentrations between 0 and 5,000 mg/kg dw. The examined endpoints were survival of the worms, number of juveniles and body weight. At the end of the test samples of overlying water and sediment were taken for analysis. The measured sediment concentrations ranged between 224 mg/kg dw and 3,600 mg/kg dw. All effect values were related to the measured concentrations.

Up to the highest test concentration no effects on the survival of *Tubifex* were observed. Also in the dry weight of the adult worms no statistically significant difference was found between the control and the worms exposed to DODMAC. However, for the endpoint number of juveniles, a concentration effect was observed. A NOEC of 1,515 mg/kg dw and a LOEC of 2,484 mg/kg dw was found. Using a linear interpolation method, a mean EC_{10} of 550 mg/kg dw and an EC_{50} of 3,022 mg/kg dw was calculated.

A further sediment test with *Caenorhabditis elegans,* a bacterivorous nematode that is primary found in terrestrial soils but also in aquatic sediments, was recently performed with DHTDMAC (BSB, 2000). An artificial sediment with an organic content of 2 % was used. Test endpoints were growth, egg production and fertility. Before the start of the test, 0.25 ml of a bacterial suspension (E. coli in M9-medium) was added to each test vessel as food for the nematodes. Afterwards, 10 juvenile nematodes of the first stage were added to the vessels, containing 0.5 g sediment, 0.5 ml test solution and 0.25 ml bacterial suspension. The vessels were incubated for 72 h at 20 °C on a shaker. At the end of the test, the nematodes were heat killed and stained with "Rose Bengal". After extracting the nematodes from the sediment, body length and number of eggs inside the body were determined. A NOEC of 1,350 mg/kg dw and a LOEC of 2,030 mg/kg dw related to nominal concentrations was found.

DHTDMAC (77% active ingredient, 1.7% MTTMAC) was applied in a partial life cycle test with *Chironomus riparius* in natural lake water (Roghair, 1992). The water of the Lake Veluwe (Netherlands) contained 1-4 mg/l suspended solids and 7.1 - 9.3 mg/l DOC (pH = 8.5, 320 mg/l $CaCO_3$). Eggs not older than 24 hours were exposed in a static renewal system for 28 days. In one experiment larval weight, mortality, behaviour and appearance were affected with similar sensitivity and the NOEC for all was 0.8 mg/l (nominal concentration of active ingredient). In a second experiment the most sensitive endpoint was retardation in development with a NOEC of 1.4 mg/l. Besides a 96h LC_{50} of 7.1 mg/l was given by the authors for the second instar larvae.

The effects of natural sediment and river water containing DHTDMAC on *Paratanytarsus parthenogenica* were assessed in a static test system over 20 days (Lewis & Wee, 1983). Samples collected from different points along the Rapid Creek, South Dakota, contained 2 to 67 mg/kg DHTDMAC in the sediment and 0.008 to 0.092 mg/l in the water. Midge eggs exposed to these concentrations showed no significant difference in larval survival and adult emergence relative to the control with laboratory water.

Roghair et al. (1992) determined the acute effect of the technical product (77 % DHTDMAC, 1.7 % MTTMAC) on the pond snail *Lymnea stagnalis* in pond water without sediment. A 96h-LC_{50} of 18 mg/l and a 96h-EC_{50} of 7.5 mg/l (reduced movements and withdrawal into the shell) was found. In 2 additional tests over a period of several weeks (29 resp. 26 days) the authors studied the effect of the test substance on snail mortality and reproduction. At the lowest non-lethal concentration of 1 mg/l the following sublethal effects were observed: retracted and curled antennae, depressed locomotory activity, withdrawal into the shell and decreased food intake. A NOEC of 320 µg/l was obtained.

For the derivation of the $PNEC_{sed}$ only such tests can be used in which the test organisms were exposed to whole sediment spiked with the test substance. Among the above cited tests with sediment organisms four tests are appropriate for the effects assessment of sediment: the studies by Pittinger et al., Conrad et al., Comber/Conrad and BSB. For *Chironomus riparius* a NOEC of 876 mg/kg dw was found. *Lumbriculus variegatus* was less sensitive to adsorbed DODMAC. A NOEC of about 5,000 mg/kg dw was found for this sediment ingesting worm. For the nematode *Caenorhabditis elegans* a NOEC of 1,350 mg/kg dw was derived. The NOEC found for the oligochaete *Tubifex tubifex* was with 1,515 mg/kg dw in the same range with the NOECs from the other tests. However, a EC_{10}-value of 550 mg/kg dw could be calculated that is used a basic value for the PNEC derivation.

The other available tests with sediment organisms were conducted in the absence of sediment. As sediment was missing, the bioavailability and toxicity of DODMAC cannot be assessed with these tests. Sediment bioassays have to address all possible routes of exposure (uptake via body surfaces to substances dissolved in the overlying water and in the pore water and to adsorbed substances by direct contact or via ingestion of contaminated sediment particles) However, exposure to bound substance is not considered in tests being conducted in water only.

For the derivation of the PNECsed an assessment factor of 10 is applied to the EC_{10} of 550 mg/kg dw obtained for *Tubifex tubifex*, as long-term tests with species representing three different living and feeding conditions and therefore different exposure pathways are available.

Therefore: **$PNEC_{sed}$ =** 550 mg/kgdw / 10 = **55 mg/kgdw**

In accordance to the TGD, the $PNEC_{sed}$ can be estimated approximately from the $PNEC_{water}$ with the equilibrium partitioning method. With a $PNEC_{river\ water}$ of 6.2 µg/l and a partitioning coefficient of 10,000 l/kg (related to dw), the $PNEC_{sed}$ would be estimated to 62 mg/kg dw. However, as DODMAC strongly adsorbs to sediments, according to the TGD an additional factor of 10 was applied to take uptake via ingestion of sediment into account. Therefore the $PNEC_{sed}$ has to be reduced to 6.2 mg/kg dw. However, the $PNEC_{sed}$ derived from sediment tests has a higher priority and is therefore used for the risk assessment.

Microorganisms

There are several tests concerning toxicity of DHTDMAC to bacteria which can be used for the derivation of a $PNEC_{WWTP}$, but no test was conducted with DODMAC. In each case laboratory water was used.

Table 3.17 Toxicity of DHTDMAC to bacteria

Inoculum	Endpoint	Effect Conc.	Substance	Reference
Pseudomonas putida	18h EC_{50}	48 / 58 mg/l	DHTDMAC	UBA, 1992
Secondary effluent	5d EC_{50}	2.0 / 6.5 mg/l	DHTDMAC	UBA, 1992
Activated sludge	3h EC_{50}	520 mg/l	DHTDMAC	UBA, 1992
Nitrifying bacteria	>119h IC_{50}	2.1 mg/l	DHTDMAC	Wagner & Kayser, 1990
Anaerobic bacteria	3h EC_{10} 3h EC_{50} 3h EC_{100}	80 mg/l 220 mg/l 420 mg/l	DHTDMAC	Hoechst, 1989

The toxicity of DHTDMAC to *Pseudomonas putida* was investigated in a growth inhibition test according to a German DIN-guideline (Bringmann & Kühn method; UBA, 1992). In two tests EC_{50}-values of 48 and 58 mg/l were derived after 18 hours (nominal values, graphically extrapolated).

Secondary effluent of a domestic wastewater treatment plant was used as inoculum in a closed-bottle inhibition test (OECD 301D, UBA, 1992). The graphically extrapolated EC_{50}-values of two tests were 2.0 and 6.5 mg/l (nominal concentrations) after a test duration of 5 days.

In an activated sludge respiration inhibition test (OECD 209) inoculum from a predominantly domestic wastewater treatment plant was used (UBA, 1992). A 3h EC_{50} of 520 mg/l was derived graphically from the dose response curve. The corresponding statistically derived value was 267 mg/l (nominal concentrations).

The toxicity of DHTDMAC to nitrifying bacteria enriched in a laboratory wastewater treatment plant (domestic sludge originally) was investigated in a manometric respirometer test (Wagner & Kayser, 1990). The test duration in the reference was referred to between 119 and 254 hours for different substances and was stopped when the nitrification of the controls was completed. The IC_{50} for inhibition of respiration was 2.1 mg/l active ingredient of DHTDMAC (a carrier solvent was used).

Anaerobic bacteria from a domestic wastewater treatment plant were exposed to DHTDMAC in an OECD 209 test (Hoechst, 1989). The inhibition of respiration was measured after 3 hours and the EC_{10} was 80 mg/l, the EC_{50} = 220 mg/l.

Using different safety factors according to the sensitivities of the test systems and the mean effect values the lowest PNEC-values are as follows:

Pseudomonas putida	EC_{50} = 53 mg/l, SF = 100	PNEC = 0.53 mg/l
Nitrifying bacteria	EC_{50}= 2.1 mg/l, SF = 10	PNEC = 0.21 mg/l
Secondary effluent	EC_{50}= 4.3 mg/l, SF = 100	PNEC = 0.043 mg/l

With all these PNECs it has to be considered that the microorganism toxicity derived in laboratory water tests has to be handled with care as a high influence of the composition of the wastewater (e.g. suspended particles, complexing agents) can be assumed, which is the same phenomenon as in surface water tests. Moreover the lowest $PNEC_{microorganisms}$ of 0.043 mg/l seems to be unrealistic as it is reported that wastewater treatment plants operate at DHTDMAC concentrations of 3 to 8 mg/l (Section 3.1.2.1). However, it is not documented whether the treatment process would be more effective without this DHTDMAC load in the influent and how less adapted plants might react. Nitrifying bacteria were found to be the most sensitive microorganisms with the lowest EC_{50} of 2.1 mg/l on which the risk assessment should be based (**$PNEC_{microorganism}$ = 0.21 mg/l**) to ensure that the most sensitive treatment process can take place.

3.2.2 Atmosphere

There are no effect data available.

3.2.3 Terrestrial compartment

As there is no terrestrial test with DODMAC results with DHTDMAC are cited below, because so far there is no proof that the toxicity of both substances varies significantly. The effect values are all nominal values and are not converted to a standard soil of a defined organic carbon content, because this does not seem to be adequate as the bioavailability of DODMAC/DHTDMAC is not determined by the organic matter content alone but also by other soil parameters e.g. ionic binding. The different test concentrations were prepared at maximum one day before the start of the test and adsorption was rapid.

Table 3.18 Toxicity of DHTDMAC to terrestrial organisms

Species	Endpoint	Effect Conc.	Substance	Reference
Sinapis alba *Triticum aestivum* *Linum utisatissimum*	14d EC_5 14d EC_{50} 14d EC_5 14d EC_5	1,400 mg/kg 3,540 mg/kg > 1,000 mg/kg > 1000 mg/kg	DHTDMAC	Pestemer et al., 1991
Sorghum bicolor *Helianthus annuus*	28d EC_{50} NOEC 28d EC_{50} NOEC	2,530 mg/kg 1,000 mg/kg 2,930 mg/kg 1,000 mg/kg	DHTDMAC	Windeatt, 1987
Avena sativa *Brassica rapa*	14d NOEC 14d NOEC	≥ 1,000 mg/kg ≥ 1,000 mg/kg	DHTDMAC	Stanley & Tapp, 1982
Eisenia fetida	14d NOEC	≥ 1,000 mg/kg	DHTDMAC	Coulson et al., 1989
Lycopersicum escul. *Lactuca sativa* *Hordeum vulgare*	NOEC (growth)	≥ 40 g/kg (dw)	DHTDMAC	Topping & Waters, cited in ECETOC 1993
soil microorganisms	14w NOEC 28d NOEC	≥ 400 mg/kg ≥ 365 mg/kg	DHTDMAC DHTDMAC	Procter & Gamble, 1992 Täuber et al., 1986

The toxicity of DHTDMAC (75% purity; named DSDMAC in the reference) to plant seedlings was tested by Pestemer et al. (1991) in a loamy sandy soil (1.3% organic carbon, 9.9% clay, 54.3 sand, 35.7 silt). Seedlings with developed cotyledons were exposed for 14 days. Related to fresh weight reduction the most sensitive species was *Sinapis alba* with an EC_5 of 1,400 mg/kg dry weight and an EC_{50} of 3,540 mg/kg dry weight. For *Triticum aestivum* and *Linum utisatissimum* the EC_5-values were above 1,000 mg/kg dw. In a germination test DHTDMAC concentrations up to 3.2 g/l had no inhibiting effect on *Lepidium sativum* (Pestemer et al. 1991).

In another study (Windeatt, 1987) the influence of DHTDMAC (76.1% active ingredient = quartenary ammonium) on the emergence of plant seedlings and the early growth stages of

Sorghum bicolor and *Helianthus annuus* were investigated. Potting compost with about 80% sand/gravel and 20% silt/clay including 4% organic matter was used as substrate. The highest test concentration of 10 g active ingredient of DHTDMAC per kg dry soil had no significant effect on the emergence of seeds after 7 days. After further 21 days the EC_{50} for fresh weight reduction of the seedlings was 2530 mg/kg for *Sorghum bicolor* and 2,930 mg/kg for *Helianthus annuus* (active ingredient in dry soil). 1,000 mg/kg was the highest test concentration with no growth effect. For *Phaseolus aureus* the 28 d EC_{50} was > 10 g/kg.

Similar results were reported for *Avena sativa* and *Brassica rapa* (Stanley & Tapp, 1982, cited in ECETOC, 1993). Plant seedlings exposed after germination for 14 days showed no reduction of growth at 1,000 mg DHTDMAC/kg dry soil (OECD draft guideline, 1981, no further details available).

Eisenia fetida was exposed to DHTDMAC (solved in methanol, 76.1% active ingredient) incorporated into artificial soil consisting of 9.4% organic matter, 70% fine sand and 20% kaolinite clay (Coulson et al., 1989). At the only concentration of the definitive test with 1,000 mg active ingredient/kg dry soil no mortality, no significant reduction in body weight nor any behavioral effects were observed after 14 days.

Concerning the toxicity of DHTDMAC to soil microorganisms two studies are cited in the ECETOC report (1993) for which no test protocols are availble. However, they can give a rough indication on possible effects. Soil respiration was measured with soil samples amended with 12.3 g activated sludge and 365 mg DHTDMAC per kg standard soil (Täuber et al, 1986). After 28 days no depression of oxygen uptake could be measured. In a study of Procter & Gamble (1992) two different soils containing 400 mg DHTDMAC/kg produced 96 and 119% carbon dioxide compared to the controls over 14 weeks.

Assuming that two trophic levels are covered with long-term data for plants (Windeatt, 1987) and micro-organisms, an assessment factor of 50 could be applied and the following PNEC is calculated:

$$\mathbf{PNEC_{soil}} \geq 1{,}000 \text{ mg/kg} / 50 \geq \mathbf{20\ mg/kg}$$

With this approach it was accepted that not every test could be validated, but if the terrestrial data are evaluated as a whole this seems to be acceptable in this special case. In case it would turn out that DHTDMAC might be more toxic than DODMAC the PEC/PNEC-ratio for DODMAC should be even saver.

3.2.4 Secondary poisoning

The bioconcentration of DODMAC in fish is only low (cf. Section 3.1.1.4). Thus biomagnification via the route fish $\rightarrow$ fish-eating mammal or bird can be excluded.

In addition, bioaccumulation tests with the endobenthic species *Lumbriculus variegatus* and *Tubifex tubifex* also show a low bioaccumulation potential.Therefore, bioaccumulation via the food chain is not to be expected for DODMAC.

3.3 RISK CHARACTERISATION

Interpreting the following results it has to be kept in mind that the exposure calculation is only based on DODMAC which is the major component of DHTDMAC. As all emissions into the environment are DHTDMAC emissions, and the toxicity of the other components is similar, the risk caused by the technical product is underestimated.

3.3.1 Aquatic compartment

3.3.1.1 Production

Site A

$PEC_{local,bulk}/PNEC_{river\ water}$ = 0.22 / 6.2 = 0.035
$C_{eff}/PNEC_{wwtp}$ = 2.3 / 210 = 0.011
$PEC_{local,sed}/PNEC_{sed}$ = 2.9 / 55 = 0.05

Sites B, C, D and E

Generally no emissions into the hydrosphere occur.

Site F

$PEC_{local,bulk}/PNEC_{river\ water}$ = 0.15 / 6.2 = 0.024
$C_{eff}/PNEC_{wwtp}$ = 0.05 / 210 = 0.0002
$PEC_{local,sed}/PNEC_{sed}$ = 2.0 / 55 = 0.036

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.

3.3.1.2 Processing to activated bentonites

Site 1

The results are:

$PEC_{local,bulk}/PNEC_{river\ water}$ = 0.14 / 6.2 = 0.023
$PEC_{local,sed}/PNEC_{sed}$ = 1.7/55 = 0.03

The risk assessment indicates that a risk to the environment is not to be expected.

Site 2

$PEC_{local,bulk}/PNEC_{river\ water}$ = 0.19 / 6.2 = 0.031
$PEC_{local,sed}/PNEC_{sed}$ = 2.5 / 55 = 0.045

The risk assessment indicates that a risk to the environment is not to be expected.

Site 3

There are no emissions into the hydrosphere.

Site 4

$PEC_{local,bulk}/PNEC_{river\ water}$ = 0.19 / 6.2 = 0.031
$PEC_{local,sed}/PNEC_{sed}$ = 2.5 /55 = 0.045

The risk assessment indicates that a risk to the environment is not to be expected.

Site 5

$PEC_{local,bulk}/PNEC_{river\ water}$ = 0.43 / 6.2 = 0.069
$PEC_{local,sed}/PNEC_{sed}$ = 5.7 / 55 = 0.1

The initial risk assessment indicates that a risk to the environment is not to be expected..

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.

3.3.1.3 Use of activated bentonites as lacquer additive

$PEC_{local,bulk}/PNEC_{river\ water}$ = 0.14 / 6.2 = 0.023
$PEC_{local,sed}/PNEC_{sed}$ = 1.7 / 55 = 0.03

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.

3.3.1.4 Emissions via household sewage

The PEC/PNEC (both based on river water, cf. Sections 3.1.6 and 3.2.1) ratios for the use of fabric softeners, car washing agents and hair conditioners are (all figures related to DODMAC):

Table 3.19 PEC/PNEC ratios for use of fabric softeners, car washing agents and hair conditioners

	1989/90	1998
$PEC_{local,bulk}/PNEC_{river\ water}$	10.5 / 6.2 = 1.7	0.54 / 6.2 = 0.087
$C_{eff}/PNEC_{wwtp}$	42 / 210 = 0.2	4.0 / 210 = 0.019
$PEC_{local,sed}/PNEC_{sed}$	137 / 55= 2.5	7.0 / 55= 0.12

The risk assessment based on consumption figures for the former use (period 1989/90) indicates that even if the household sewage is purified in a municipal wwtp, a risk to both aquatic and benthic organisms is expected. For the aquatic compartment an improvement of effect data is not possible as there are data from 3 trophic levels already available. Also the exposure data can not be improved to lead to a PEC/PNEC ratio of < 1. It has to be concluded that the former use of DHTDMAC as fabric softener led to a risk for the aquatic environment. However, the risk assessment is performed on the basis of recent emission data, and no conclusion is drawn from this scenario.The risk assessment based on the consumption figures from 1998 (uses as fabric softener, car washing agents, hair conditioners) doesn't indicate a risk for aquatic and sediment organisms.

However, it should be considered that the present risk assessment is based on DODMAC only which is the major component of the technical product DHTDMAC. A risk assessment of DHTDMAC would lead to PECs which are higher by a factor of 2.4, while the PNECs are identical (as the toxicity of both substances is equal, cf. Section 3.2).

The DHTDMAC emissions via household sewage decreased substantially in the last decade, since the substance was largely replaced in fabric softeners. The consumption figures for the period 1996 to 1998 (cf. Section 2) show no clear tendency. It has to be ensured that the use of DHTDMAC in fabric softeners, car washing agents and hair conditioners should not increase in the future.

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.

3.3.2 Atmosphere

Because an extremely low volatility of DODMAC is to be expected, no significant exposure of the atmosphere is assumed.

3.3.3 Terrestrial compartment

The $PEC_{local,soil}/PNEC_{soil}$ ratio due to the emissions via household sewage is

for 1989/90: PEC/PNEC = 5.3 / 20 = 0.27
for 1998: PEC/PNEC = 0.49 / 20 = 0.025

The risk assessment indicates that a risk to soil organisms due to the current uses of DHTDMAC in fabric softeners, car washing agents and hair conditioners is not to be expected.

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.

3.3.4 Secondary poisoning

The bioconcentration of DODMAC in fish is only low (cf. Section 3.1.1.4). Thus biomagnification via the route fish $\rightarrow$ fish-eating mammal or bird can be excluded.

In addition, bioaccumulation tests with the endobenthic species *Lumbriculus variegatus* and *Tubifex tubifex* also show a low bioaccumulation potential.Therefore, bioaccumulation via the food chain is not to be expected for DODMAC.

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.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 General discussion

DODMAC is not produced or used as an isolated product but is applied exclusively as the main component in DHTDMAC (42 % DODMAC). Therefore the occupational exposure is described for the manufacture and use of DHTDMAC. The exposure assessment is performed for the component DODMAC (see Sections 4.1.1.2.3 and 4.1.1.2.4).

DHTDMAC is marketed in three forms:

- paste-like preparation containing app. 75 % DHTDMAC (32 % DODMAC)
- aqueous emulsion containing app. 16 % DHTDMAC (7 % DODMAC)
- powder containing app. 95 % DHTDMAC (40 % DODMAC)

As a chemical intermediate DHTDMAC is used for the production of organic clays. The substance is mainly applied in diluted preparations (2 - 8 %), no direct uses of DHTDMAC are known for this application. DHTDMAC is used in the laundry / cleaning products industry (fabric softeners, car cleaning products) as well as in the chemico-technical and the cosmetic industries (e. g. hair cosmetics).

The produced quantities of DHDTMAC have declined during the last years from 35 040 t in 1993 to 5 651 t in 1998 (actual information on the quantity imported into the EU are not available). This decrease is caused by replacing DHTDMAC by other substances, especially in the case of fabric softeners (see Chapter 2). No actual pattern concerning the quantities used in the different industrial areas is known and detailed information on the quantities used in car cleaning agents is not available. It cannot be excluded, that at present significant quantities of the substance are still processed further to preparations which are used in the mentioned sectors within the EU. Therefore the assessment of occupational exposure includes uses of DHTDMAC in fabric softeners, in personal care products and in car cleaning products.

Additional uses of DHTDMAC are mentioned in the literature: the refining of cane sugar, use as antistatic agents, corrosion inhibitors and disinfection agents. These uses are regarded to be not relevant.

On account of the physico-chemical properties of the substance (ionic substance, vapour pressure estimated by EPI program to 10^{-15} Pa, EPA 1996) inhalative exposure to vapours is assumed to be negligible and exposure to dusts at the workplace during the handling of the powdery substance must be taken into consideration. Taking into account the corrosive effect of the paste-like preparation containing 75 % DHTDMAC (32 % DODMAC), it is expected that repeated daily dermal contact is avoided. Dermal exposure is to be considered when the powdered substance or diluted preparations are handled.

Consumers are exposed to DHTDMAC (DODMAC) contained in linen softeners and hair cosmetics.

4.1.1.2 Occupational exposure

Occupational exposure limit values for DODMAC are not known.

4.1.1.2.1 Production and further processing in the chemical industry and further processing in the cosmetic industry

Production

DHTDMAC is batch-wise manufactured in closed systems at elevated temperature and pressure during app. 10 hours. The primary product is a paste-like preparation containing 75 % DHTDMAC (32 % DODMAC) in a water/isopropanol mixture being further processed to a powder containing 95 % DHTDMAC (40 % DODMAC) or to an aqueous preparation containing 16 % DHTDMAC (7 % DODMAC). The powder is obtained by subsequent spray drying and the aqueous emulsion is manufactured by mixing the liquefied paste-like preparation with water (BUA, 1995).

Three manufacturers provide information about the production process: Two of them produce the paste-like preparation throughout the year. The third provides information about the production of the powdery substance (95 % DHTDMAC, 1994: 150 t), produced only by one company at one production site. The substance is produced campaign wise (5-6 times/year) with a duration of approximately 2-10 days, resulting in max 60 days/year. During production six workers over three shifts/working day (2 workers over 8 hours/shift) are employed. During bagging respiratory equipment is worn (Hoechst Marion Roussel, 1998). The collective of exposed people amounts to 20 worker per plant when the paste-like preparation is produced. According to information provided by the manufacturer, only 3 workers are involved in the production of the powder. The workers wear gloves and safety goggles.

On account of the physico-chemical properties of the substance (ionic substance, vapour pressure estimated to 10^{-15} Pa, EPA 1996) inhalative exposure to dusts at the workplaces during the handling of the powdery substance must be taken into consideration. On account of the corrosive effect of the paste-like primary product (75 % DHTDMAC, 32 % DODMAC), which is also assumed for the 16 % aqueous solution, it is assumed that during the production of DHTDMAC daily repeated skin contact is avoided to a large extent by using personal protective equipment. In this case dermal exposure is assessed to be low. During activities like filling, transfer, cleaning, maintenance and repair work, potential exposure is assumed only by single contacts. The corresponding exposure level is assessed applying the EASE model (see Section 4.1.1.2.3).

For the handling of powders the low permeation properties of powders in general and the highly accepted use of gloves in the base chemical industry leads to the assessment of low dermal exposure, independent of the suitability of the material of the gloves.

Production of personal care products

According to the information provided by one manufacturer, the powdery form of DHTDMAC (containing 95 % DHTDMAC, 40 % DODMAC) is used in the cosmetic industry (e. g. hair-care products). The content of DHTDMAC in personal care products amounts to app. 2 % (0.8 % DODMAC). These products are produced under sanitary conditions. It is assumed that, in view of the very high sanitary requirements, the plants or workplaces (e. g. workplaces for filling operations) are equipped with suitable exhaust ventilation systems.

In general inhalative and dermal exposure in the cosmetic industry are assumed to occur during sampling, filling, transfer, cleaning, maintenance and repair work. On account of the physico-chemical properties of the substance (ionic substance, vapour pressure estimated to 10^{-15} Pa, EPA, 1996) inhalative exposure to vapours is negligible and exposure to dusts at the workplaces during the handling of the powdery substance must be taken into consideration. The manufacture of cosmetics requires facilities that maintain high standards of quality and cleanliness (good manufacture practices). Therefore it can be assumed that, as a rule, immediate skin contact is avoided to a large extent and that the use of gloves is highly accepted within the cosmetic industry.

Because of the low permeation properties of powders in general and the highly accepted use of gloves dermal exposure is assessed to be low independent of the suitability of the material of the gloves.

Workplace measurements

One single measurement result of total dust (calculated from two unknown results of filter samples over one hour), measured during bagging of the powdery substance, was submitted by the producer (Hoechst Marion Roussel, 1998). It amounts to 0.95 mg/m^3 and of app. 0.4 mg/m^3 (with respect to the concentration of app. 40 % DODMAC in DHTDMAC). The bagging process and the tasks of the workers are not described in detail. Therefore the representativity of this single measurement result is not clear.

4.1.1.2.2 Occupational exposure in fields of use in the further processing industry, outside the chemical industry

Further processing

DHTDMAC is used in the laundry/cleaning products industry (fabric softeners, car cleaning products), for the manufacture of organophilic bentonites as well as in the chemico-technical and the cosmetic industries (see above). It is assumed that the further processing is performed within the chemical industry as well as in (smaller) formulation companies. Within the chemical industry, it is assumed that open systems are equipped with suitable local exhaust ventilation. In principle it cannot be excluded that open systems without suitable technical ventilation equipment are also employed and that no personal protective equipment is worn, e. g. in chemical small and medium sized enterprises (Voullaire, Kliemt, 1995).

Production of fabric softeners

Fabric softeners are produced by mixing the liquefied paste-like preparation containing 75 % DHTDMAC (32 % DODMAC) with water. According to information provided by one producer, the DHTDMAC content in the final products amounts to 4 - 8 % (1.7 % - 3.4 % DODMAC). Taking into account the corrosive effect of the paste-like preparation, daily repeated skin contact is avoided to a large extent by using personal protective equipment. In this case dermal exposure is assessed to be low. During activities like filling, transfer, cleaning, maintenance and repair work, potential exposure is assumed only by single contacts. The corresponding exposure level is assessed applying the EASE model (see Section 4.1.1.2.3).

Production of car cleaning agents

DHTDMAC is an ingredient (4 %, 1.7 % DODMAC, see Chapter 4.1.1.2) of car cleaning products and of car polishing products. There is only little information about the production of cleansers. In a NIOSH walk-through survey (1980) through a plant which was engaged in the packaging of commercial aerosols and lotions, the compounding and packaging of a spot remover is described (Orris, Daniels, 1980). Some of the ingredients were hand charged into mixers, which were closed afterwards.

There is a lack of information concerning the quantity as well as the form (powder, preparation) of DHTDMAC being further processed to car cleaning products. Unless other information will be provided, it is assumed that car cleaning products are produced comparably to fabric softeners on the basis of the paste-like preparation containing 75 % DHTDMAC. Taking into account the corrosive effect of the paste-like preparation, daily repeated skin contact is avoided to a large extent by using personal protective equipment. In this case dermal exposure is assessed to be low. During activities like filling, transfer, cleaning, maintenance and repair work, potential exposure is assumed only by single contacts. The corresponding exposure level is assessed applying the EASE model (see Section 4.1.1.2.3).

Production of organic clays

Organic clays (organophilic bentonites) are produced by mixing and kneading a suspension of bentonite with the aqueous emulsion containing 16 % DHTDMAC (7 % DODMAC). This procedure intensifies the ion-exchange reaction of the ions bound to the clay and the $DHTDMA^+$-ions (Winnacker, Küchler, 1983). It is assumed that the $DHTDMA^+$-ions are almost irreversible bound to the clay. Because it is not clear whether the diluted emulsion is corrosive and because of the lack of information about the suitability of the materials of the gloves, which are recommended by the producers, dermal exposure to the substance must be taken into account. The estimation of the dermal exposure levels according to the EASE model is used (see Section 4.1.1.2.3).

Use of organic clays within the oil industry and the automotive industry

App. 70 % of the produced organic clays are applied in drilling muds applied in the oil industry. The remaining 30 % are used for the formulation of lacquers which are applied in the automobile industry. In the oil industry, drilling muds are mainly handled in circuits. Since the concentration of organic clay in drilling muds amounts to 2 % (Kirk-Othmer, 1996) the DHTDMAC-concentration is < 1 % (< 0.42 % DODMAC). Unless further information is provided, on account of the low concentration of DHTDMAC (DODMAC), dermal exposure is assumed to be not critical.

Lacquers containing organic clays are applied in the automotive industry. These lacquers are normally applied in spray booths, which operate automatically. Because of the automatic process, inhalative exposure to aerosols are largely avoided. The content of DHTDMAC is not known. For a rough estimation a concentration of 5 % DHTDMAC (2.1 % DODMAC) is assumed and a solid concentration in the aerosol of app. 50 % is considered. On account of the low concentration of DODMAC in the aerosol and the automatic lacquering process, inhalative and dermal exposure are assumed to be not critical. Additionally, the strong ionic bond formed between the clay and the DHTDMAC makes direct contact of worker with the substance DHTDMAC more unlikely.

Skilled trade sector

With regard to the use of final products which contain DHTDMAC, such as fabric softeners, car cleaning products and hair-care products, special attention must be paid to dermal exposure to hair-care products in the hairdressing trade and to the use of car cleaning products. If no personal protective equipment (gloves) is used, regular, frequent skin contact with the substance is to be assumed in these areas.

It cannot be excluded that car washing agents containing 4 % DHTDMAC (1.7 % DODMAC) are used for high pressure cleaning of cars. For this case, exposure to aerosols has to be taken into consideration.

4.1.1.2.3 Inhalation and dermal exposure estimation according to the EASE model

See Appendix 1.

The exposure levels are estimated for DHTDMAC. From these values the exposure to DODMAC is calculated.

Inhalative exposure

Exposure to dusts when the powdery substance is handled in the chemical and cosmetic industry

Input parameters:	non-dispersive use dry manipulation exposure-type is dust LEV (local exhaust ventilation) present
Estimated exposure level:	2 - 5 mg/m^3 DHTDMAC

Production of the powdery substance: Considering a purity of 95 % DHTDMAC, a content of 42 % DODMAC in DHTDMAC, the exposure level amounts to

0.8 - 2.0 mg/m^3 DODMAC

Further processing of the powdery substance in the cosmetic industry: Considering a purity of 95 % DHTDMAC in the powder, a content of 42 % DODMAC in DHTDMAC and assuming a duration and frequency of exposure of app. 2 hours / day the exposure level amounts to

0.2 - 0.5 mg/m^3 DODMAC

Dermal exposure

Production and use of the corrosive paste-like preparation and of the aqueous emulsion also assumed to be corrosive; potential dermal exposure during drumming, cleaning, maintenance and repair works

Input parameters:	T = 20°C non dispersive use direct handling

incidental

Estimated exposure level: 0 – 0.01 mg /cm^2/day DHTDMAC

Production of the 75 % paste-like preparation, further processing to the aqueous preparation (16 % DHTDMAC), to fabric softeners and car cleaning agents: Considering an amount of 75 % DHTDMAC in the preparation and a content of 42 % DODMAC in DHTDMAC, the exposure level is estimated to

0 - 0.03 mg/cm^2/day DODMAC

Production of the 16 % aqueous emulsion, further processing to organic clays: Considering an amount of 16 % DHTDMAC in the preparation and a content of 42 % DODMAC in DHTDMAC, the exposure level is estimated to

0 - 0.007 mg/cm^2/day DODMAC

Production and use of the powdery substance in the cosmetic industries, dermal exposure during sampling, filling, transfer, cleaning, maintenance

Input parameters: T = 20 °C
non dispersive use
direct handling
intermittent

Estimated exposure level: 0.1 - 1 mg/cm^2/day DHTDMAC

Production of the powder and uses in industrial areas and in the cosmetic industry: Considering a purity of content of 95 % DHTDMAC in the powder and a content of 42 % DODMAC in DHTDMAC, the exposure level amounts to

0.04 - 0.4 mg/cm^2/day DODMAC

Use of hair-care products in the skilled trade sector

Input parameters: T = 20 °C
wide-dispersive use
direct handling
extensive

Estimated exposure level: 5 - 15 mg/cm^2/day DHTDMAC

Considering an amount of 2 % DHTDMAC in the product and a content of 42 % DODMAC in DHTDMAC, the exposure level amounts to

0.04 - 0.13 mg/cm^2/day DODMAC

Use of car cleaning products in the skilled trade sector

Input parameters: T = 20 °C
wide-dispersive use

direct handling
intermittent

Estimated exposure level: 1 - 5 $mg/cm^2/day$ DHTDMAC

Considering an amount of 4 % DHTDMAC in the product and a content of 42 % DODMAC in DHTDMAC, the exposure level amounts to

0.02 - 0.08 $mg/cm^2/day$ DODMAC

4.1.1.2.4 Integrated assessment

General

In the following, all exposure levels refer to exposure to DODMAC, which is the main component of DHTDMAC. The concentration of DODMAC in DHTDMAC amounts to 42 %. Measured data on the level, duration and frequency of exposure are not available. Therefore the exposure is assessed applying the EASE model. On account of the physico-chemical properties of the substance (ionic substance, vapour pressure estimated by EPI program to 10^{-15} Pa, EPA 1996) inhalative exposure to vapours during production, further processing and use is assumed to be negligible. If the powdery substance is handled, exposure to dusts has to be taken into consideration.

DHTDMAC is marketed in the form of a paste-like preparation containing 75 % DHTDMAC (32 % DODMAC). In addition, an aqueous emulsion containing 16 % DHTDMAC (7 % DODMAC) as well as a powdery form of DHTDMAC (purity 95 %, 40 % DODMAC) are placed on the market. DHTDMAC is used in the laundry/cleaning products industry (fabric softeners, car cleaning products), in the manufacture of organophilic bentonites as well as in the chemico-technical and the cosmetic industries (e.g. hair cosmetics). Although some applications of DHTDMAC, e. g. as a softener, are largely reduced during the last years, it cannot be excluded, that at the moment significant quantities of the substance are still being produced in the EU and that preparations containing DHTDMAC are still used outside the chemical industry.

3 of 6 manufacturers provided information on the production and further processing of DHTDMAC, but not all of them described the workplaces and activities, the duration and frequency of exposure to a sufficient extent.

Production and further processing within the chemical industry and further processing in the cosmetic industry

Production and further processing

DHTDMAC is batch-wise manufactured in closed systems. The primary product is a paste-like preparation containing 75 % DHTDMAC (content of DODMAC 32 %) in a water/isopropanol mixture. Therefrom powdery DHTDMAC (purity: 95 %, containing 40 % DODMAC) is manufactured by subsequent spray drying. An aqueous emulsion (containing 16 % DHTDMAC, 7 % DODMAC) is obtained when the liquefied paste-like preparation is mixed with water. According to the information provided by 2 producers the paste-like preparation (containing 75 % DHTDMAC, 32 % DODMAC) is produced throughout the year. The collective of exposed people amounts to 15 - 20 workers per production site.

On account of the corrosivity of the paste-like preparation which is also assumed for the 16 % aqueous emulsion, in general, gloves and eye protection are worn to avoid skin contact and daily repeated dermal exposure is assessed to be low. During activities like filling, transfer, cleaning, maintenance and repair work, potential exposure is assumed only by single contacts. The estimation of a potential dermal exposure by single contacts according to the EASE model amounts to 0 - 0.03 mg/cm^2/day and 0 - 0.007 mg/cm^2/day DODMAC, respectively. Considering an exposed area of 420 cm^2 (palms of two hands), the potential dermal exposure is assessed to 0 - 13 mg/person/day and to 0 - 3 mg/person/day, respectively.

When the powdery substance is produced, inhalative exposure to dusts at the workplace during filling, sampling and maintenance work has to be taken into consideration. According to the information of the company DHDTMAC is produced campaign wise with an exposure duration and frequency of 8 hours/shift and max. 60 days/year. The single measurement result of app. 0.4 mg/m^3 (see Chapter 4.1.1.2.1. workplace measurements) is in good agreement with the EASE estimate (see Chapter 4.1.1.2.3.) of about 0.8 - 2 mg/m^3 DODMAC, because the representativity of this single measurement result is not clear, the EASE estimate is taken for assessing the risks.

Taking into account the low permeation properties of powder and the high acceptance of using gloves within the chemical industry, daily dermal exposure to dusts is assessed to be low, even if unsuitable material is worn. If no gloves are used, dermal contact may occur during filling, transfer, cleaning, maintenance and repair. The corresponding exposure level is estimated according to the EASE model to 0.04 - 0.4 mg/cm^2/day DODMAC. Considering an exposed area of 420 cm^2 (palms of two hands) the exposure level amounts to level of 17 - 170 mg/person/day. It should be noticed, that because of the high acceptance of using gloves, in general, dermal exposure is assessed as low.

Production of personal care products

According to the information provided by one manufacturer, the powdery form of DHTDMAC is used in the cosmetic industry. Therefore inhalative exposure to dusts at the workplace during filling, weighing, cleaning, maintenance and repair works must be taken into consideration. In the cosmetic industry, closed systems can be assumed in most cases, where either continuous production or batch processing are employed. It is to be assumed that, in view of the very high sanitary requirements, the plants or workplaces (e. g. workplaces for filling operations) are equipped with suitable exhaust ventilation systems. The estimation of the exposure to dusts is performed in application of the EASE model. Assuming a duration of exposure of 2 hours per day, the inhalative exposure to dusts results to 0.2 - 0.5 mg/m^3 DODMAC. The manufacture of cosmetics requires facilities that maintain high standards of quality and cleanliness (good manufacturing practices). Therefore it can be assumed that, as a rule, the use of gloves is highly accepted. Taking also into account that the permeation properties of powders are low, in general, dermal exposure is assessed to be low, independent of the suitability of the material of the gloves. If no gloves are used, dermal contact may occur during filling, transfer, cleaning, maintenance and repair. The corresponding exposure level is estimated according to the EASE model to 0.04 - 0.4 mg/cm^2/day DODMAC. Considering an exposed area of 420 cm^2 (palms of two hands) the exposure level amounts to 17 - 170 mg/person/day. It should be noticed, that because of the high acceptance of using gloves, in general, dermal exposure is assessed as low.

Occupational exposure in fields of use in the further processing industry, outside the chemical industry

It is assumed that the preparations are manufactured within the chemical industry as well as in (smaller) formulation companies. Within the chemical industry, it is to be assumed that open systems are equipped with suitable local exhaust ventilation. In principle it cannot be excluded that open systems without suitable technical ventilation equipment are also employed and that no personal protective equipment is worn, e.g. in chemical small and medium sized enterprises (Voullaire, Kliemt, 1995).

Production of fabric softeners

Fabric softeners are produced by mixing the liquefied paste-like preparation containing 75 % DHTDMAC (content of DODMAC: 32 %) with water. On account of the corrosivity of the paste-like preparation, in general, gloves and eye protection are worn to avoid skin contact and daily repeated dermal exposure is assessed to be low. During activities like filling, transfer, cleaning, maintenance and repair work, potential exposure is assumed only by single contacts. The potential dermal exposure by single contacts is assessed according to the EASE model with regard to the concentration of 75 % DHTDMAC (32 % DODMAC) in the preparation to 0 - 0.03 mg/cm^2/day. Considering an exposed area of 420 cm^2 (palms of two hands) it estimated to 0 - 13 mg/person/day DODMAC.

Production of car cleaning agents

There is a lack of information concerning the quantity as well as the form (powder, preparation) of DHTDMAC being further processed to car cleaning products. Unless other information will be provided, it is assumed that car cleaning products are produced comparably to fabric softeners on the basis of the paste-like preparation containing 75 % DHTDMAC (32 % DODMAC). On account of the corrosivity of the paste-like preparation the assessment of the dermal exposure will be the same than for the production of fabric softeners.

Production and use of organic clays

Organic clays (organophilic bentonites) are produced by mixing and kneading a suspension of bentonite with an aqueous emulsion containing 16 % DHTDMAC (content of DODMAC: 7 %). On account of the corrosivity of the 16 % aqueous emulsion, in general, gloves and eye protection are worn to avoid skin contact and daily repeated dermal exposure is assessed to be low. During activities like filling, transfer, cleaning, maintenance and repair work, potential exposure is assumed only by single contacts. The potential dermal exposure by single contacts is assessed according to the EASE model with regard to the concentration of 16 % DHTDMAC (7 % DODMAC) in the preparation to 0 - 0.007 mg/cm^2/day. Considering an exposed area of 420 cm^2 (palms of two hands) it is estimated to 0 - 3 mg/person/day DODMAC.

Organic clays are used in lacquers which are applied within the automotive industry and in drilling fluids applied in the oil industry. Unless other information is obtained, inhalative exposure to aerosols and dermal exposure are assumed to be not critical (see Chapter 4.1.1.2.2).

Occupational exposure within the skilled trade sector

Special attention must be paid to dermal exposure to hair-care products in the hairdressing trade and to the use of car cleaning and polishing. It is to be assumed, that gloves are not worn.

For the use of hair-care products the exposure level is assessed assuming daily extensive dermal contact e.g. during shampooing. The estimation of exposure according to the EASE model considering a concentration of 2 % DHTDMAC (0.8 % DODMAC), a duration of exposure of 5 hours per day and an exposed area of 840 cm^2 (hands) amounts to 34 - 110 mg/person/day DODMAC.

During the use of car cleaning and car polishing products immediate dermal contact may occur when cleaning and laying on activities are performed. It is to be assumed, that car polishing agents are applied without dilution with water. The dermal exposure is estimated according to the EASE model. Considering a concentration of DHTDMAC of 4 % (1.7 % DODMAC) and an exposed area of 1,300 cm^2 (hands and parts of the forearms) the daily dermal exposure amounts to 26 - 105 mg/person/day DODMAC. It may be that car cleaning agents are further diluted.

The inhalative exposure to aerosols during cleaning using high pressure equipment cannot be estimated yet, because there is a lack of data and information. On account of the low concentration of DHTDMAC (4 % DHTDMAC, 1,7 % DODMAC) and the further dilution of the cleaning agents for cleaning purposes (app. 10 %), the inhalative exposure to aerosols is assumed to be not critical.

The following table shows the exposure data of DODMAC which are relevant for occupational risk assessment.

Table 4.1 Summary of exposure data

Exposure scenario	Form of exposure	Activity	Duration and frequency	Inhalative exposure to DODMAC		Dermal exposure to DODMAC			
				Level of exposure shift average [mg/m³]	Method	Level of exposure [mg/cm²/day]	Exposed area [cm²]	Shift average [mg/p/day]	Method
Chemical industry (inclusive cosmetic industry)									
manufacturing of a preparation containing 75 % DHTDMAC	vapour, paste	filling, transfer, cleaning, maintenance, repair work	shift length, daily single contacts	negligible[1)]	exp. judg. ---	low 0 - 0.03	420 (palms of two hands)	low[2)] 0 - 13	exp. judg. EASE
manufacturing of a preparation containing 16 % DHTDMAC	vapour, emulsion	filling, transfer, cleaning, maintenance, repair work	shift length, daily **single contacts**	negligible[1)]	exp. judg. ---	**low** **0 - 0.007**	420 (palms of two hands)	**low[2)]** **0 - 3**	**exp. judg.** EASE
manufacturing of powder containing 95 % DHTDMAC	dust, powder	filling, transfer, cleaning, maintenance, repair work	8 hours/shift/ not daily (approx. 60 days/year) with PPE without PPE	0.8 - 2.0 ---	EASE ---	low 0.04.- 0.4	420 (palms of two hands)	low 17 - 170	exp. judg. EASE
production of personal care products, use of the powder containing 95 % DHTDMAC	dust, powder	weighing, filling, cleaning, maintenance, repair work	2 hours/daily with PPE without PPE	0.2 - 0.5 (with LEV) ---	EASE	low 0.04 - 0.4	420 (palms of two hands)	low 17 - 170	exp. judg. EASE

Exposure scenario	Form of exposure	Activity	Duration and frequency	Inhalative exposure to DODMAC		Dermal exposure to DODMAC			
				Level of exposure shift average [mg/m³]	Method	Level of exposure [mg/cm²/day]	Exposed area [cm²]	Shift average [mg/p/day]	Method
Industrial area									
production of fabric softeners, use of preparations containing 75 % DHTDMAC	vapour, paste	weighing, filling, cleaning, maintenance, repair work	2 hours/daily single contacts	negligible[1]	exp. judg.	low 0 - 0.03	420 (palms of two hands)	low[2] 0 - 13	exp. judg. EASE
production of car cleaning agents, use of preparations containing 75 % DHTDMAC	vapour, paste	weighing, filling , cleaning, maintenance, repair work	2 hours/daily single contacts	negligible[1]	exp. judg.	low 0 - 0.03	420 (palms of two hands)	low[2] 0 - 13	exp. judg. EASE
production of organic clays (use of emulsions containing 16 % DHTDMAC)	vapour, emulsion	weighing, filling, cleaning, maintenance, repair work	2 hours/daily **single contacts**	negligible[1]	exp. judg.	**low** **0 - 0.007**	420 (palms of two hands)	**low**[2] **0 - 3**	**exp. judg.** **EASE**
Skilled area									
use of hair-care products containing 2 % DHTDMAC	vapour, solution	shampooing	5 hours/daily	negligible[1]	exp. judg.	0.04 - 0.13	840 (hands)	34 - 110	EASE
use of car polishing and car cleaning products containing 4 % DHTDMAC	vapour, solution aerosol	cleaning, laying on spraying	shift length, daily	negligible[1] [3]	exp. judg.	0.02 - 0.08	1 300 (hands and part of the forearms)	26 - 105	EASE

1) on account of the very low vapour pressure (estimated to 10^{-15} Pa)
2) corrosive effect of the 75 % **resp. 16 %** preparation
3) cannot be estimated yet, assumed to be not critical

4.1.1.3 Consumer exposure

DHTDMAC is used as a fabric softener in hand laundering products. Textiles may also contain the substance after washing. Moreover, DHTDMAC is used by consumers in the form of cosmetic products (hair care products) in a maximum concentration of 2% (voluntary reporting to the BgVV, 1996).

According to the Swedish product register, DHTDMAC (DODMAC) is used in paints/lacquers and thus, by consumers.

Dermal exposure

The following exposure estimations have been performed in agreement with the TGD (Chapter 2). Furthermore, the values recommended by Colipa (1989) and the Scientific Committee for Cosmetology (1994) are taken as a basis.

Softeners in hand laundering

For dermal exposure to DHTDMAC during hand laundering it is assumed that 30 g of a product containing 10% of DHTDMAC are used in a volume of 5,000 ml of water (DHTDMAC concentration 0.6 mg/ml).

The total amount (A_{der}) which is exposed via the dermal route is given by the equation:

$$A_{der} = C_{der} \cdot T_{der} \cdot S_{der},$$

where C_{der} is the concentration of the substance in the solution, T_{der} is the thickness of layer on skin (0.0024 cm, EPA) and S_{der} is the surface area of exposed skin of both hands and \ forearms (= 1980 cm²).

According to this equation the consumer will be exposed to a total amount of about 3 mg DHTDMAC per event. Related to body weight (60 kg) the acute dermal exposure amounts to 50 µg/kg bw per event.

Assuming a twice-weekly use (= 104 uses/year) an exposure of ~14 µg DHTDMAC (6 µg DODMAC)/kg bw/d results as yearly average for this application.

Exposure to DHTDMAC by wearing softened fabrics:

Assessment of exposure to DHDTMAC by wearing softened fabrics is based on the following assumptions:

- Average weight of product that is deposited in a fabric is 1 mg/cm² (w),
- Weight fraction in the product is 0.1(w_f),
- Surface area which is exposed to the fabric is ~17400 cm² (total body) (S_{der}),
- Duration of contact to skin is 24 h (t),
- Fraction of DHTDMAC (m_f) migrating from fabric to skin is based on a value of <0.08% per hour (Hollies et al., 1982).

The total amount (A_{der}) for dermal exposure via wearing of softened fabrics is calculated by the equation:

$$A_{der} = w \cdot w_f \cdot S_{der} \cdot t \cdot m_f.$$

The calculation results a total amount of about 34_mg of DHTDMAC to which the skin may be exposed. This amount leads to a dermal exposure of ~550 µg DHTDMAC (230 µg DODMAC) kg bw/d.

Exposure via cosmetics

Hair care products contain a maximum of 1-2% DHTDMAC (up to 0.8% DODMAC). Hair care products can be used as products which are rinsed off (e.g. hair conditioner) or as products which remain in the hair.

A daily single amount of 12 g of a hair care product which will be rinsed off (rinse-off product) will result in a consumer exposure to 40 µg DHTDMAC (~17 µg DODMAC)/kg bw per day in consideration of a rinse-off coefficient of 10% and a partition coefficient of 10% (Scientific Committee for Cosmetology, 1994).

According to the exposure estimates given by the Scientific Committee for Cosmetology (1994) for non-rinse off products a partition coefficient of 10% (that means, 90% on hair, 10% on scalp) was used. For the rinse off products in addition a rinse off coefficient of 10 % was used (that means 90% of the substance is washed out). Thus, out of the residual 10% of the substance 9 % will be retained on the hair, whereas 1 % remains on the scalp.

For daily use of a hair care product which is remaining on head there is no “rinse-off effect”. Thus, assuming a daily use of a single amount of 12 g a hair care product which will remain in the hair, and a partition coefficient of 10%, an exposure to ~400 µg DHTDMAC (~ 170 µg DODMAC)/kg bw per day will result.

Combined dermal exposure

Assuming that a consumer will use haircosmetics and will perform a hand wash laundry and wears a cloth which is washed with DHTDMAC (DODMAC) containing softener, a person will be exposed to the substance in an amount in the up to 0.5 mg DODMAC)/kg bw range per day.

Lacquers

Exposure to DHTDMAC (DODMAC) from lacquers where the substance is present as chemisorbate in organophile bentonites can be excluded since the substance is irreversibly bound thus it cannot be released.

Car cleansing agents

According to the present information there is no data on the further use of car cleansing agents containing DHTDMAC by consumers.

<u>Other routes of exposure (dust - inhalatory)</u>

Inhalatory exposure through dust can be neglected in private applications.

<u>Conclusions</u>

DHTDMAC (DODMAC) is a component in products for private use. The sum of all types of exposure (reasonable worst case) is in the upper microgram/kg bw and day range (up to 500 µg/kg bw/d) when the products are used as intended.

Remark:

For estimation of consumer exposure, standard assumptions of typical uses have priority; where this is not practicable, more arbitrary assumptions are used. Under these variable circumstances, it is not possible to estimate an exact individual exposure.

4.1.1.4 Humans exposed via the environment

Just as the environmental exposure, two scenarios are calculated: based on the consumption figures of DHTDMAC as fabric softener in 1989/90 reflecting the former use (cf. Section 3.1.2.2.4) and the figures from 1998 reflecting the actual situation where the consumption has been decreased substantially.

Intake via drinking water

There are monitoring data for the production of drinking water from surface waters in the Netherlands available (Versteegh, 1992). DHTDMAC was measured in surface waters and bank filtrates. **In Table 4.2**, the corresponding DODMAC concentrations [µg/l] are given, considering that DHTDMAC contains 42% DODMAC.

Table 4.2 Concentrations of measured DHTDMAC and calculated DODMAC

Medium	measured DHTDMAC [µg/l]	calculated DODMAC [µg/l]	Remarks
bank filtrate surface water	- 14.4 (mean 3.3) - 21.8 (mean 8.4)	- 6.0 (mean 1.4) - 9.2 (mean 3.5)	corresponding surface water and bank filtration measurements
bank filtrate surface water	1.9 - 6.0 (mean 2.8)	0.8 - 2.5 (mean 1.2)	not known if the values correspond

From the PEC calculation of groundwater below agricultural soil fertilized with sludge, a $PEClocal_{soil,porewater}$ of 0.48 µg/l (1989/90) resp. 0.044 µg/l (1998) for DODMAC was obtained (cf. Section 3.1.2.2).

For the pollution of drinking water produced from surface waters, the PEC_{local} for the waterphase (cf. Section 3.1.5) is an adequate basis for a local worst case scenario. According to the TGD, a purification factor of 1/4 (hypothetical log Pow of >5 considering the strong adsorption) has to be chosen:

1989/90 $\Rightarrow C_{drw}$ = 8.4 µg/l / 4 = 2.1 µg/l
1998 $\Rightarrow C_{drw}$ = 0.42 µg/l / 4 = 0.11 µg/l

As a worst-case approach, the C_{drw} values calculated from the production from surface water are chosen. With a consumption of 2 l/d and a body weight of 70 kg the daily intake is

1989/90 $\Rightarrow$ **$DOSE_{drw}$ = 0.06 µg kg bw^{-1} d^{-1}**
1998 $\Rightarrow$ **$DOSE_{drw}$ = 0.003 µg kg bw-1 d^{-1}**

Intake via fish

The concentration in fish is calculated from the $PEC_{local,bulk}$ (10.5 µg/l for 1989/90 and 0.54 µg/l for 1997) and the BCF from the river water test:

1989/90 $\mathbf{C_{fish}}$ = 10.5 µg/l · 13 l/kg = **140 µg/kg**
1998 $\mathbf{C_{fish}}$ = 0.54 µg/l · 13 l/kg = **7.0 µg/kg**

With a daily consumption of 115 g fish, the intake is

1989/90 ⇒ $\mathbf{DOSE_{fish} = 0.23\ µg\ kg\ bw^{-1}\ d^{-1}}$
1998 ⇒ $\mathbf{DOSE_{fish} = 0.012\ µg\ kg\ bw^{-1} \cdot d^{-1}}$

Intake via plants

The concentration in plants can be estimated from the plant uptake test (cf. Section 3.1.1.4). With a soil concentration of 2 mg/kg, plant concentrations up to 0.05 mg/kg were found in the test. With a $PEClocal_{agr.soil}$ of 4.8 mg/kg (1989/90) resp. 0.44 mg/kg (1998), concentrations in plants up of 0.12 mg/kg (1989/90) and 0.011 mg/kg (1997) are expected.

Assuming a consumption of daily 1.2 kg leaf crops and 384 g root crops, the maximum intake is

1989/90 ⇒ $\mathbf{DOSE_{plant} = 2.7\ µg\ kg\ bw^{-1}\ d^{-1}}$
1998 ⇒ $\mathbf{DOSE_{plant} = 0.25\ µg\ kg\ bw^{-1}\ d^{-1}}$

Intake via meat and milk

Because no log Pow / C_{plant} correlation is opportune for DODMAC and no monitoring data are available, a concentration in meat or milk can not be calculated. However, it can be assumed that cattle eating DHTDMAC contaminated plants will adsorb the substance in the guts and do not accumulate it in the meat and milk to a large extend (comparable with fish), so this exposure pathway should be not significant.

Total daily intake for humans

The single doses are summarized:

1989/90 ⇒ $\mathbf{DOSE_{tot} = 3.0\ µg\ kg\ bw^{-1}\ d^{-1}}$
1998 ⇒ $\mathbf{DOSE_{tot} = 0.27\ µg\ kg\ bw^{-1}\ d^{-1}}$

Because the risk assessment based on the local concentrations (which represent a worst-case approach) results that there is no concern (cf. Section 4.1.3.3), the estimation of the European average intake (which should be derived from regional environmental concentrations) is not necessary.

4.1.1.5 Combined exposure

A person who is exposed indirectly to DODMAC through the environment may also be exposed through different dermal applications. However, in such cases these activities will dominate the total exposure resulting in maximum value of up to 1 mg/kg bw/d.

4.1.2 Effects assessment: Hazard identification and Dose (concentration) - response (effect) assessment

4.1.2.1 Toxico-kinetics, metabolism and distribution

After dermal administration of 10 mg (≈ 30µCi) ^{14}C-labelled DODMAC to the back of each of four rabbits over a 5 · 8 cm area most of the radioactivity remained at the site of application (88 ± 2.3%). Only traces of administered radioactivity were detected over a 72 h-period in urine (0.15 %), faeces (0.16 %), exhaled carbon dioxide (0.27 %), other skin (0.2%) and cage wash (0.3%) (Drotman, 1977).

In in-vitro-studies on human abdominal skin no absorption of DODMAC was detected (no further information was given, Drotman, 1977).

These experimental findings are supported by the physicochemical properties of DODMAC being insoluble in water and existing as a quaternary ammonium salt in an ionic state, uncharged molecules, however, are absorbed. Furthermore, DODMAC has a molecular weight of about 580 g/mol, usually only substances with lower molecular weight are absorbed.

Therefore, the dermal absorption and the concentration of DODMAC in the skin can be assumed to be very low.

No data are available on toxicokinetics and metabolism of DODMAC using the oral or inhalation routes of exposure.

4.1.2.2 Acute toxicity

Animal data

Oral

In rats, the acute oral toxicity of DODMAC has proven to be low with LD_{50} values well above 2000 mg/kg bw. In a Limit-test according to OECD guidelines 401 with DHTDMAC (97 ± 1% purity, max. 3% water), 2,000 mg/kg of the substance (with sesame oil as vehicle) caused no mortality; clinical symptoms are mentioned but not qualified (Hoechst AG 1986a, unpublished report).

In another test with rats, LD_{50} values of 11,300 (9,600-12,200) mg/kg bw for males and of 13,000 (11,200-15,100) mg/kg bw for females were detected, using a 20% aqueous solution of a test substance called "distearyl dimethylammonium chloride" (no data on purity): Various doses of this 20% aqueous solutions of DODMAC were orally given to male and female rats (observation period 12 days): No mortality occurred after application of 6,900 mg/kg to 10 males, no mortality occurred after application of 8,300 mg/kg to 10 females, 14,400 mg/kg killed 7/8 males and 6/9 females, deaths were observed on days 1-7. Thus, oral LD_{50} values of 2,260 mg/kg for male rats and 2,600 mg/kg for female rats might be stated for the undiluted "distearyl dimethylammonium chloride" used in this study. Toxic signs: Depression of spontaneous movement, diarrhea, piloerection, abdominal distention. No data on necropsy are reported (Suzuki et al., 1983).

Inhalation

In a Limit-test with male rats according to Regulations for the Enforcement of the Federal Hazardous Substances Act of the USA, a test substance called “ArquadR 2HT-75” (no information on chemical identity) demonstrated a LC_{50} value > 180 mg/l/1 hour: A group of 10 male rats was exposed to the test material in an inhalation chamber for 1 hour. The concentration of the test material in the chamber atmosphere was determined to be 180 mg/l of mist. At the conclusion of the 1-hour exposure period the animals were removed from the chamber. Observations were made continuously of the appearance and behavior of the animals during the exposure period and at frequent intervals thereafter for a total of 14 days. No mortalities occurred. Clinical signs during exposure: “Excited” activity upon initiation, preening, excessive masticatory movements, excessive salivation stains, damp hair coats, lacrimation, serosanguineous stains around the nose, labored respiration. All rats exhibited normal appearance and behavior on the first post-exposure day and throughout the remainder of the study. Necropsy revealed no significant gross pathological alterations (AKZO Chemicals Inc. 1974, unpublished report).

Dermal

In rats, a dermal LD_{50} of more than 2000 mg/kg bw was detected in a Limit-test according to OECD guidelines with a substance called “Praepagen WK hochkonz” (probably DODMAC with a purity of approx. 97% as judged on the basis of producer information (BUA, 1997): The test substance was applied for 24 hours as an aqueous suspension occlusively to the skin of 5 male and 5 female rats using a dose of 2,000 mg/kg bw. No mortality was observed, skin dryness but no other substance related clinical symptoms were observed, no pathologic signs were detected at necropsy (Hoechst AG 1988a, unpublished report).

Human data

Human data on the acute toxicity of DODMAC are not available.

Conclusion:

Human data on the acute toxicity of DODMAC are not available. In rats, the substance exhibited only low acute toxicity with oral LD_{50} > 2,000 mg/kg bw, dermal LD_{50} > 2,000 mg/kg bw and inhalation LC_{50} > 180 mg/l/1 hour. According to the acute toxicity figures DODMAC is not to be classified.

4.1.2.3 Irritation

Animal data

In a test with rabbits according to OECD guidelines 404, moderate skin irritation was detected for DODMAC (purity approx. 97%): Three albino rabbits were tested with 0.5 g of the substance pasted with isotonic saline using semi-occlusive patches. All animals revealed mild to moderate erythema (mean scores for 24, 48 and 72 observation periods: 2/1/0.3) that reversed within 14 days. In addition, the treated skin areas were sporadically dry-rough, discolored light brown and demonstrated fine or coarse scales during the observation period of 14 days. Edema were not seen (Hoechst AG 1986c, 1986d, unpublished reports).

Technical grade DODMAC, containing 77% dimethyldioctadecylammonium chloride, 11.3% isopropanol and 11.7% water, however, causes corrosion after a 4-hours contact with the skin of rabbits: A test with 6 rabbits according to OECD 404 (semi-occlusive application of 0.5 ml for 4 hours) resulted in moderate irritation, the effects increased after the day of application till exhibition of severe necrosis after a 14-day observation time (Hoechst AG 1989a, unpublished report).

After instillation of dialkyldimethylammonium chloride (97 ± 1% purity, max. 3% water) into the eyes of rabbits, risk of serious damage to eyes was stated based on results of a test according to OECD guidelines 405 (only short abstract submitted not including details like irritation scores): The eyes were exposed to 100 mg of the test substance for an exposure time of 24 hours, number of test animals not given (Hoechst AG 1986b, abstract of an unpublished report).

Data on respiratory irritation are not available. However, in the acute inhalation study (AKZO, 1974, cf. Section 4.1.2.2) clinical signs of toxicity were reported, but all rats exhibited normal appearance and behavior on the first post-exposure day and throughout the remainder of the study.

Human data

Human data on local irritation/corrosion caused by DODMAC are not available.

Conclusion

Human data on local irritation/corrosion caused by DODMAC are not available. Judged on the basis of tests with rabbits, the pure substance causes severe effects to the eyes, but only moderate effects to the skin of rabbits, while technical grade DODMAC containing approximately 12% isopropanol causes skin corrosion. Based on the reported data, pure DODMAC is classified "Xi, irritant" and labeled "R 41, risk of serious damage to eyes", while technical grade "DODMAC" (containing approximately 12% isopropanol) is to be classified "C, corrosive" and labeled "R 34, causes burns".

4.1.2.4 Corrosivity

Animal data

Pure DODMAC exhibits only moderate skin irritation in rabbits, that is not to be labeled according to EU regulations (Hoechst AG, 1986c). Technical grade DODMAC however, containing 77% dimethyldioctadecylammonium chloride, 11.3% isopropanol and 11.7% water, causes corrosion after a 4-hour contact with the skin of rabbits: a test with 6 rabbits (semi-occlusive application of 0.5 ml for 4 hours) resulted in moderate irritation, the effects increased after the day of application till exhibition of severe necrosis after a 14-day observation time (Hoechst AG 1989a, unpublished report).

Human data

Human data on local irritation/corrosion caused by DODMAC are not available.

Conclusion

Human data on local irritation/corrosion caused by DODMAC are not available. Pure DODMAC exhibits only moderate skin irritation in rabbits, while the technical grade substance (containing 12% isopropanol) demonstrated severe corrosive properties. The relevance of such data for the assessment of the skin irritant properties of pure DODMAC is questionable. However, the local corrosivity of technical grade DODMAC is crucial for the evaluation of results of toxicological testing performed in order to assess acute effects after application of DODMAC. Based on the reported data, technical grade "DODMAC" (containing approximately 12% isopropanol) is to be classified “C, corrosive” and labeled “R 34, causes burns” according to the EU legislation.

4.1.2.5 Sensitisation

Animal data

Within “epicutaneous sensibilization testing” with guinea pigs (similar to a Buehler test), a substance called “Arquad 2 HT-75 (12%ig in Aqua dest.)” proved to exhibit no sensitizing properties. The relevance of this test is not known, because there are no data on the chemical identity of the test substance. Twenty guinea pigs received 0.5 ml of the 12% Arquad solution each for 6-hours occlusive skin exposure times at days 1, 7 and 14. After 2 weeks in addition to the test animals, 10 control animals received 0.5 ml of the test solution. The application sites of all animals were depilated 18-24 hours after the last exposure and the resulting skin lesions assessed. None of the guinea pigs exhibited any positive reactions at any observation time within the study (IBR International Bio-Research 1978, unpublished report).

A guinea pig maximization test was conducted by Hoechst (1989b).The concentrations used in this study have been adjusted due to the severe local corrosivity of the tested technical grade DODMAC containing 77% dimethyldioctadecylammonium chloride, 11.3% isopropanol and 11.7% water (cf. Section 4.1.2.3). Thus, a substance concentration of 0.04% was used for induction and a concentration of 0.1% for challenge. Concentrations necessary for hazard assessment of pure DODMAC (slightly skin irritating), however, should be much higher. Therefore, due to the far to low concentrations in the Hoechst study with the technical grade substance this guinea pig maximization test is not appropriate to conclude on the sensitizing potential of DODMAC.

Dimethyldioctadecylammonium chloride and most of the polyoxyethylene alkyl ethers were tested for enhancement of skin allergy responses to 4-ethoxymethylene-2-phenyloxazolone and 2,4,6-trinitrochlorobenzene (both are allergy-inducing agents) in guinea pigs and mice. A high enhancement coefficient was detected (Nakano 1976).

Human data

In a repeated insult test with a DHTDMAC preparation containing 78% DHTDMAC, 8% other quaternary ammonium chlorides, 1% free amine plus hydrochlorides, 9% ethanol, and 3% water, no evidence of delayed contact hypersensitivity was observed: One hundred thirty-six human volunteers were tested to investigate the skin sensitization potential of a 2.5% aqueous solution of the DHTDMAC preparation (DODMAC content of 0.82%). All applications were by 24-hour contact occlusive patches. One hundred twenty-seven subjects completed all phases of the experimental plan (induction: 3 weeks of substance application, with 3 applications per week; challenge: patches applied approximately 17 days after the last induction application). There were few incidences of irritation during the induction, no delayed contact hypersensitivity was observed at challenge (i.e., no subjects exhibited reaction scores of grade 1 or greater during challenge) (Procter and Gamble, 1985).

Three University Centers participated in a study on contact dermatitis caused by irritants and/or sensitizing agents in housewives and cleaners occupationally exposed to new detergents and hygiene products in the domestic and extradomestic environment in Italy. The first step was to collect generic data on the use of the products and possible complaints by means of a questionnaire published in a weekly magazine. Nearly 2,000 women answered, indicating 824 different products as alleged noxious agents for the skin. The second part of the investigation was carried out at the dermatology centers involved in the study according to a standard design which included eliciting the history of occupational and nonoccupational exposures, medical and dermatological history, clinical examination with special regard to the patterns of hand eczema and other cutaneous feature and diagnostic patch tests, combined with the above examination, to differentiate irritant from allergic reactions. The study included 1,719 female subjects selected on the basis of their working activity as housewife or professional cleaner, exposed to contact with household and hygiene products: 1,100 of them were patients affected with hand contact dermatitis; 619 women with other mild diseases (cutaneous or mucosal) were considered as controls. Within this study, a 0.1% aqueous solution of "distearyl-dimethyl ammonium chloride" was tested. Judged on the basis of information from producers (BUA, 1997), this "distearyl-dimethyl ammonium chloride" normally is a preparation containing < 79% DHTDMAC, appr. 12% isopropanol, 10-12% water. No positive reaction was registered with a 0.1% aqueous solution of this DODMAC containing substance (DODMAC content of 0.033%) (Meneghini et al., 1995).

Animal or human data on respiratory sensitization are not available.

<u>Conclusion</u>

DODMAC is used in cosmetics for the treatment of hair (as a nearly 100% pure substance, proven to cause only moderate skin irritation) and in detergents (normally in the form of a mixture of approximately 75% of DODMAC dissolved in 25% isopropanol/water, proven to cause skin corrosion). Thus, evaluation of information on sensitization testing with "DODMAC" is difficult, because such testing has to use substance concentrations that have proven to cause only slight skin irritation. Slight irritant effects are elicited with minimal concentrations of technical grade DODMAC, while pure DODMAC needs much higher concentrations in order to cause similar effects.

Based on human patch tests and on tests with guinea pigs, it can be concluded that DODMAC does not induce skin sensitization in humans. DODMAC is reported to enhance significantly skin allergy to chemical substances in tests with guinea pigs and mice. However, there is no need for labeling according to EU regulations.

4.1.2.6 Repeated dose toxicity

<u>Animal data</u>

Since DODMAC is a major component of DHTDMAC, it is expected that the toxicity of both these chemicals is the same.

Oral administration:

In a 28-day toxicity study of Hoechst AG (1990) sesame oil containing approx. 90% DODMAC, 5% water and 5% isopropanol was administered by gavage at doses of 0, 20, 100, and 500 mg/kg of DODMAC to Wistar rats. Dosages were calculated on nominal concentration values. Although histopathology only included heart, lung, kidneys, adrenals, stomach, small and large intestine, the study was accepted as valid according to the requirements of the Annex V method B.7. Beginning at the 8th day (females) and 14th day (males) of treatment some high dose animals showed squatting position, abnormal gait, disregular and noisy breathing. Reduced spontaneous activity, retracted flanks and distended abdomen were also seen in some high dose females. Body weight gain was slightly (non-significantly) lower in high dose males and females compared to the control values. Hematology revealed significantly reduced reticulocyte counts in high dose males which were within the normal range for this species, sex and age, whereas no other red cell parameter was changed. Mean values for segmented neutrophile ratio were increased in high dose males and females due to abnormal rates in two males and three females. Lower concentrations of albumin and the albumin-globulin ratio and higher γ-globulin values were observed in males of the high dose group (all changes were significant). Absolute and relative organ weights of the adrenals were determined to be significantly increased in high dose males. Adrenal weights of high dose females were also higher than controls, however adrenals from three females only were weighted. Macroscopically, enlargement of the adrenals was seen in one female and discoloration of the adrenal surface was evident in three females of the high dose group. Corresponding to these observations in the adrenals, two females had cortical necrosis with peripheral granulocytic infiltration, one of this was hemorrhagic. Furthermore in a single high dose female ulceration of the forestomach was found.

The NOAEL from this study was considered to be 100 mg/kg bw/d.

In another oral study which is not consistent to the test protocols of current guidelines for subchronic or chronic studies, DHTDMAC was administered to Sprague-Dawley derived albino rats at 0, 0.2, 1.0, 10, or 500 mg/kg bw/d in feed (EPA/OTS, 1992). After 91 days on test, 20 animals/sex each from the 500 mg/kg groups and the control groups and 10 animals from the remaining groups were selected for blood collection and necropsy. Groups of 20 animals/sex at doses of 0, 0.2, 1.0 and 10 mg/kg were selected for blood collection and necropsy after 180 days on test. Additionally 10 animals/sex from these groups were sacrificed after discontinuation of treatment at day 180 and recovery until the day 270. Data on mortality, clinical observations, body weights, food consumption, anatomical pathology and organ weights were collected. At day 91 adrenals and intestinal lymph nodes (anterior and ileocecocolic lymph nodes) were examined histopathologically from all animals sacrificed. In the 500 mg/kg dose groups and control groups, heart, liver and spleen, were also examined. Histopathologic examination was performed on all above-listed organs from all animals sacrificed on day 180. From recovery animals killed on day 270 no other than the anterior mesenteric lymph nodes were examined histopathologically. No test substance related clinical findings or deaths were observed. At the 91-day sacrifice, statistically significant effects were seen in animals of the 500 mg/kg dose group which had lower body weights, decreased body weight gain, decreased feed efficiency and decreased absolute liver and kidney weights in males and increased relative liver weights in females. Microscopic lesions in the adrenal glands of males and females treated at 500 mg/kg were increased incidence of cortical hydropic degeneration and sinusoidal reticuloendothelial cell hyperplasia in the sinusoids of the inner cortex and especially for females, increased incidence of cortical necrosis of cells in the inner cortex with mixed inflammatory cell infiltration. Other histopathologic findings in the high dose group included accumulations of foamy macrophages and sinusoidal reticuloendothelial hypercellularity in enlarged mesenteric lymph nodes, and an increased incidence of chronic liver inflammation (13/20 males and 19/20 females vs. 6/20 males and 4/20 females in control groups). No relevant treatment-related finding was observed in dosed groups at day 180 or 270 of the study, therefore the NOAEL from this 6-month study is 10 mg/kg bw/d (corresponding to 4 mg DODMAC/kg bw/d). The report is incomplete in that all appendices are lacking.

In an early study on beagle dogs (IBT, 1971), no test substance-related effects were seen following 90 days of administration of 0, 14, 140 and 2,800 ppm DHTDMAC in feed (4 males and 4 females/group). Dosage per kg body weight per day was 3.8, 42.4, and 756 mg/kg in males and 4.8, 47.6 and 935.2 mg/kg in females. The study included clinical signs, food consumption, body and organ weights, selected parameters on hematology, clinical chemistry and urinalysis on days 45 and 90, and histopathology of numerous organs/tissues. The study report did not contain summary incidence tables on mean values and no certificates on analytical concentrations and stability.

Dermal application

Although a dermal repeated dose study in animals concordant with the guideline test protocol is not available, the following study on rabbits give some information on DODMAC effects via the dermal route.

20 dermal applications (5 days/week) of 2 ml/kg bw of a 0, 0.2 and 2% aqueous solution containing approx. 75% DODMAC and a mixture of isopropanol and water (bw/d dosage = 0, 4 and 40 mg/kg bw) on clipped skin of 3 male and 3 female rabbits (Gelbsilber)/group induced local skin irritative effects but no clinical or morphological sign of substance-induced systemic toxicity (Hoechst AG, 1974). Skin effects were described to be slight redness, exsiccation, superficial fissures, foldings, dark discoloration and in one animal hemorrhagia without any corresponding microscopic change. In the high dose group, 6/6 animals were affected versus 5/6 animals in the low dose groups, the effects were seen earlier on high dose animals (from the 2nd day versus the 3rd day of treatment) and the duration of effects tended to be longer in the high dose groups. However, severity grades of the lesions observed were only reported for some of them, so that mean severity scores can not be estimated accurately. Analytical certificates on concentrations and stability of DODMAC in the test solutions were not available. The study included clinical signs, some parameters on hematology and clinical chemistry, organ weights (nine organs) and histology (18 organs/tissues). The dermal NOAEL for systemic effects was 40 mg/kg bw/d; the dermal LOAEL for local skin effects was 4 mg/kg bw/d.

Inhalation application

No repeated dose inhalation study is available.

<u>Human data</u>

Not available.

<u>Summary</u>

Subacute and subchronic studies in rats revealed that oral administration of DODMAC as well as DHTDMAC induced degeneration of adrenal cortical cells at high dosages of 500 mg/kg bw/d (Hoechst AG, 1990, EPA/OTS, 1992). From the Hoechst study (Hoechst AG, 1990), higher percentages of neutrophil granulocytes and relative γ-globulinemia observed in the subacute study were interpreted to represent responsive inflammatory reactions to adrenal necrosis. Additionally, the behavioral and respiratory abnormalities as well as effects on the body weight gain observed at this dosage in the subacute DODMAC study were considered as unspecific toxic effects. Considering abnormal gait and reduced spontaneous activity of treated animals it can not be excluded that they were induced by the isopropanol component of the test substance. Isopropanol may also be responsive for the irritative effect inducing stomach ulceration in one high dose females (see skin irritation Section 4.1.2.3), as no macroscopic lesions were reported in the EPA feeding study (EPA/OTS 1992). However the contribution of isopropanol cannot be predicted, because of methodical differences in the spectrum of organs investiged microcopically. Following 91 days of treatment with 500 mg/kg DHTDMAC (EPA/OTS, 1992), relevant findings besides the adrenal lesions were higher frequencies of chronic liver inflammation in comparison to the control groups and sinusoidal reticuloendothelial hyperplasia and numerous foamy macrophages in the mesenteric lymph nodes possibly due to intracellular accumulation of test substance or its degradation products. At dosages below 500 mg/kg bw/d, no significant toxic effect could be identified up to 100 mg/kg bw/d of DODMAC in the subacute toxicity study and up to 10 mg/kg bw/d DHTDMAC (corresponding to 4 mg/kg bw/d DODMAC) in the 6-month study.

Subacute dermal administration of DODMAC (with isopropanol) on clipped rabbit skin induced slight local irritation at dosages of 4 and 40 mg/kg bw/d on 20 days (5 days/week) but no indication on systemic toxicity.

NOAEL for the oral route

No-observed-adverse-effect-level (NOAEL): 100 mg/kg bw/day (rat/oral 28 d study).

The Hoechst study (1990) was accepted as valid study and is therefore the most appropriate to derive a NOAEL for quantitative risk assessment procedures. A NOAEL of 100 mg/kg bw/d of DODMAC results from this oral 28-day rat study. The combined subchronic/chronic study on DHTDMAC (EPA/OTS, 1992) is not considered for the derivation of a NOAEL because of methodical defaults (absence of clinical chemistry examinations, histopathological examinations of only a few organs).

NOAEL for the dermal route

No-observed-adverse-effect-level (NOAEL) for systemic effects: The estimated NOAEL of 40 mg/kg bw/d from the rabbit study (Hoechst AG, 1974) should not be taken for the risk assessment procedures. The oral rat study (Hoechst AG, 1990) is considered to be more reliable than this dermal rabbit study.

No-observed-adverse-effect-level (NOAEL) for local effects on the skin: The only information available was the dermal rabbit study (Hoechst AG, 1974) revealing that the LOAEL for skin irritation was 0.2% aqueous solution of 75% DODMAC and a water-isopropanol mixture (appr. 4 mg/kg bw/d).

4.1.2.7 Mutagenicity

In vitro

The substance, Präpagen WK, tested in all studies consists of 90% dimethyldioctadecylammonium chloride, 5% water, 5% isopropanol.

A bacterial mutation assay was negative in doses up to 2500 µg/plate without and with Aroclor 1254 induced S-9 mix in Salmonella typhimurium strains TA98, TA100; TA1535, TA1537, TA1538 and E.coli WP2uvrA. Concentrations from 1000 µg/plate upwards induced toxic effects (Hoechst AG, 1982).

An in vitro chromosomal aberration assay with V79 cells was negative in concentrations up to 50 µg/ml with and without metabolic activation at fixation time of 18 h and 28 h after start of treatment. With and without S-9 mix cells were treated 4 h with the test substance. The highest doses led to weak cytotoxicity as measured by mitotic index. In a pre-experiment 100 µg/ml were totally toxic. The test was performed according Annex V guideline B10 (Hoechst AG, 1989c). In a further cytogenetic study with V79 cells (May, 1996) for the detection of chromosomal aberrations the test-1substance exhibited already at 80 µg/ml cytotoxic effects. The analysis of chromosomal aberrations in the concentration-range of 15 to 80 µg/ml revealed a negative result, with and without metabolic activation.

In vivo

No data available.

Conclusion

There is no hint on mutagenic properties of the tested substance from the performed in vitro tests.

4.1.2.8 Carcinogenicity

There are no experimental animal data on DODMAC or DHTDMAC. There are no data from mutagenicity which give concern on carcinogenic properties of the test substances.

4.1.2.9 Toxicity for reproduction

Animal data

For distearyldimethylammoniumchloride (GENAMIN DSAC, 96.8% active compound) a GLP conform Reproduction/Developmental Toxicity Screening Test according to OECD Guideline 421 had been performed (RBM Exp. No. 990376) in 1999. Groups of 10 rats (CRL:CD (SD) BR) per sex were treated with dosages of 0, 62.5, 125, and 500 mg/kg bw/day by gavage (administration volume 10 ml/kg bw/day) using corn oil as a vehicle for the control group. Males were treated daily from two weeks before mating, during mating and until a dosing period of a total of 28 days had been completed. Females were treated daily from two weeks before mating until the 4 th day of lactation. Subsequently these females were sacrificed with their pups.

At daily doses of 500 mg/kg bw one male and one female died after 12 respectively 10 treatments. Clinical observations revealed dyspnea, soft stools in all females and almost all males. Half of the females also showed slight to moderate dilation of the abdomen. Body weight loss of about 14 to 15 g was observed in both sexes during the first week of treatment. Further, statistically significantly lower mean daily food consumption was observed in the males during the premating period and in the dams during the first week of pregnancy. Statistically significantly lower mean dam body weights were observed after 14 and 20 days of gestation and at the day of birth after delivery. No toxicologically relevant effects were observed at dosages of 125 and 62.5 mg/kg bw/day.

At sacrifice of the parental animals no significant differences were found on the organ weights of uterus, ovaries, testes and epididymides. Histopathology of testes, epididymides and of the ovaries of the animals of the 500 mg/kg dose groups were reported not show any compound related changes. No substance related changes were reported for the evaluation of testicular stages of spermatogenesis performed in the PAS-hematoxylin stained sections.

At the dosages of 62.5 and 125 mg/kg/day all of the 10 paired females revealed to be sperm positive after mating, all revealed to be pregnant and all delivered live litters. The numbers of corpora lutea had not been evaluated during this study. At 500 mg/kg/day, from the 9 paired females 7 revealed to be sperm positive (77 %) after mating, 6 out of 9 (67 %) revealed to be pregnant, and 5 out of 6 (83 %) delivered live litters. One animal revealed to have fully resorbed. Mean pre-coital time was longer in this group (about 6.1 days) when compared to the controls and the lower dosage groups (1.5 to 2.1 days).

After birth, for the animals treated with 62.5 or 125 mg/kg/day there were no substance related biological differences in their pregnancy outcome in comparison to the control group. At 500 mg/kg /day, the percentage of postimplantation losses was increased to 19 % per litter in comparison to about 6 % per litter in the controls and in the lower treatment groups, thus resulting in a statistically significantly lower rate of live borns of 83 % in comparison to 94 % in the controls and in the lower treatment groups. Viability index on postnatal day 4 was in the range of those of the controls and the lower treatment groups.

For all dose groups under investigation no statistically significant differences were found for the body weights of male and female pups at birth and on postnatal day 4. It is not reported whether pups had been evaluated for any external abnormalities.

No studies on reproductive toxicity of distearyldimethylammoniumchloride with other application routes are available.

No-observed-adverse-effect level (NOAEL)/reproductive toxicity: 125 mg/kg bw/day.

Other information

From a very poorly documented study DODMAC was reported not to show any embryo/fetotoxic activity when applied on the skin of pregnant rats (4 · 4 cm, 0.5 ml ethanolic solution per animal) during the period of organogenesis (6.-15. day of gestation) at dosages (indicated as 0, 22, 33, or 50 mg/ animal and day) sufficient to cause so-called “adverse” maternal reactions, however only in terms of local skin reactions in the dams (Palmer, 1983). The significance of the results of this study for the evaluation of an inherent potential for reproductive toxicity of DODMAC is highly questionable. Due to the well known very poor dermal absorption, the topical route of application is considered not to be suited for these purposes. In addition, since this study does not provide any data whether the substance has been systemically available at all, the rapporteur does not follow the interpretation of the authors of the results of their study.

Further, there is some information from studies with structurally related substances.

Dicetyldimethylammonium chloride (single sc. doses of 50 or 200 mg/kg bw on day 7, 9, 11, 13, or 15 of pregnancy) did not show any specific teratogenic potential in mice, however, there was an increase in the incidence of fetuses with split or bifurcated cervical vertebral arches in all doses (Inoue and Takamuku, 1980).

Another study with cetyltrimethylammonium bromide (single ip doses of 10.5 or 35.0 mg/kg bw on day 8, 10, 12, or 14 of pregnancy) showed an increased incidence of malformations, principally cleft palate and minor skeletal defects in the skull and sternum and increased fetal mortality at the high dose in mice (Isomaa and Ekman, 1975).

Conclusion

There are no human data on the reproductive toxicity of distearyldimethylammoniumchloride. The potential to adversely affect reproduction and development was investigated at a screening level during a study according to OECD Guideline 421 with the oral route of administration. During this study clear signs of general toxicity were observed after repeated administration of 500 mg/kg bw/day in both sexes, a dosage which also led to impaired reproductive performance. Based on the reduced mating, fertility and gestation indices in the 500 mg/kg dose group a NOAEL for reproductive toxicity of 125 mg/kg/day can be estimated from this study.

4.1.3 Risk characterisation

4.1.3.1 General aspects

According to the different exposure scenarios, consumers are dermally exposed to DHTDMAC (DODMAC). Other exposure routes are of minor importance. Local responses at the site of administration are of importance. Dermal absorption is expected to be extremely low.

Human data on the acute toxicity and on local irritation/corrosion caused by DODMAC are not available. In rats, the acute oral, inhalation and dermal toxicity of DODMAC is low. Pure dimethyldioctadecylammonium chloride causes serious damage to the eyes but only moderate irritation to the skin of rabbits. Data on respiratory irritation are not available. Technical grade DODMAC, however, has proven corrosive to the skin of rabbits because of a high content of isopropanol.

DODMAC enhances the allergic potency of other chemical substances, but does not seem to cause skin sensitization by itself as judged on the basis of tests with relevant concentrations of DODMAC.

Following repeated oral exposure of 500 mg/kg bw/d of DODMAC degeneration of adrenal cortex was induced. Comparable lesions in the adrenals were also seen after 500 mg/kg bw/d DHTDMAC, additional effects were reticuloendothelial hyperplasia and accumulation of foamy macrophages of mesenteric lymph nodes and increased incidence of chronic liver inflammation. No adverse effects were reported up to 100 mg/kg bw/d DODMAC in subacute oral studies

(NOAEL). After repeated dermal application to rabbits, local irritation but no systemic toxic effects were observed up to 40 mg/kg bw/d (NOAEL), a systemic LOAEL was not determined.

There is no information on the effects after prolonged inhalative exposure to rodents neither on the health effects in humans via any route.

There is no evidence of a genotoxic potential of DODMAC.

There are no data on carcinogenic effects.

There are no human data on the reproductive toxicity of distearyldimethylammoniumchloride. The potential to adversely affect reproduction and development was investigated at a screening level during a study according to OECD Guideline 421 with the oral route of administration. During this study clear signs of general toxicity were observed after repeated administration of 500 mg/kg bw/day in both sexes, a dosage which also led to impaired reproductive performance. Based on the reduced mating, fertility and gestation indices in the 500 mg/kg dose group a NOAEL for reproductive toxicity of 125 mg/kg/day can be estimated from this study.

No specific human population at risk could be identified within the general population.

4.1.3.2 Workers

A summary of the effects which are relevant for occupational risk assessment is listed in **Table 4.3**.

Table 4.3 Summary of effects relevant for workplace risk assessment (DODMAC)

	Inhalation	Dermal
Acute toxicity	LC50 > 180 mg/l/1 h no lethality	LD50 > 2 000 mg/kg no lethality
Irritation/Corrosivity	threshold for local effects in the respiratory tract unknown	eye: serious damage to the eye skin: the pure substance was moderately irritating (not sufficient for classification), the technical grade substance was corrosive
Sensitization	no case reports; not suspected to be a respiratory sensitizer	no skin sensitizer
Repeated dose toxicity (systemic)	based on oral rat study: extrapolated NAEC: 29 mg/m³	based on oral rat study: extrapolated NAEL: greater than 290 mg/p/d
Repeated dose toxicity (local)	threshold for local effects in the respiratory tract unknown	No valid data available
Mutagenicity	available data are not indicative of a genotoxic potential	
Carcinogenicity	no carcinogenicity study not suspected to be carcinogenic	
Reproductive toxicity	based on oral rat study: extrapolated NAEC: 220 mg/m³	based on oral rat study: extrapolated NAEL: >2200 mg/p/d

For the purpose of risk assessment it is assumed that inhalation of dust and skin contact are the main routes of exposure. Oral exposure is not considered to be a significant route of exposure.

For the following risk characterisation exposure estimates for the component DODMAC are used (see Section 4.1.1.1).

Acute toxicity

Dermal contact

Acute dermal toxicity is considered to be very low. Firstly, the dermal LD_{50} for rats is estimated to be greater than 2,000 mg/kg. There was no lethality at this dose level. Secondly, percutaneous absorption is known to be very low. The highest value for dermal exposure was calculated to be 170 mg/person/d (2 mg/kg/d; see **Table 4.1**). Comparison of this level of exposure with acute dermal toxicity data clearly shows, that acute dermal risks are not considered of 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.

Inhalation

There was no lethality in rats at extremely high exposure levels (180 000 mg^3 for 1 hour). During normal use of DODMAC occupational exposure at this extreme level can be excluded. Therefore acute inhalation risks are not considered of 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.

Irritation/Corrosivity

Dermal contact

Pure DODMAC (97 %) showed mild to moderate skin irritation in rabbits; the degree of local effects is not considered sufficient for classification. Technical grade DODMAC (containing 11.7 % water and 11.3 % isopropanol) however was corrosive in rabbits. Local skin effects of DODMAC seem to be strongly influenced by isopropanol that might improve solubility and contact to skin.

There are no experimental data concerning the acute irritating effect of dilutions of technical grade DODMAC. For preliminary assessment of solutions of technical grade DODMAC it is proposed with reference to the preparations directive to consider dilutions greater than 10 % of technical grade DODMAC as corrosive, and those between 5 % and 10 % as irritating to the skin.

In a subacute dermal rabbit study slight irritation effects are reported following administration of a 0.2 % aqueous solution of technical grade DODMAC. Because irritation scores are incompletely reported, the validity of this study is considered insufficient for risk assessment purposes.

The exposure scenarios summarized in **Tables 4.1 or 4.3** show that there is either handling of corrosive preparations (dilutions of greater than 10 % of technical grade DODMAC) or handling of dilutions of less than 5 % of technical grade DODMAC, which are not considered irritating to the skin.

Skin contact is avoided during handling of corrosive preparations by using personal protective equipment. Potential exposure is assumed only by single contacts. Therefore conclusion ii is reached.

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

While pure DODMAC only showed mild to moderate skin irritation in rabbits, it caused serious damage to the eyes of rabbits. There are no experimental data describing eye irritation effects following exposure to dilutions of DODMAC. With reference to the considerations concerning local skin effects, serious damage to the eyes is anticipated for dilutions with greater than 10 % DODMAC; dilutions between 10 % and 5 % of the substance are considered to be irritating to the eye. Applying the same rationale as for skin irritation, conclusion ii is reached for eye irritation as well.

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.

Inhalation

In an acute inhalation toxicity test with rats signs of respiratory tract irritation are reported at an extremely high single concentration (180,000 $mg/m^3/h$). Based on this limited information, acute irritation potency due to inhalation exposure does not seem to be severe. Referring to these toxicological data and the occupational exposure levels described (**Table 4.1**) relevant acute respiratory tract irritation is not suspected to occur during normal use.

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.

Sensitization

Dermal contact

Based on animal and human data, DODMAC is not considered to be a skin sensitizer. Dermal contact to DODMAC is not anticipated to result in relevant cases of contact allergy.

DODMAC is reported to enhance skin allergy response to known sensitizers. This extra risk of combined exposures (DODMAC and known sensitizer) is considered to be effectively covered for preparations that are classified with R 43 (> 1 % for the sensitizing substance(s) in the preparation).

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.

Inhalation

Asthmatic reactions following exposure to DODMAC so far have not been reported. Structurally related compounds are not known to be respiratory sensitizers. Because DODMAC is not suspected to be a respiratory sensitizer, inhalation exposure is not assumed to result in relevant cases of asthmatic reactions.

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

Dermal contact (local)

This chapter provides no additional information compared with the preceding chapter “irritation/corrosivity, dermal contact”. Please refer to the according passage.

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 (systemic effects)

With reference to the hazard assessment the NOAEL of 40 mg/kg bw/d from the subacute dermal rabbit study is not used for dermal risk assessment. The oral rat study is considered to be more reliable than the dermal rabbit study.

The NOAEL of 100 mg/kg/d (rat, oral, subacute) has to be converted to the anticipated human NAEL for chronic dermal exposure.

For duration adjustment (subacute/chronic) the factor of 1/6 is used (BAU 1994). This duration factor is derived from empirical data for various existing chemicals individually tested with different durations of exposure. The factor 1/6 will probably result in some sort of “central tendency” estimate. A NAEL (rat, oral, chronic) of app. 17 mg/kg/d is estimated. Cross-species scaling on a metabolic rate basis (factor 1/4) yields an anticipated NAEL (human, oral, chronic) of app. 4.2 mg/kg/d. Quantitative information on oral absorption is not available. Therefore for a route-to-route extrapolation the preliminary assumption is made, that the oral absorption is equal to or probably higher than the low dermal absorption. Assuming a human body weight of 70 kg a NAEL (human, dermal, chronic) greater than 290 mg/person/d and a LAEL greater than 1,460 mg/person/d is estimated.

For reasons of comparability the NAEL without duration adjustment and metabolic rate scaling is calculated as well. Assuming a dermal absorption equal to or lower than the oral one, a NAEL greater than 100 mg/kg/d is anticipated. For a worker of 70 kg bodyweight a NAEL greater than 7,000 mg/person/d will result. This NAEL is 24-fold higher than the adjusted dermal NAEL greater than 290 mg/person/d.Based on general toxicological knowledge oral absorption is probably higher than dermal absorption. If, for instance, oral absorption is only 10 times greater than dermal absorption, the estimated dermal NAEL of greater than 290 mg/person/d had to be replaced by a dermal NAEL of 2,900 mg/person/d.

The relevant information for the assessment of systemic chronic toxicity due to dermal contact (exposure, NAEL, MOS) is listed in **Table 4.3**.

The NAEL of > 290 mg/kg/d derived by duration adjustment, metabolic rate scaling and route-to-route extrapolation and the NAEL of > 7,000 mg/kg/d whose extrapolation is restricted to route-to-route extrapolation are compared with the relevant exposure scenarios.

The exposure scenarios with relevant repeated dermal exposure are

- “use of hair-care products” (skilled trade),
- “use of car polishing and car cleaning products” (skilled trade).

It has to be mentioned that the exposure assessment for the 2 scenarios is solely based on EASE calculations without use of personal protective equipment.

These MOS values have been calculated under the assumption that the (unknown) oral absorption is equal to the very low dermal absorption. However, based on general toxicological knowledge oral absorption of DODMAC is probably higher than dermal absorption. If, for instance, oral absorption of DODMAC is only 10 times greater than dermal absorption all MOS values (those with and without modification) are ten times greater than the MOS values listed in the table.

Because of these considerations all MOS values calculated are considered to be of 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.

Table 4.4 MOS values [repeated dose toxicity (systemic, dermal)] of DODMAC

Exposure scenario	Duration/ Frequency	Shift average value [mg/p/day]	MOS[3] [NAEL > 7,000 mg/p/day]	MOS[3] (extrap.) [NAEL > 290 mg/p/day]	Con-clusion
Chemical industry (inclusive cosmetic industry)					
manufacturing of a preparation containing 75 % DHTDMAC, activity: filling, transfer, cleaning, maintenance, repair work	shift length, daily	low[1]	high	high	ii
manufacturing of a preparation containing 16 % DHTDMAC, activity: filling, transfer, cleaning, maintenance, repair work	shift length, daily	low[1]	high	high	ii
production of personal care products, use of the powder containing 95 % DHTDMAC, activity: weighing, filling, cleaning, maintenance, repair work	2 h/daily	low[2]	high	high	ii
Industrial area					
production of fabric softeners, use of preparations containing 75 % DHTDMAC, activity: weighing, filling, cleaning, maintenance, repair work	2 h/daily	low[1]	high	high	ii
production of car cleaning agents, use of preparations containing 75 % DHTDMAC, activity: weighing, filling, cleaning, maintenance, repair work	2 h/daily	low[1]	high	high	ii
Production of organic clays (use of emulsions containing 16% DHTDMAC), activity: weighing, filling, cleaning, maintenance, repair work	2 h/daily	low[1]	high	high	ii
use of hair-care products containing 2 % DHTDMAC, activity: shampooing	5 h/daily	34 - 110	> 64 - 206	3 - 9	ii
use of car polishing and car cleaning products containing 4 % DHTDMAC, activity: cleaning, laying on	shift length, daily	26 - 105	> 67 - 269	> 3 -11	ii

1 corrosive effect of the 75 % resp. 16 % preparation
2 expert judgment (PPE)
3 If oral absorption is 10 times greater than dermal absorption all MOS values listed have to be multiplied by the factor of 10

Inhalation (systemic effects)

Since repeated inhalation toxicity was not investigated, the subacute oral rat study is used for the assessment of systemic toxicity. For human health risk assessment the experimental NOAEL of 100 mg/kg/d (rat, oral, subacute) has to be converted to the anticipated human NAEC for chronic inhalation exposure.

For duration adjustment (subacute/chronic) a factor of 1/6 is used (BAU 1994). A NAEL (rat, oral, chronic) of app. 17 mg/kg/d is estimated. Cross-species scaling on a metabolic rate basis (factor 1/4) yields an anticipated NAEL (human, oral, chronic) of app. 4.2 mg/kg/d. For a route-to-route extrapolation a body weight of 70 kg, a respiratory volume of 10 m^3/8 h and an equivalent inhalatory and oral uptake are assumed, resulting in a NAEC (human, inhalation, chronic) of app. 29 mg/m^3 and a LAEC of app. 145 mg/m^3. Effects on the adrenals are assumed.

For reasons of comparability the NAEC without duration adjustment and metabolic rate scaling is calculated as well. The experimental NOAEL of 100 mg/kg/d will correspond to a human NAEL of 7,000 mg/person/d. Assuming that a worker of 70 kg inhales 10 m^3 air per working day and that an adjustment factor for inhalatory uptake is not necessary, a NAEC of 700 mg/m^3 will result. This NAEC is about 24-fold higher than the adjusted value of 29 mg/m^3.

Table 4.5 MOS values [repeated dose toxicity (systemic, inhalative)] of DODMAC

Exposure scenario	Duration/ Frequency	Shift average value [mg/m^3]	MOS [NAEC: 700 mg/m^3]	MOS (extrap.) [NAEC: 29 mg/m^3]	Con- clusion
Chemical industry (inclusive cosmetic industry)					
manufacturing of preparations containing 75 % DHTDMAC, activity: filling, transfer, cleaning, maintenance, repair work vapour	shift length, daily	negligible[1]	very high	very high	ii
manufacturing of preparations containing 16 % DHTDMAC, activity: filling, transfer, cleaning, maintenance, repair work vapour	shift length, daily	negligible[1]	very high	very high	ii
production of personal care products, use of the powder containing 95 % DHTDMAC, activity: weighing, filling, cleaning, maintenance, repair work					
dust	2 h/daily	0.2 - 0.5[2]	1 450 - 3 500	58 - 145	ii
Industrial area					
production of fabric softeners, use of preparations containing 75% DHTDMAC, activity: weighing, filling, cleaning, maintenance, repair work vapour	2 h/daily	negligible[1]	very high	very high	ii
production of car cleaning agents, use of preparations containing 75 % DHTDMAC, activity: weighing, filling, cleaning, maintenance, repair work vapour	2 h/daily	negligible[1]	very high	very high	ii
production of organic clays, use of emulsions containing 16 % DHTDMAC, activity: weighing, filling, cleaning, maintenance, repair work vapour	2 h/daily	negligible[1]	very high	very high	ii

Table 4.5 continued overleaf

Table 4.5 continued

Exposure scenario	**Duration/ Frequency**	**Shift average value [mg/m³]**	**MOS [NAEC: 700 mg/m³]**	**MOS (extrap.) [NAEC: 29 mg/m³]**	**Con-clusion**
Skilled area					
use of hair-care products containing 2 % DHTDMAC, activity: shampooing vapour	5 h/daily	negligible[1]	very high	very high	ii
use of car polishing and car cleaning products containing 4 % DHTDMAC, activity: cleaning laying on vapour	shift length, daily	negligible[1]	very high	very high	ii
activity: spraying aerosol		[3]	very high	very high	ii

[1] on account of the very low vapour pressure (estimated to 10^{-5} Pa)
[2] EASE (with LEV)
[3] cannot be estimated yet; assumed to be not critical

Systemic health risks due to chronic inhalation exposure are not expected (see **Table 4.4**).

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.

Inhalation (local)

The data from acute irritation testing (eye and skin) and the limit test on acute inhalation with a very high concentration indicate an irritation potential. Respiratory tract irritation potency in acute inhalation testing seems to be low. Local effects in the respiratory tract after repeated inhalation cannot be quantified. Due to physico-chemical properties (e. g. high molecular weight, salt-like character) an exposure to the vapour is not considered to be relevant. A chronic dust exposure is estimated (EASE) for the production of personal care products (2 h/d, shift average: 0.2 - 0.5 mg/m^3), but not in the skilled trade area (see **Table 4.4**). Since the respiratory tract irritation threshold cannot be assessed on the basis of the available data, the corresponding risk for the exposure scenario cannot be estimated. Based on the above information, especially the lack of dust exposure in the skilled trade area, further investigation of chronic respiratory tract irritation seems not to be of immediate 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.

Combined exposure (systemic effects)

There are no workplace scenarios with relevant chronic inhalation and chronic dermal exposure as well. Therefore risks of combined exposure are not considered of 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.

Mutagenicity

Available base set data do not reveal a genotoxic potential. Based on these data mutagenic effects are not anticipated to occur.

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

There are no carcinogenicity data available. Based on negative mutagenicity test results, DODMAC is not suspected to be a carcinogen. Corresponding risks at the workplace are not anticipated to occur.

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.

Reproductive toxicity (fertility impairment, developmental toxicity)

An oral screening study (OECD 421) with DODMAC has been performed in rats. During this study clear signs of general toxicity were observed after repeated administration of 500 mg/kg/d in both sexes, a dosage which led to impaired reproductive performance. Based on the reduced mating, fertility and gestation indices in the 500 mg/kg/d dose group a NOAEL for reproductive toxicity of 125 mg/kg/d can be estimated from this study and used for risk assessment.

Dermal contact

According to the principle described in the chapter on repeated dose toxicity (dermal systemic effects) a human dermal NAEL for reproductive toxicity is estimated. Using a factor of ¼ for cross-species scaling and assuming a reduced systemic availability after dermal exposure a NAEL of >2,200 mg/person/d is calculated for a body weight of 70 kg. A comparison of this value with the highest dermal exposure levels of 170 mg/person (acute) and 110 mg/person/d (chronic) results in extrapolated MOS values of >13 and >20. Both are considered to be high enough to derive no concern.

In addition a direct MOS is calculated for a body weight of 70 kg. Comparing the respective dose of >8,750 mg/person/d (70 x 125) with the dermal exposure levels (170 mg/person (acute) and 110 mg/person/d (chronic)) MOS values of >51 and >80 are calculated. The MOS are considered to be high enough, covering cross species scaling (factor ¼) and further uncertainties of an assessment on the basis of animal data. No concern is derived.

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.

Inhalation

On the basis of the oral NOAEL of 125 mg/kg/d a human NOAEC for reproductive toxicity is estimated. Using a factor of ¼ for cross-species scaling and assuming an equivalent inhalatory and oral uptake a human NAEC of 220 mg/m^3 is calculated for a body weight of 70 kg and a respiratory volume of 10 m^3/8 h (125 x 70 x $(4 \times 10)^{-1}$). A comparison of this concentration with the highest exposure of 2 mg/m^3 (acute) and 0.5 mg/m^3 (chronic) results in extrapolated MOS values of 110 and 440. Both are considered to be high enough to derive no concern.

In addition a direct MOS is calculated comparing the concentration of 875 mg/m^3 ($125 \cdot 70 \cdot 10^{-1}$) with the highest exposure of 2 mg/m^3 (acute) and 0.5 mg/m^3 (chronic). MOS values of 440 and 1,750 are calculated. Both are considered to be high enough, covering cross species scaling (factor ¼) and further uncertainties of an assessment on the basis of animal data. No concern is derived.

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.

Conclusions of the occupational risk assessment

In the occupational risk assessment of DODMAC health risks of workers were evaluated for dermal and inhalation exposure. Overall no concern (conclusion ii) was derived for all toxicological endpoints.

4.1.3.3 Consumers

Acute toxicity

Human data on the acute toxicity of DODMAC are not available. In rats, the substance exhibited only low acute toxicity with oral LD_{50} > 2,000 mg/kg bw, dermal LD_{50} > 2,000 mg/kg bw and inhalation LC_{50} > 100 mg/l/1 hour. The acute toxicity of DODMAC is not to be labeled according to EU legislation.

Following the exposure assessment, consumers are not expected to be exposed to DODMAC (DHTDMAC) in the range of hazardous doses, which can be derived from acute oral or inhalation figures based on animal LD50/LC50 values. Therefore, the substance is of no concern in relation to acute oral or dermal toxicity.

Consumer exposure may occur as a result of using hair cosmetics and softeners containing DHTDMAC. The total amount available for potential uptake by the skin is estimated to be in up to 0.5 mg DODMAC/kg bw and day. Following dermal exposure to rats a LD_{50} of more than 2000 mg/kg bw was established with pure DODMAC (~ 97% purity). Taking into account the poor dermal absorption of the substance across the skin the margin of safety between the estimated combined exposure of humans and the dermal LD_{50} (rat) is considered 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.

Irritation/Corrosivity

Human data on local irritation/corrosion caused by DODMAC are not available. In a test with rabbits according to OECD guidelines moderate skin irritation was detected for dimethyldioctadecylammonium chloride (purity approx. 97%). However, technical grade DODMAC, containing 77% dimethyldioctadecylammonium chloride, 11.3% isopropanol and 11.7% water caused corrosion after a 4-hours contact with the skin of rabbits. Serious damage to the eyes of rabbits is reported after instillation of dialkyldimethylammoniumchloride (97 ± 1% purity, max. 3% water) into the eyes of rabbits.

Based on the reported data, pure DODMAC is classified "Xi, irritant" and labeled "R 41, risk of serious damage to eyes", while technical grade "DODMAC" (containing approximately 12% isopropanol) is to be classified "C, corrosive" and labeled "R 34, causes burns".

According to the dermal exposure scenarios for hair cosmetics and softeners (reasonable worst case) it can be assumed that irritant concentrations of the substance will not occur.

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.

Sensitization

DODMAC is used in cosmetics for the treatment of hair. Moreover, consumer exposure may occur as a result of using softeners. The evaluation of the various information on sensitization testing with DODMAC is difficult, because such testing has to use substance concentrations that have proven to cause only slight skin irritation. Slight irritant effects are elicited with minimal concentrations of technical grade DODMAC, while pure DODMAC needs much higher concentrations in order to cause similar effects.

Based on human patch tests and on tests with guinea pigs, it can be concluded that DODMAC does not induce skin sensitization in humans and thus, has not to be labeled according to EU legislation.

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

Consumers may be dermally exposed to DODMAC (DHTDMAC) via cosmetics and softeners up to 0.5 mg/kg bw/day. An inhalation exposure through dust can be neglected.

Subacute and subchronic studies in rats revealed that oral administration of DODMAC as well as DHTDMAC induced degeneration of adrenal cortical cells at high dosages of 500 mg/kg bw/d. Higher percentages of neutrophil granulocytes and relative γ-globulinemia observed in the subacute study (Hoechst, 1990) were interpreted to represent responsive inflammatory reactions to adrenal necrosis. Considering abnormal gait and reduced spontaneous activity of treated animals it can not be excluded that they were induced by isopropanol as a component of the test substance. Isopropanol may also be responsive for the irritative effect inducing stomach ulceration in one high dose female. Relevant findings in the 6-month study (EPA/OTS, 1992) on treatment with 500 mg/kg DHTDMAC (corresponding to 200 mg/kg DODMAC) besides the adrenal lesions were higher frequencies of chronic liver inflammation in comparison to the control groups and sinusoidal reticuloendothelial hyperplasia and numerous foamy macrophages in the mesenteric lymph nodes following 91 days. At dosages below 500 mg/kg bw/d, no significant toxic effect could be identified up to 100 mg/kg bw/d of DODMAC in the subacute toxicity study (NOAEL) and up to 10 mg/kg bw/d DHTDMAC in the 6-month study.

Subacute dermal administration of DODMAC (with isopropanol) on clipped rabbit skin induced local irritation but no indication of systemic toxicity up to 40 mg/kg bw/day (NOAEL), a systemic LOAEL was not determined.

For the decision on the appropriateness of MOS, the following aspects regarding the critical effect as well as exposure have been considered and taken into account:

Overall confidence in the database

The data taken into account for performing the risk characterization have been evaluated with regard to their reliability, relevance and completeness according to Section 3.2 of the TGD. The data were published in peer reviewed journals or submitted to the Competent Authority in private reports being adequately detailed and in accordance with internationally recognized guidelines and to GLP.

The findings of all studies are not contradictory so that the judgement can be based on the database.

There are no reasons to assume limited confidence.

Uncertainty arising from the variability in the experimental data

The two studies on rats cited above allow to conclude on the NOAEL of severe systemic health effects during oral administration. The range varied from 10 mg/kg bw/d to 100 mg/kg bw/d. The NOAEL of 100 mg/kg bw/d (degeneration of adrenocortical cells) was derived from the 28-day gavage study (Hoechst, 1990) which was well performed and the results were in conformity with the findings of the other studies. The combined subchronic/chronic study on DHTDMAC (EPA/OTS, 1992) is not considered for the derivation of a NOAEL because of methodical defaults (absence of clinical chemistry examinations, histopathological examinations of only a few organs).

There are no reasons to assume a special extent of uncertainty which have to be taken into account.

Intra- and interspecies variation

Specific investigations about the toxicokinetic behaviour and metabolism of the substance are not available. Therefore there is concern, which has to be expressed in the magnitude of the MOS.

Nature and severity of the effect

The main effect considered as “critical effect” is the degeneration of adrenocortical cells (irreversible, serious health effect).

There are no reasons to assume that the effects shown in the animal experiments are limited to the species tested, thus being not of relevance for humans. Because of the seriousness of the effect there is concern, which has to be expressed in the magnitude of the MOS.

Dose response relationship

In rats no steep dose response relationship is observed for the systemic effects (NOAEL 100 mg/kg bw/d, LOAEL 500 mg/kg bw/d).

Therefore, there is no reason to assume concern which has to be expressed in an increased MOS taking into account the exposure level.

Differences in exposure (route, duration, frequency and pattern)

Dermal route

Following the exposure assessment, the consumer may be exposed dermally to DODMAC via usage of softeners and hair cosmetics. The validity of the dermal subacute rabbit study is limited due to the lack of a LOAEL and the low dose level tested. Therefore an oral study is used for determining a MOS.

There are no reasons to assume that special concern can be derived from this procedure concerning different routes. There are rather arguments for considering a lower concern due to the poor dermal absorption.

Human population to which the quantitative and/or qualitative information on exposure applies

Following the dermal exposure there is no reason to assume a special risk for elderly, children or other people suffering from special diseases like obesity or persons with high bronchial reactivity.

Other factors

There are no other factors known requiring a peculiar margin of safety.

MOS for dermal exposure scenario

The calculation of the combined dermal exposure due to hair cosmetics and softeners leads to an external exposure of up to 0.5 mg DODMAC/kg bw/d. The margin of safety between the

dermal external exposure level < 0.5 mg/kg bw/d

and the

oral NOAEL of 100 mg/kg bw/d

is judged to be sufficient. Because of the poor dermal absorption of the substance, the internal exposure will be much lower.

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.

<u>Mutagenicity</u>

A bacterial mutation test and two in vitro chromosomal aberration tests produced negative results. There is no evidence of a genotoxic potential of the substance.

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.

Cancerogenicity:

There is no concern about the cancerogenic potency of DODMAC on the basis of repeated dose toxicity or mutagenicity data.

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.

Reproductive toxicity

Following the exposure assessment consumers may be dermally exposed to DODMAC (DHTDMAC) via cosmetics and softeners up to amounts of 0.5 mg/kg bw/day.

Data from a screening study according to OECD Guideline 421 with oral administration to rats did not give evidence for adverse effects up to doses of 125 mg/kg bw/d. Based on reduced mating, fertility and gestation indices in the 500 mg/kg bw/d dose group a NOAEL for reproductive toxicity of 125 mg/kg bw/day was estimated from this study.

For the decision on the appropriateness of MOS, the following aspects regarding the critical effect as well as exposure have been considered and taken into account:

Overall confidence in the database

The data taken into account for performing the risk characterization have been evaluated with regard to their reliability, relevance and completeness according to Section 3.2 of the TGD. The data were submitted to the Competent Authority in a private report being adequately detailed and in accordance with internationally recognized guidelines and to GLP (cf. Section 4.1.2.9).
There are no reasons to assume limited confidence.

Uncertainty arising from the variability in the experimental data

No special concerns have to be raised from this point.

Intra- and interspecies variation

There are no indication to limit the findings to a single species.

Nature and severity of the effect

Certain influences on reproduction have been observed after treatment with DODMAC at the maternal toxic dose of 500 mg/kg bw (cf. Section 4.1.2.9).

There are no reasons to assume that the effects shown in the animal experiments are limited to the species tested, thus being not of relevance for humans. Therefore, there is concern, which has to be expressed in the magnitude of the MOS.

Dose-response-relationship

No steep dose-response relationship is observed (NOAEL 125 mg/kg bw/d) whereas the mentioned effects occurred at high doses leading to maternal toxicity (500 mg/kg bw/d).

There is no reason to assume concern which has to expressed in an increased MOS taking into account the exposure level.

Differences in exposure (route, duration, frequency and pattern)

Following the exposure assessment, the consumer may be dermally exposed. The estimated external body burden with an assumed absorption of 100% is compared with an oral NOAEL from a Screening study according OECD Guideline 421.

There are no reasons to assume that special concern can be derived neither from this procedure nor from the available toxicokinetic information concerning different routes inasmuch as absorption was set with 100%.

MOS for

Dermal exposure scenario

The estimated dermal exposure is <0.5 mg/kg bw/d. The margin of safety between the

external exposure level of < 0.5 mg/kg bw/d

and the

oral NOAEL of 125 mg/kg bw/d

is judged to be sufficient, even if it is taken into account that properties of DODMAC to adversely affect reproduction could be evaluated only from an OECD 421 screening test.

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.

4.1.3.4 Humans exposed via the environment

Indirect exposure via the environment is calculated using data for oral intake via drinking water, fish and plants (local concentration, worst-case approach). On the basis of these data, a total daily dose of 0.27 µg/kg bw/d is calculated.

Repeated dose toxicity

In a repeated dose toxicity study (rat, oral, 28-day study) the NOAEL for substance-related toxic effects was 100 mg/kg bw/d (cf. Section 4.1.3.3 Repeated dose toxicity).

MOS for the exposure scenario: Humans exposed via the environment

The margin of safety between the

estimated exposure level of 0.27×10^{-3} mg/kg bw/d

and the

oral NOAEL of 100 mg/kg bw/d

is judged to be sufficient, even if special considerations on intra- and interspecies variation and the nature and severity of the effects are taken into consideration and being aware that the exposure calculation is based on a worst case model calculation.

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.

Reproductive toxicity

From the results of an OECD-Guideline 421 study with oral application to rats a NOAEL for reproductive toxicity of 125 mg/kg bw/d was estimated (cf. Sections 4.1.2.9 and 4.1.3.3).

MOS for exposure scenario: Humans exposed via the environment

The margin of safety between the
estimated exposure level of 0.27 x 10^{-3} mg/kg bw/d
and the
oral NOAEL of 125 mg/kg bw/d

is judged to be sufficient taking into account that the calculated local concentrations represent a worst case approach (cf. Section 4.1.1.3). The substance is of no concern in relation to indirect exposure via the environment.

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.

4.1.3.5 Combined Exposure

A person who is exposed indirectly to DODMAC through the environment may also be exposed through different dermal applications. These activities will dominate the total exposure resulting in maximum value of up to 1 mg/kg bw/d.

Repeated dose toxicity

MOS for Combined exposure scenario

A NOAEL of 100 mg/kg bw/d was derived from an oral 28-day study on rats (cf. Sections 4.1.2.6, and 4.1.3.3). The margin of safety between the

estimated exposure level of < 1 mg/kg bw/d
and the
NOAEL (oral) of 100 mg/kg bw/d

is judged to be sufficient. Because of the poor dermal absorption of the substance, the internal exposure will be much lower. Thus, the substance is of no concern in relation to combined 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.

Reproductive toxicity

From the OECD Guideline 421 study on rats a NOAEL of 125 mg/kg bw/d was derived for reproductive toxicity (cf.Sections 4.1.2.9 and 4.1.3.3). The margin of safety between the

calculated exposure level of < 1 mg/kg bw/d

and the

NOAEL (oral) of 125 mg/kg bw/d

is judged to be sufficient even taking into consideration that the properties of DODMAC to adversely affect reproduction could be evaluated only from an OECD 421 screening test. However, due to the poor dermal absorption of the substance the internal exposure will be lower. Thus, the substance is of no concern in relation to combined 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.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

DODMAC has no explosive or oxidising properties due to structural reasons and is not flammable. Therefore with regard to physico-chemical properties and with regard to the occupational exposure (described in Section 4.1.1.2) and consumer exposure (described in Section 4.1.1.3) DODMAC is not expected to cause specific concern relevant to human health. There is no need for further information and/or testing with regard to physico-chemical properties (conclusion ii).

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.

4.2.1 Risk characterisation

4.2.1.1 Workers

With regard to the physico-chemical properties and with regard to the occupational exposure described in Section 4.1.1.2, DODMAC is not expected to cause specific concern relevant to human health.

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.

5 RESULTS

5.1 ENVIRONMENT

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.

The risk assessment shows that the production of DODMAC, the processing to and use of acitvated bentonites as well as the use as fabric softeners, car washing agents and hair conditioners does not indicate a risk to the environment. However, it should be considered that the present risk assessment is based on DODMAC only which is the major component of the technical product DHTDMAC. A risk assessment of DHTDMAC would lead to higher PEC/PNEC ratios.

The DHTDMAC consumption figures for the period 1996 to 1998 (cf. Section 2) show no clear tendency. It has to be ensured that the use of DHTDMAC in fabric softeners, car washing agents and hair conditioners should not increase in the future.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

5.2.1.1 Workers

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.

5.2.1.2 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.

5.2.1.3 Humans exposed via the environment

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.

5.2.1.4 Combined 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.

5.2.2 Human health (risks from physico-chemical properties)

DODMAC has no explosive or oxidising properties due to structural reasons and is not flammable. Therefore with regard to physico-chemical properties and with regard to the occupational exposure and consumer exposure, DODMAC is not expected to cause specific concern relevant to human health.

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.

6 REFERENCES

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ABBREVIATIONS

ADI	Acceptable Daily Intake
AF	Assessment Factor
ASTM	American Society for Testing and Materials
ATP	Adaptation to Technical Progress
AUC	Area Under The Curve
B	Bioaccumulation
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft
BCF	Bioconcentration Factor
BMC	Benchmark Concentration
BMD	Benchmark Dose
BMF	Biomagnification Factor
bw	body weight / *Bw*, *b.w.*
C	Corrosive (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
CA	Chromosome Aberration
CA	Competent Authority
CAS	Chemical Abstract Services
CEC	Commission of the European Communities
CEN	European Standards Organisation / European Committee for Normalisation
CMR	Carcinogenic, Mutagenic and toxic to Reproduction
CNS	Central Nervous System
COD	Chemical Oxygen Demand
CSTEE	Scientific Committee for Toxicity, Ecotoxicity and the Environment (DG SANCO)
CT_{50}	Clearance Time, elimination or depuration expressed as half-life
d.wt	dry weight / dw
dfi	daily food intake
DG	Directorate General
DIN	Deutsche Industrie Norm (German norm)
DNA	DeoxyriboNucleic Acid
DOC	Dissolved Organic Carbon
DT50	Degradation half-life or period required for 50 percent dissipation / degradation
DT90	Period required for 50 percent dissipation / degradation
E	Explosive (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
EASE	Estimation and Assessment of Substance Exposure Physico-chemical properties [Model]

EbC50	Effect Concentration measured as 50% reduction in biomass growth in algae tests
EC	European Communities
EC10	Effect Concentration measured as 10% effect
EC50	median Effect Concentration
ECB	European Chemicals Bureau
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECVAM	European Centre for the Validation of Alternative Methods
EDC	Endocrine Disrupting Chemical
EEC	European Economic Communities
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EN	European Norm
EPA	Environmental Protection Agency (USA)
ErC50	Effect Concentration measured as 50% reduction in growth rate in algae tests
ESD	Emission Scenario Document
EU	European Union
EUSES	European Union System for the Evaluation of Substances [software tool in support of the Technical Guidance Document on risk assessment]
F(+)	(Highly) flammable (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
FAO	Food and Agriculture Organisation of the United Nations
FELS	Fish Early Life Stage
GLP	Good Laboratory Practice
HEDSET	EC/OECD Harmonised Electronic Data Set (for data collection of existing substances)
HELCOM	Helsinki Commission -Baltic Marine Environment Protection Commission
HPLC	High Pressure Liquid Chromatography
HPVC	High Production Volume Chemical (> 1000 t/a)
IARC	International Agency for Research on Cancer
IC	Industrial Category
IC50	median Immobilisation Concentration or median Inhibitory Concentration
ILO	International Labour Organisation
IPCS	International Programme on Chemical Safety
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database (existing substances)
IUPAC	International Union for Pure and Applied Chemistry
JEFCA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
Koc	organic carbon normalised distribution coefficient

Kow	octanol/water partition coefficient
Kp	solids-water partition coefficient
L(E)C50	median Lethal (Effect) Concentration
LAEL	Lowest Adverse Effect Level
LC50	median Lethal Concentration
LD50	median Lethal Dose
LEV	Local Exhaust Ventilation
LLNA	Local Lymph Node Assay
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
LOED	Lowest Observed Effect Dose
LOEL	Lowest Observed Effect Level
MAC	Maximum Allowable Concentration
MATC	Maximum Acceptable Toxic Concentration
MC	Main Category
MITI	Ministry of International Trade and Industry, Japan
MOE	Margin of Exposure
MOS	Margin of Safety
MW	Molecular Weight
N	Dangerous for the environment (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC
NAEL	No Adverse Effect Level
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
NOEC	No Observed Effect Concentration
NTP	National Toxicology Program (USA)
O	Oxidizing (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational Exposure Limit
OJ	Official Journal
OSPAR	Oslo and Paris Convention for the protection of the marine environment of the Northeast Atlantic
P	Persistent
PBT	Persistent, Bioaccumulative and Toxic
PBPK	Physiologically Based PharmacoKinetic modelling
PBTK	Physiologically Based ToxicoKinetic modelling
PEC	Predicted Environmental Concentration

pH	logarithm (to the base 10) (of the hydrogen ion concentration {H^+}
pKa	logarithm (to the base 10) of the acid dissociation constant
pKb	logarithm (to the base 10) of the base dissociation constant
PNEC	Predicted No Effect Concentration
POP	Persistent Organic Pollutant
PPE	Personal Protective Equipment
QSAR	(Quantitative) Structure-Activity Relationship
R phrases	Risk phrases according to Annex III of Directive 67/548/EEC
RAR	Risk Assessment Report
RC	Risk Characterisation
RfC	Reference Concentration
RfD	Reference Dose
RNA	RiboNucleic Acid
RPE	Respiratory Protective Equipment
RWC	Reasonable Worst Case
S phrases	Safety phrases according to Annex III of Directive 67/548/EEC
SAR	Structure-Activity Relationships
SBR	Standardised birth ratio
SCE	Sister Chromatic Exchange
SDS	Safety Data Sheet
SETAC	Society of Environmental Toxicology And Chemistry
SNIF	Summary Notification Interchange Format (new substances)
SSD	Species Sensitivity Distribution
STP	Sewage Treatment Plant
T(+)	(Very) Toxic (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
TDI	Tolerable Daily Intake
TG	Test Guideline
TGD	Technical Guidance Document [1]
TNsG	Technical Notes for Guidance (for Biocides)
TNO	The Netherlands Organisation for Applied Scientific Research
UC	Use Category
UDS	Unscheduled DNA Synthesis
UN	United Nations
UNEP	United Nations Environment Programme
US EPA	Environmental Protection Agency, USA
UV	Ultraviolet Region of Spectrum

UVCB	Unknown or Variable composition, Complex reaction products of Biological material
vB	very Bioaccumulative
vP	very Persistent
vPvB	very Persistent and very Bioaccumulative
v/v	volume per volume ratio
w/w	weight per weight ratio
WHO	World Health Organization
WWTP	Waste Water Treatment Plant
Xn	Harmful (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
Xi	Irritant (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)

Appendix 1

Substance:
DHTDMAC (DODMAC)

Computer model used:
USES 1.0
(Uniform Sytem for the Evaluation of substances)
Category of consumer products:
Cosmetics (hair softeners)
Results:
Dermal uptake by consumer:
0.0225 mg/kg b.w. and day

Name:	DODMAC, dermal 5	
CAS-No.:	107-64-2	
EC-notification no.:	EINECS no.:	
Molecular weight [g.mol-1]:	586.5	
Mol. Formula:		
PARAMETER STATUS		
Scenario:	Dermal No consumer exposure in scenario 5	exposure
Timescale of exposure:	Chronic	Acute
Weight Frac. chem. in product [-]:	0.03 S	??
Number of events per period [events.d-1]:	0.375 S	??
DERMAL EXPOSURE IN SCENARIO 5:	ACTUAL	DEFAULT
UPTAKE BY CONSUMER	CALCULATED	

Inhalatory uptake by consumer [mg.kg-1.d-1]:	??
Oral uptake by consumer [mg.kg-1.d-1]	??
Dermal uptake by consumer [mg.kg.-1d.-1]:	0.0225

REGIONAL: CONCENTRATIONS IN HUMAN INTAKE CALCULATED

Substance:
DHTDMAC (DODMAC)

Computer model used:
USES 1.0
(Uniform Sytem for the Evaluation of substances)
Category of consumer products:
Linen softeners and wool detergents
Results:
Dermal uptake by consumer:
10.99 mg/kg b.w. and day (wool detergents)
18.32 mg/kg b.w. and day (linen softeners)

Name:	DODMAC, dermal 5	
CAS-No.:	107-64-2	
EC-notification no.:	EINECS no.:	
Molecular weight [g.mol-1]:	586.5	
Mol. Formula:		
PARAMETER STATUS		
Scenario:	Dermal No consumer exposure in scenario 4	exposure
Timescale of exposure:	Chronic	Acute
Weight Frac. chem. in product [-]:	0.06 S	??
Number of events per period [events.d-1]:	0.375 S	??
DERMAL EXPOSURE IN SCENARIO 5:	ACTUAL	DEFAULT
UPTAKE BY CONSUMER	CALCULATED	

Inhalatory uptake by consumer [mg.kg-1.d-1]:	??
Oral uptake by consumer [mg.kg-1.d-1]	??
Dermal uptake by consumer [mg.kg.-1d.-1]:	10.99

REGIONAL: CONCENTRATIONS IN HUMAN INTAKE CALCULATED

Substance:
DHTDMAC (DODMAC)

Computer model used:
USES 1.0
(Uniform Sytem for the Evaluation of substances)
Category of consumer products:
Car polish and car cleansing agents
Results:
Dermal uptake by consumer:
8.143 mg/kg b.w. and day

Name:	DODMAC, dermal 5	
CAS-No.:	107-64-2	
EC-notification no.:	EINECS no.:	
Molecular weight [g.mol-1]:	586.5	
Mol. Formula:		
PARAMETER STATUS		
Scenario:	Dermal No consumer exposure in scenario 4	exposure
Timescale of exposure:	Acute	Acute
Weight Frac. chem. in product [-]:	0.04 S	??
Number of events per period [events.d-1]:	0.125 S	??
DERMAL EXPOSURE IN SCENARIO 5:	ACTUAL	DEFAULT
UPTAKE BY CONSUMER	CALCULATED	

Inhalatory uptake by consumer [mg.kg-1.d-1]:	??
Oral uptake by consumer [mg.kg-1.d-1]	??
Dermal uptake by consumer [mg.kg.-1d.-1]:	8.143

REGIONAL: CONCENTRATIONS IN HUMAN INTAKE CALCULATED

European Commission

**EUR 20397 EN/2 – European Union Risk Assessment Report
Dimethyldioctadecylammonium chloride (DODMAC),
Volume 14 published in 2002 with Addendum 2009**

Editors: K. Aschberger, O. Cosgrove, S. Pakalin, A. Paya-Perez, S. Vegro.

Luxembourg: Office for Official Publications of the European Communities

2009 – VIII pp., 121 pp. – 17.0 x 24.0 cm

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The report provides the comprehensive risk assessment of the substance dimethyldioctadecylammonium chloride (DODMAC). It has been prepared by Germany in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to man and the environment, laid down in Commission Regulation (EC) No. 1488/94.

The evaluation considers the emissions and the resulting exposure to the environment and the human populations in all life cycle steps. Following the exposure assessment, the environmental risk characterisation for each protection goal in the aquatic, terrestrial and atmospheric compartment has been determined. For human health the scenarios for occupational exposure, consumer exposure and humans exposed via the environment have been examined and the possible risks have been identified.

The risk assessment for dimethyldioctadecylammonium chloride concludes that there is at present no concern for the environment or for human health. There is at present no need for further information and/or testing or for risk reduction measures beyond those that are being applied already.

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European Commission – Joint Research Centre
Institute for Health and Consumer Protection
former Toxicology and Chemical Substances (TCS)
European Chemicals Bureau (ECB)

European Union Risk Assessment Report
(with addendum 2009)

dimethyldioctadecylammonium chloride
(DODMAC)

CAS No: 107-64-2 EINECS No: 203-508-2

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