SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides

EC No 295-835-2

CAS No 92129-33-4

Evaluating Member State(s): Italy

Dated: 10 October 2019

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2015

Before concluding the substance evaluation a Decision to request further information was issued on: 16 June 2017.

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides were originally selected for substance evaluation in order to clarify concerns about:

- wide dispersive use
- exposure of environment
- high (aggregated) tonnage

Additional concerns identified during the evaluation:

- skin irritation/corrosion
- eye irritation/corrosion

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Not applicable.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State to the following conclusions, as summarised in the table below.

Table 1

CONCLUSION OF SUBSTANCE EVALUATION Conclusions	Tick box
Need for follow-up regulatory action at EU level	X
Harmonised Classification and Labelling	X
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

After the notification of the final decision on substance evaluation, the registrant updated the registration dossier and CSR, not including the exposure scenario "Formulation of pastilles". This use is therefore not supported anymore by the active registrations. Since the final decision on substance evaluation was referred to justification for non-default assumption regarding release factors in the aquatic compartment of the exposure scenario "Formulation of pastilles", the concern related to the environmental risk characterization ratios (RCR) for aquatic compartment does not longer exist.

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised Classification and Labelling

On the basis of the available information, a harmonized classification of the substance is proposed by eMSCA, as a follow-up at EU level for the following hazard category: Skin Corr. 1C, Eye Dam. 1, Aquatic Acute 1 and Aquatic Chronic 1.

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

Not applicable.

4.1.3. Restriction

Not applicable.

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Not applicable.

5.2. Other actions

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

A harmonized classification of the substance is proposed as a follow-up at EU level for Skin Corr. 1C, Eye Dam. 1, Aquatic Acute 1 and Aquatic Chronic 1.
The eMSCA has the intention to prepare an Annex XV dossier with a proposal for harmonized classification and labelling. The intention will be included in the RoI tentatively by the first half of 2021.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides was originally selected for substance evaluation in order to clarify concerns about:

- exposure/Wide dispersive use
- exposure of environment
- high (aggregated) tonnage

Additional concerns raised during the evaluation have been identified about:

- skin irritation/corrosion
- eye irritation/corrosion

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Environmental Exposure and risk characterisation	eMSCA reccomends the registrant to provide detailed information on operational conditions and risk management measures, which are clear and well documented in order to justify the adoption of release factors different from the default ERC ones. For one ES the RCR for aquatic compartment was greater than one adopting default ERC values. The updated registration dossier and CSR do not contain the above-mentioned ES.
Skin Irritation/Corrosion	eMSCA supports the classification of Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides as Skin Corr. 1C therefore a revision of the harmonized classification for this end point should be performed.
Eye Irritation/Eye Damage	eMSCA supports the classification of Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides as Eye Dam. 1 therefore a revision of the harmonized classification for this end point should be performed.
Environmental hazard	eMSCA supports the classification of Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides as Aquatic Acute 1 and Aquatic Chronic 1. Because of differences in self classifications (including M-factors) in the C&L inventory a revision of the harmonized classification for this end point should be performed.

7.2. Procedure

The Substance evaluation of the Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides has started in March 2015.
The initial grounds for concern were related to: exposure/wide dispersive use, exposure of environment, high (aggregated) tonnage.
In the course of the evaluation, the evaluating MSCA identified additional concerns regarding skin irritation/corrosion and eye irritation/ serious eye damage.
The evaluating MSCA considered that further information was required to clarify the above mentioned concerns. Therefore, it prepared a draft decision pursuant to Article 46(1) of the REACH Regulation to request further information. It submitted the draft decision to ECHA on 17 March 2016.
The eMSCA notified the draft decision to the competent authorities of the other Member States and ECHA for proposal(s) for amendment, requesting to submit information on the registered substance regarding environmental exposure-related request (justification for non-default assumption regarding release factors).
As no amendments were proposed, on 16 June 2017 ECHA took the decision according to Articles 52(2) and 51(3) of the REACH Regulation.
After the notification of the final decision on substance evaluation, the registrant updated the registration dossier and CSR, not including the exposure scenario "Formulation of pastilles". This use is therefore not supported anymore by the active registrations.

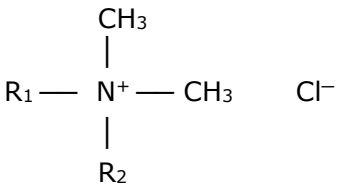
7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides
EC number:	295-835-2
CAS number:	92129-33-4
Index number in Annex VI of the CLP Regulation:	--
Molecular formula:	C16/C16: C34H72N.Cl C16/C18: C36H76N.Cl C18/C18: C38H80N.Cl (see also Table 5)
Molecular weight range:	C16/C16: 530.4 C16/C18: 558.4 C18/C18: 586.5
Synonyms:	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chlorides (DHTDMAC, EC 263-090-2, CAS 61789-80-8)

Type of substance ☐ Mono-constituent ☐ Multi-constituent ☒ UVCB

Structural formula:



where both R_1 and R_2 consist of a linear saturated C16 or C18 alkyl chain

UVCB substance

Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides is an oleochemical of UVCB nature due to the variability in the carbon chain lengths distribution.
Degree of purity: 100% w/w.

Based on the conventions in OECD 193 (*OECD guidance for characterising oleochemical substances for assessment purposes*), the substance should be named more precisely quaternary ammonium compounds, di-C16-18-(even numbered)-alkyldimethyl, chlorides. Molecular formula and molecular weight were indicated in Table 4 only for those constituents which, according to the qualitative/quantitative criteria under OECD 193, should be considered for the characterisation of the substance.

Based on the available analytical information and following the application of the qualitative/quantitative criteria under OECD 193, quaternary ammonium compounds, di-C16-18(even numbered)-alkyldimethyl, chlorides (EC 295-835-2, CAS 92129-33-4) and quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, chlorides (DHTDMAC, EC 263-090-2, CAS 61789-80-8) can be concluded to be the same UVCB oleochemical. The latter was therefore included under synonyms in Table 4.

Table 5

CONSTITUENT **Constituents**	**Typical concentration**	**Concentration range**	**Remarks**
Dihexadecyldimethylammonium chloride (EC 217-325-0, CAS 1812-53-9, C34H72N.Cl)	Confidential information	Confidential information	To be considered for the characterisation of the substance, according to OECD 193 criteria
Hexadecyldimethyloctadecylammonium chloride (CAS 32288-33-8, C36H76N.Cl)	Confidential information	Confidential information	To be considered for the characterisation of the substance, according to OECD 193 criteria
Dimethyldioctadecylammonium chloride or DODMAC (EC 203-508-2, CAS 107-64-2, C38H80N.Cl)	Confidential information	Confidential information	To be considered for the characterisation of the substance, according to OECD 193 criteria

7.4. Physico-chemical properties

Table 6

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Solid (solvent-free)
Melting/freezing point	62.1°C (EU A.1) The result was obtained on a structurally-related oleochemical, i.e. quaternary ammonium compounds, di-C14-18-alkyldimethyl, chlorides (CAS 68002-59-5) *The read-across approach for physical-chemical properties is not generally recommended. Testing according to EU A.1/OECD 102 should be carried out on the registered substance (possibly by DSC, which allows the determination of the melting point and the boiling point of a substance in a single test)**
Boiling point	627.53°C (estimation by MPBPVP program provided by EPI suite published by the US EPA) The estimation was carried out for a structurally-related oleochemical, i.e. quaternary ammonium compounds, di-C14-18-alkyldimethyl, chlorides (CAS 68002-59-5) *The read-across approach for physical-chemical properties is not generally recommended. No justification for not providing an experimental result was given, either. Therefore, testing according to EU A.2/OECD 103 should be carried out on the registered substance (possibly by DSC, see above)**
Relative density	D^{20}_4 is 0.903 (OECD 109) *The purity of the test item is missing**
Vapour pressure	3 E(-09) Pa at 25°C (estimation by the modified Grain method) The estimation was carried out for DDAC (CAS 7173-51-5), which is a different substance, though structurally-related. *The read-across approach for physical-chemical properties is not generally recommended. No justification for not providing an experimental result was given, either. Moreover, the eMSCA is aware of existing experimental studies for DDAC, showing a VP value 1000-fold higher than the one expected by the modified Grain method at 25°C. Therefore, testing according to EU A.4/OECD 104 should be carried out on the registered substance**
Surface tension	37 mN/m at 23°C (ISO 304; Du Noûy ring) Test item: 0.5 g/L solution in water
Water solubility	38 mg/L at 23°C

	(critical micelle concentration, CMC) *Water solubility should usually be determined experimentally (testing should almost always be possible). Here, CMC was used as a "surrogate", without any sound justification for not submitting experimental data on water solubility.* *A knowledge of the CMC is indeed very important for surfactants, e.g. as a measure of their efficiency and for the derivation of a calculated Kow (to avoid the artefact of unrealistically low Kow values). Nevertheless, CMC and water solubility are two different issues. Precipitation and micelle formation are similar but not the same phenomena. Additionally, the study summary on the CMC determination indicates that a "1 g/L stock solution was prepared". Seemingly, a solubility higher than the CMC value (38 mg/L) can be expected. Moreover, the substance is marketed as a technical concentrate in polar solvents (water/alcohols).* *In conclusion, testing according to EU A.6 or OECD 105 should be carried out, to determine the water solubility of the registered substance**
Partition coefficient n-octanol/water (Log Kow)	Log Kow at 25°C: 8.2 for C16/C16 8.4 for C16/C18 8.4 for C18/C18 (OECD 123 – low stirring method) *The substance is surface-active. According to OECD 123 "APPLICABILITY OF THE TEST", the slow stirring method is applicable to substances that do not display significant interfacial activity. Therefore, the above log Kow values are not reliable and cannot be used to predict the substance partitioning behaviour.* *On the other hand, experimentally-determined and higher-tier sorption and BCF/BAF figures are available in the IUCLID dossier, which can be relied on to predict the substance fate in the environment.* *Kow is also necessary as input parameter in environmental exposure estimation models and algorithms. So, a calculated Kow value is necessary, to be derived by solubility in octanol and critical micelle concentration in water (so to avoid the artefact of unrealistically low Kow values)**
Flash-point	Not applicable. The solvent-free substance is solid at room temperature
Flammability	Not a flammable solid (EU A.10)
Auto-flammability	Auto-ignition temperature: 396°C ± 5°C (EU A.15) *The purity of the test item is missing.* *Though the test material was reported to be a solid, EU A.15 "Auto-ignition temperature (Liquids and Gases)" was used instead of EU A.16 "Relative self-ignition temperature of solids". No justification was provided**

Explosive properties	Not explosive, based on the lack of structural alerts
Oxidising properties	Not oxidizing, based on the lack of structural alerts
Granulometry	Not applicable. The solvent-free substance is a solid paste. Besides, the substance is marketed/ used as a technical concentrate
Stability in organic solvents and identity of relevant degradation products	Data waiving. Required only if critical
Dissociation constant	Not required. The substance does not possess any acidic/basic group
Viscosity	Data waiving. The solvent-free substance is solid at room temperature

***** *Text in italics is eMSCA's comment/observation*

7.5. Manufacture and uses

7.5.1. Quantities

Table 7

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☐ 100 – 1000 t	☒ 1000- 10,000 t	☐ 10,000-50,000 t
☐ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

This substance is manufactured and/or imported in the European Economic Area in 1 000+ tonnes per year.
This substance is used by consumers, by professional workers (widespread uses), in formulation or re-packing, at industrial sites and in manufacturing.

Consumer Uses
This substance is used in cosmetics and personal care products.
Other release to the environment of this substance is likely to occur from indoor use as processing aid.

Widespread uses by professional workers
This substance is used in leather treatment products and plant protection products.
This substance is used in agriculture, forestry and fishing areas.
This substance is used in the following activities or processes at workplace: transfer of chemicals, mixing in open batch processes, closed, continuous processes with occasional controlled exposure, closed batch processing in synthesis or formulation, batch processing in synthesis or formulation with opportunity for exposure, roller or brushing applications and non-industrial spraying.
Release to the environment of this substance can occur from processing aids at industrial sites. Other release to the environment of this substance is likely to occur from outdoor use and indoor use as processing aid.

Formulation or re-packing
This substance is used in the following activities or processes at workplace: transfer of chemicals, closed, continuous processes with occasional controlled exposure, closed processes with no likelihood of exposure, closed batch processing in synthesis or formulation, transfer of substance into small containers, mixing in open batch processes and batch processing in synthesis or formulation with opportunity for exposure.
Release to the environment of this substance can occur from industrial use: formulation of mixtures and formulation in materials.

Uses at industrial sites
This substance has an industrial use resulting in manufacture of another substance (use of intermediates).
This substance is used in the following activities or processes at workplace: transfer of chemicals, closed batch processing in synthesis or formulation, closed processes with no likelihood of exposure, batch processing in synthesis or formulation with opportunity for exposure, mixing in open batch processes, closed, continuous processes with occasional controlled exposure, transfer of substance into small containers, roller or brushing applications and treatment of articles by dipping and pouring.
Release to the environment of this substance can occur from industrial use as an intermediate step in further manufacturing of another substance (use of intermediates) and in the production of articles.

Manufacture
This substance is used in the following activities or processes at workplace: transfer of chemicals at dedicated facilities, closed batch processing in synthesis or formulation, transfer of substance into small containers, batch processing in synthesis or formulation with opportunity for exposure, closed processes with no likelihood of exposure and production of mixtures or articles by tabletting, compression, extrusion or pelletisation.
Release to the environment of this substance can occur from industrial use: manufacturing of the substance.

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

The substance is not currently listed on Annex VI of CLP Regulation ((EC) No 1272/2008).

7.6.2. Self-classification

The following hazard classes are present in the C&L Inventory:
Flam. Liq. 3, H226
Skin Corr. 1C, H314
Skin Irrit. 2, H315
Eye Dam. 1, H318
Aquatic Acute 1, H400 with M-factor acute = 1
Aquatic Chronic 1, H410 with M-factor chronic= 10 in ECHA web site (1 in CSR)

Environmental fate properties

Quaternary ammonium compounds, di-C16-18(even numbered)-alkyldimethyl, chlorides are readily biodegradable and removed at 95% from waste waters in sewage treatment plant. On the basis of an experimental BCF value of 13 L/kg, bioaccumulation of the substance is expected to be low.

7.6.3. Degradation

No data are available in the registration dossier on hydrolysis and phototrasformation in air, water and soil. Concerning biotic degradation, a key study with reliability 1 was performed according to a standard test protocol (OECD test guideline 301D, Ready Biodegradability Closed Bottle test). Quaternary ammonium compounds, di-C16-18(even numbered)-alkyldimethyl, chlorides was not biodegraded after 28 d (3%).
The registrant concluded that the substance is not readily biodegradable and based on the available information, the eMSCA can support this conclusion.
Regarding the degradation in sewage treatment plant, based on the results of a study performed according to OECD 303 A (Simulation Test - Aerobic Sewage Treatment. A: Activated Sludge Units), the registrant concluded that at least 95% of the substance is removed from waste waters after passing the treatment unit. The eMSCA, based on the available information, can support this conclusion.

7.6.4. Environmental distribution

Concerning the adsorption/desorption the registrant proposed a log Kp = 4.22, based on read-across approach. A justification in support of read-across approach from DODMAC to DHTDMAC has been provided by the registrant. The eMSCA can support this conclusion and the read-across approach.

7.6.5. Bioaccumulation

Concerning bioaccumulation the registrant concluded the substance is not bioaccumulative on the basis of a key study with reliability 1 performed in *Lepomis macrochirus* (BCF whole body w.w. in river water= 13 L/kg). Based on available information, the eMSCA can support this conclusion.

7.7. Environmental hazard assessment

7.7.1. Aquatic compartment (including sediment)

7.7.1.1. Fish

The acute toxicity key test was based on a read across approach with the substance DODMAC (CAS 107-64-2). Based on the available information the eMSCA can support the read across approach and concludes that the substance is chronically toxic to fish (LC50 freshwater of 21.3 mg/L; LC50 marine water of 59.3 mg/L; NOEC freshwater of 0.23 mg/L).

7.7.1.2. Aquatic invertebrates

Both the acute and chronic toxicity key tests were based on a read across approach with the substance DODMAC (CAS 107-64-2). Based on the available information, the eMSCA can support the read across approach and concludes that the substance is chronically toxic to invertebrates (LC50 freshwater of 3.1 mg/L; LC50 marine water of 3.3 mg/L; NOEC freshwater of 0.38 mg/L).

7.7.1.3. Algae and aquatic plants

The registrant concluded that the substance is acutely and chronically toxic to algae (LC50 freshwater of 0.48 mg/L; LC50 marine water of 0.24 mg/L; NOEC freshwater of 0.062; NOEC marine water of 0.1 mg/L), and based on the available information, the eMSCA can support this conclusion.

7.7.1.4. Sediment organisms

The registrant concluded the substance is not toxic to sediment organisms based on a read across approach with the substance DODMAC. The EC_{10} value was obtained with *Tubifex tubifex* (550 mg/kg dw). A justification in support of read-across from DODMAC to the registered substance has been provided by the registrant. The eMSCA can support this conclusion and the read-across approach.

7.7.1.1. Other aquatic organisms

The registrant did not report any information.

7.7.2. Terrestrial compartment

The terrestrial toxicity potential of quaternary ammonium compounds, di-C16-18(even numbered)-alkyldimethyl, chlorides has been reviewed in the frame of a European Risk Assessment (RAR) published in 2002 by German Authorities. Based on RAR information, the registrant concluded that N-C16-C18(even numbered)-alkyl-N,N-dimethyl-C16-C18(even numbered)-alkyl-1-aminium chloride is not highly toxic to terrestrial organisms depending on operational conditions of exposure.

7.7.3. Microbiological activity in sewage treatment systems

Concerning the toxicity to aquatic micro-organism the registrant concluded that Nitrifying bacteria are the most sensitive microorganisms with the lowest EC_{50}=2.1 mg/L. Based on the available information, the eMSCA can support this conclusion.

7.7.4. PNEC derivation and other hazard conclusions

Table 9

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	$PNEC_{aqua\text{-}freshwater}$: 6.2 µg/L	Assessment factor: 10 Data from long-term toxicity tests of 3 throphic levels are available and the most sensitive species was algae with a NOEC value of 0.062 mg/L, therefore this value and an assessment factor of 10 are used for deriving the PNEC
Marine water	$PNEC_{aqua\text{-}marine\ water}$: 0.62 µg/L	Assessment factor: 100 Acute toxicity data are available for marine species of 3 throphic levels and are similar to those obtained in the freshwater compartment. Since there are no data of long-term results from marine species, results from the freshwater compartment are used for the calculation of this PNEC and an assessment factor of 100 is applied

Intermittent releases to water	$PNEC_{aqua\text{-}intermittent\ releases}$: 2.4 µg/L	Assessment factor: 100 This PNEC is based on the lowest L(E)C50 values obtained in the frame of the acute toxicity tests. An assessment factor of 100 applies. The most sensitive species being marine algae (LC50 marine water of 0.24 mg/L), this test is used for deriving the PNEC
Sediments (freshwater)	$PNEC_{sediment}$ calculated on the basis of one of eight studies on sediment organisms included in the RAR. The EC10 value used for the PNEC derivation is from one of the test with DODMAC (Comber and Conrad, 2000). In particular, for the derivation of the $PNEC_{sediment}$ the EC10 value of 550 mg/kg dw obtained for Tubifex tubifex was used.: $PNEC_{sediment(freshwater)}$ = 55 mg/kg dw	Assessment factor: As long-term tests with species representing three different living and feeding conditions and therefore different exposure pathways are available, assessment factors of 10 and 50 were used for $PNEC_{sediment(freshwater)}$ and $PNEC_{sediment(marine\ water)}$ respectively.
Sediments (marine water)	$PNEC_{sediment}$ calculated on the basis of one of eight studies on sediment organisms included in the RAR. The EC10 value used for the PNEC derivation is from one of the test with DODMAC (Comber and Conrad, 2000). In particular, for the derivation of the $PNEC_{sediment}$ the EC10 value of 550 mg/kg dw obtained for Tubifex tubifex was used.: $PNEC_{sediment(marine\ water)}$ = 11 mg/kg dw	Assessment factor: As long-term tests with species representing three different living and feeding conditions and therefore different exposure pathways are available, assessment factors of 10 and 50 were used for $PNEC_{sediment(freshwater)}$ and $PNEC_{sediment(marine\ water)}$ respectively.
Sewage treatment plant	PNECSTP=0.21 mg/l The calculation of PNECSTP is based on the result of the study with nitrifying bacteria that were found to be the most sensitive organisms.	Assessment Factor: 10 Since nitrifying bacteria are tested (EC50 value of 2.1 mg/), an assessment factor of 10 is applied.
Soil	$PNEC_{soil}$ calculated on the basis of the 28d NOEC >365 mg/kg from one of the tests with DHTDMAC (Täuber et al., 1986): $PNEC_{soil}$= 7.3 mg/kg dw	Assessment factor: 50 Applied to the lowest of two trophic levels covered with long-term data: plants (NOEC=1000 mg/kg) and micro- organisms (28d NOEC >365 mg/kg).

7.7.5. Conclusions for classification and labelling

Based on available information, the eMSCA can support the conclusion of the registrant about the classification of the substance.

Aquatic Acute 1 – H400 with M-factor = 1
Aquatic Chronic 1 – H410 with M-factor = 1

7.8. Human Health hazard assessment

7.8.1. Toxicokinetics

7.8.2. Acute toxicity and Corrosion/Irritation

The acute systemic toxicity of quaternary ammonium compound, di-C16 -18 -alkyldimethyl, chloride by oral, dermal and inhalation routes was investigated by testing technical grade dihydrogenated tallow alkyl dimethyl ammonium chloride (DHTDMAC, 70 to 75% active in isopropanol/water) as well as pure dioctadecyldimethylammonium chloride (DODMAC, 97% in water).

7.8.2.1. Acute oral toxicity

Concerning the oral acute toxicity the registrant presented three experimental studies. Two of these are valid studies and are supported by the result of a third study for which only the executive summary of the study report is available.

The key study submitted in the registration dossier was conducted according to OECD TG 401. Based on a preliminary study, indicating no deaths in 2 males and 2 female rats at 5000 mg/kg bw, the main experiment was performed at the limit dose level of 5000 mg/kg bw on rats. Under the experimental conditions, the acute median lethal dose (LD50) of quaternary ammonium compound, di-C16 -18 -alkyldimethyl, chloride was greater than 5000 mg/kg bw thus the tested substance is not classified.

The eMSCA supports this conclusion.

7.8.2.2. Acute inhalation toxicity

Concerning the acute inhalation toxicity the registrant submitted in the registration dossier an experimental study conducted according to other guideline than OECD: Revised, Federal Register, september 17, 1964. The 1 hour LC50 was found to exceed 180 mg/l. No mortalities occurred and the symptomatology restricted to the day of exposure did not indicate a toxic potential by inhalation. Additional testing for acute inhalation toxicity is scientifically not justified because of animal welfare reasons. The substance is a strong irritant for which risk reduction measures have to apply anyway. Limited existing data on acute inhalation toxicity do not indicate major concerns. This justification is in line with the conclusions of the available EU RAR (Final report 2002).

The eMSCA supports this conclusion.

7.8.2.3. Acute dermal toxicity

Concerning the acute dermal toxicity the registrant presented an experimental study conducted according to the OECD Guideline 402. The LD50 of the test material was greater 2000 mg/kg body weight in rats thus the test material is not classified for acute dermal toxicity. The eMSCA supports this conclusion.

7.8.2.4. Skin corrosion/irritation

Technical grades dihydrogenated tallow alkyl dimethyl ammonium chloride or dioctadecyldimethylammonium chloride (DHTDMAC or DODMAC, 75 to 78% active in isopropanol/water) as well as pure dioctadecyldimethylammonium chloride (DODMAC, 97% in water) were investigated for skin corrosion/ irritation in four reliable without restriction studies.

Concerning the skin corrosion/irritation end-point the registrant presented studies all performed according to the OECD guideline 404 in compliance with Good Laboratory Practice (GLP).

In a first experimental study conducted in 1996 submitted in the registration dossier, pure DODMAC (97% in water) applied to the skin of 3 rabbits under a semi-occlusive dressing, was only slightly irritating to skin following a 4-hour exposure period. In this study, skin reactions were observed approximately at 0.5, 1, 24, 48 and 72 hours after removal of the dressing and the non day 7, 14 in order to observe their reversibility. The mean scores over 24, 48 and 72 hours for individual animals were 2.0, 1.0, and 0.3 for erythema and 0.0, 0.0, and 0.0 for oedema. Whereas no oedema were observed following treatment, mild to moderate erythema occurred which reversed fully within the observation period of 14 days. Based on these results, pure quaternary ammonium compound, di-C16 -18 -alkyldimethyl, chloride should not be subject for classification and labelling requirements regarding skin irritation.
Nevertheless, in three other submitted studies reported in the registration dossier performed with DHTDMAC and/or DODMAC (75 to 78% active in isopropanol/water), severe skin irritation up to corrosive effects were observed after a 4 -hour exposure period under semi-occlusive dressing.
In other two studies reported in the registration dossier conducted in 1991 and 1989, the observed effects were interpreted as being reversible, while in another study conducted in 1989 and also reported in the registration dossier, slight to moderate erythema and oedema reactions increased over time until exhibition of necrosis. In this last study, DODMAC at 77 % active in isopropanol/water, was applied to the skin of 3 rabbits for 3 minutes or 4 hours. The skin was examined at 30, 60 minutes and 24, 48 and 72 hours after removal of the dressing. Since effects were still present after 72 hours, additional readings were performed after 7 and 14 days.
A slight transient erythema was noted in 2 animals after 3 minutes of exposure at one 24 hours following removal of the patches. No signs of irritation were observed after 48 hours and later.
After 4 hours of exposure, the skin of animals exhibited slight erythema and moderate oedema one hour after removal of the patches. At the 24 and 72-hour readings, moderate erythema and slight to moderate oedema were observed. Additionally the skin was leathery. Seven days post application moderate to severe erythema in all animals and slight oedema in one animal appeared. Swelling of the other animals could not be assessed because of induration. This was still partially the case after 14 days.
In two rabbits well-defined to severe erythema and slight oedema were observed at this time point.
The skin was also indurated, raised, scabbed, chapped, parchement-like and with fine or coarse scales. A scar had developed in two animals 14 days after the application.
Based on these results, technical grades in isopropanol/water should be classified as Skin Corr. 1C.

7.8.2.5. Serious eye damage/eye irritation

Technical grades dihydrogenated tallow alkyl dimethyl ammonium chloride (DHTDMAC, 78% active in isopropanol/water) as well as pure dioctadecyldimethylammonium chloride (DODMAC, 97% in water) were investigated for skin irritation/corrosion in two studies.
The technical grade DHTDMAC was tested in a study conducted on 1991 and submitted in the registration dossier. The potential of the test material (78% active in isopropanol/water) to induce eye irritation was assessed only in 1 rabbit for ethical considerations as severe ocular effects were anticipated according to the OECD guideline 405 and the principles of Good Laboratory Practice. A single dose of 0.1ml of the test material was instilled into one eye, the other eye was not treated and served as control. The eyes were not rinsed after administration of the test item. Ocular reactions were observed 1 hour and 24 hours later. 1 hour then 24 hours after instillation of the test substance, the ocular reactions were severe and the conjunctival chemosis (score of 4) obscured the evaluation of the reactions at the iris and cornea. The flowing of a whitish

purulent substance was also noted. Some severe ocular lesions were expected at the next reading times but taking into consideration the severity of the lesions noted after 24 hours, the animal was sacrificed for ethical grounds before the nature of the reactions concerning the iris and the cornea could have been checked. Under these experimental conditions, the test material was considered as severely damaging when administered by ocular route to rabbits. The pure DODMAC (97% in water) was tested in a study and conducted in 1986. The executive summary submitted in the registration dossier reported that the study was conducted according to OECD guideline 405. After installation of 100 mg test substance into the eyes of rabbits severe damaging reactions were observed.

Under the experimental conditions of these studies and according to the criteria laid down in Regulation EC No 1272/2008/EC (CLP Regulation), the test material should be classified as Eye Dam. 1.

7.8.3. Sensitisation

Skin sensitisation:
According to result of the human repeat insult patch test supporting by the two others studies performed in human volunteers and the guinea-pig maximization test result, the test material is not classified for skin sensitisation.
The eMSCA supports this conclusion.

Respiratory sensitisation:
The registration dossier doesn't report information on the sensitising potential of the substance via the inhalation route. As quaternary ammonium compound is not considered as a sensitizer via the dermal route the risk that the substance is a respiratory sensitizer is regarded as negligible. Based on this reasoning the substance does not need to be classified for respiratory sensitization according to the criteria laid down in the CLP Regulation. Therefore, neither further information nor additional classification is required.

7.8.4. Repeated dose toxicity

The repeated dose toxicity of quaternary ammonium compound, di-C16-18 (even numbered)-alkyldimethyl, chloride was investigated by oral and dermal routes in several subacute and subchronic studies performed in rats and dogs. Based on all available data, the substance does not require classification with regard to repeated dose toxicity according to the CLP Regulation.

The eMSCA supports this conclusion.

7.8.5. Mutagenicity

GENETIC TOXICITY IN VITRO
Dioctadecyldimethylammonium chloride (DODMAC, 90% in isopropanol/water) as well as the structural analogue Dihydrogenatedbenzylmethylammonium chloride (purity 96%) were investigated for genetic toxicity in three in vitro tests.

1- Gene mutation in bacteria:
One study on gene mutation in bacteria is available. The study predates GLP requirements but the method used is similar to the OECD guideline 471. The study gave negative results both with and without metabolic activation.

2- Chromosomal aberrations in mammalian cells:
One in vitro study on chromosome aberration is available performed according to OECD guideline 473 and Good Laboratory Practices. The results showed that the substance had not clastogenic activity in the *in vitro* mammalian chromosome aberration test with V79 chinese Hamster cells.

3- Gene mutation in mammalian cells:
The endpoint gene mutation in mammalian cells is covered in the registration dossier by read across from a respective study conducted with the structurally closely related substance 'benzyl-di-C16-18-alkylmethylammoniumchloride'. In the gene mutation study the potential of 'benzyl-di-C16-18-alkylmethylammoniumchloride' to induce mutations at the TK locus, was investigated in L5178Y mouse lymphoma cells according to OECD guideline 476 and GLP. The negative results in the 'benzyl-di-C16-18-alkylmethylammoniumchloride' suggested that also the registered substance could be not mutagenic in the *in vitro* mammalian cell gene mutation test.

Conclusion:
Based on the available data, there is no indication of a mutagenic potential for quaternary ammonium compound, di-C16 -18 -alkyldimethyl, chloride. Moreover, two evaluation reports on the structural closely related DidecylDimethylAmmonium Chloride (DDAC) have been recently published by the European Competent Authorities and conclude that the substance was of no concern for genetic toxicity (Document I- Draft Evaluation reports in the frame of the directive 98/8/EC concerning the placing of biocidal products on the market - DDAC CAS 7173 -51 -5-Product type 8 - RMS Italy, June 2015).

7.8.6. Carcinogenicity

No data available.
Limited data from repeated dose toxicity studies have not provided any indications of pre-neoplastic, neoplastic or carcinogenic effects.
Moreover, the consistently negative results from the series of in vitro genotoxicity tests assessing gene mutation and chromosomal damage do also not give any concern that the substance may have a carcinogenic potential.
Finally, two evaluation reports on the structural closely related DidecylDimethylAmmonium Chloride (DDAC) have been recently published by the European Competent Authorities and conclude that the substance was not carcinogenic in an appropriate study (Document I- Draft Evaluation reports in the frame of the directive 98/8/EC concerning the placing of biocidal products on the market - DDAC CAS 7173 -51 -5- Product type 8 - RMS Italy, June 2015).

Therefore the eMSCA concludes that based on the available data there is no concern for carcinogenicity.

7.8.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

Not evaluated.

7.8.8. Hazard assessment of physico-chemical properties

Not evaluated.

7.8.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

In the CSR, the registrant derived the DNEL using ECETOC guidance (2010). The eMSCA does not support this approach, hence the DNEL values derived by the eMSCA using the ECHA R8 Guidance are reported below.

Workers

Dermal DNEL

Identified key study for DNEL derivation is the 28-day oral toxicity study in rats which results in a NOAEL of 100 mg/kg body weight per day. A default factor of 10% skin absorption is used and no correction factor for differences in absorption between animals and human is applied so the corrected$_{\text{dermal, systemic}}$ NOAEL = 1000 mg/kg bw/d. Route to route extrapolation must be applied.

Inhalation DNEL

Identified key study for DNEL derivation is the 28-day oral toxicity study in rats which results in a NOAEL of 100 mg/kg body weight per day.
Correction for respiratory volume between rat and human: 1/ 0.38 m3 /kg bw.
Correction for activity driven differences of respiratory volumes in workers compared to workers in rest: 6.7 m^3/10 m^3.
Corrected inhalation, systemicNOAEL = 100 x 1.76 = 176 mg/m^3, route to route extrapolation must be applied.

General population/Consumers

Use of cosmetics is covered by Regulation (EC) No. 1223/2009. Although no general consumer uses is supported by the registrant, and it is not expected a significant indirect exposures via the environment an oral DNEL long-term (systemic) has been derived for completeness.
Identified key study for DNEL derivation is a 28-day oral toxicity study in rats which results in a NOAEL of 100 mg/kg body weight per day.

Table 10

CRITICAL DNELS/DMELS					
Endpoint of concern	**Type of effect**	**Critical study(ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL/ DMEL**	**Justification/ Remarks**
Workers Dermal	Long-term - systemic effects	repeated dose toxicity	NOAEL: 1000 mg/kg bw/day	DNEL=8.3 mg/kg bw/day	Route-to-route AF =0.1 (default 10% dermal absorption). Interspecies after allometric scaling AF = 4. Intraspecies for workers AF = 5. Exposure duration (from subacute to chronic) AF = 6. Dose-response AF = 1 (starting point is a NOAEL). Quality of database AF =1 (complete and consistent).
Workers Inhalation	Long-term - systemic effects	repeated dose toxicity	NOAEC: 176 mg/m³	DNEL=5.9 mg/m³	Route-to-route AF =1 (based on pulmonary physiology and clearance dynamics of particula matters / aerosols no differences in absorption rate to be expected). Allometric scaling not applicable for oral to inhalation extrapolation. Intraspecies for workers AF = 5. Exposure duration AF = 6 (subacute to chronic exposure). Dose-response AF = 1 (starting point is a NOAEL). Quality of database AF =1 (complete and consistent)
General population Oral	Long-term - systemic effects	repeated dose toxicity	NOAEL: 100 mg/kg bw/day	DNEL= 0.41 mg/kg bw/day	For the derivation the following assessment factors were

					applied: Route-to-Route: AF = 1; Interspecies extrapolation: AF=4 (allometric scaling rat to humans); Remaining differences: AF = 1 (included in variability assessment); Intraspecies variability: AF =10; Exposure duration: AF=6 (subacute to chronic, effects mainly concentration but not dose driven); Dose-response: AF=1 (no conspicious behaviour); Quality of database: AF=1 (judged sufficient for evaluation)

7.8.10. Conclusions of the human health hazard assessment and related classification and labelling

On the basis of the available information, a harmonized classification of the substance is proposed by eMSCA, as a follow-up at EU level for the following hazard category: Skin Corr. 1C and Eye Dam. 1.

7.9. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.10. PBT and VPVB assessment

Persistent assessment

Based on the results of the ready biodegradability study, the eMSCA considers the substance potentially P/vP.

Bioaccumulation assessment

Based on the results of the bioaccumulation study, the eMSCA considers the substance does not fulfil the B/vB criteria.

Toxicity assessment

The substance does not meet the T criteria in the contest of PBT assessment.

7.11. Exposure assessment

7.11.1. Human health

As reported by the registrant in the CSR, quaternary ammonium compounds, di- C16-18 (even numbered)-alkyldimethyl, chlorides only industrial uses are relevant for the exposure assessment since no exposure is expected for professional use scenarios while consumer exposure could be envisaged only for cosmetic use that is covered by Regulation (EC) No. 1223/2009.

7.11.1.1. Worker

As worker exposure is determined only by the exposure duration and relevant PROC (rather than by tonnage, which may vary use by use) exposure assessments for each PROC has been estimated using the ECETOC TRA model for each relevant PROC for each exposure scenario.

7.11.2. Environment

For the environmental exposure assessment the eMSCA used the ECHA Guidance and Technical Guidance Document (TGD 2003).

The eMSCA assessed all the exposure scenarios submitted by the registrant. Regarding the input parameters for program EUSES, the eMSCA could only examine one EUSES Summary report for Cosmetic Use. The eMSCA notes that some input parameters are not in compliance with physico-chemical properties of the substance.

The registrant did not report a distribution model of the substance in the environment. Based on physico-chemical properties and the results of sewage treatment plant simulation test and adsorption/desorption test, the substance will preferentially be distributed into water and sediment compartments. Moreover, taking into account the assumption of municipal STPs adopted as RMM and the possible use of STP sludge as agricultural fertilizer, the distribution of the substance involves also the soil compartment. The sorption of the registered substance to soil and sediment can vary in a wide range depending on the nature of the adsorbent.

The environmental exposure assessment performed by the registrant is based on the release factors for different use categories from Appendix I of TGD (2003) - part II (A/B Tables) as utilized by the program EUSES.

The eMSCA observes that in CSRs, only in the exposure scenarios (ESs) "Manufacture of coatings-organic solvent borne, water borne and solvent free products", "Manufacture of coatings-powder coatings", "Industrial application of coatings", "Professional applications of coatings" the registrant specified the source (emission tables of TGD) of release factors values but the reported values do not match with the values of A/B Tables. In the other ESs the the registrant did not specify the table sources. The registrant did not provide a clear and detailed justification, based on Risk Management Measures/Operational Conditions/substance properties.

The eMSCA recommends the registrant to provide detailed information on operational conditions and risk management measures, which are clear and well documented in order to justify the adoption of release factors different from the default ERC ones.

7.11.2.1. Aquatic compartment (incl. sediment)

Concerning the release factors adopted by the the registrant, for the exposure scenario (ES) "Formulation of pastilles" the eMSCA noted that the used release factors are not linked to specific A/B Tables of the TGD. The adopted values were one order of magnitude lower than the corresponding TGD values related to the industrial and use category declared by

the the registrant (IC3 - chemical industry. chemicals used in synthesis and to UC9 - absorbents and adsorbents). The justification provided by the registrant was a generic qualitative statement and it was not sufficient to justify the refinement. The eMSCA noted that the adopted release factors underestimate RCR values for the aquatic compartment (freshwater and marine water) for the above-mentioned ES: the use of default ERC release factors determines RCR values higher than 1.

After the notification of the substance evaluation decision, the registrant updated the registration dossier and CSR, not including the exposure scenario "Formulation of pastilles".

Moreover, in the CSRs, regional PEC values for aquatic compartment are not specified. The local PEC values reported by the registrant for each scenario shall include the contribution of regional background (regional PEC values). The eMSCA recommends the registrant to provide reliable regional PECs value in an update of the registration dossier.

In order to clarify the possible impact on the environment and potential human exposure via the environment, information on groundwater is required. The registrant did not report information about groundwater compartment and did not provide any justification. The eMSCA estimated the local PEC groundwater, by using the specific equations of TGD (2003) and the obtained value is very low (in the order of 10^{-6}).

7.11.2.2. Terrestrial compartment

The registrant provided regional PEC_{soil} values for few ES which are different from each other.

The local PEC values provided by the registrant for each scenario shall include the contribution of regional background (regional PEC values). The eMSCA recommends the registrant to provide reliable regional PECs value in an update of the registration dossier.

Moreover, the eMSCA notes that in all CSRs local PEC_{soil} values correspond with regional PEC_{soil} values, where provided, and, at the same time, with local concentrations in the soil.

7.11.2.3. Atmospheric compartment

Taking into account the substance properties, eMSCA considers the atmospheric compartment not relevant.

7.11.3. Combined exposure assessment

Not evaluated.

7.12. Risk characterisation

Environment

The eMSCA perfomed the risk assessment for all the exposure scenarios submitted by the the registrant.

During the evaluation. the eMSCA concluded that the risks are controlled except for the exposure scenario (ES) "Formulation of pastilles" for the aquatic compartment (freshwater and marine water), since the RCR values for this scenario are underestimated using the release factors adopted by the the registrant. The adopted values are one order of magnitude lower than the corresponding TGD values related to the industrial and use category declared by the the registrant (IC3 - chemical industry: chemicals used in synthesis and UC9 - absorbents and adsorbents). The use of default ERC release factors determines RCR values higher than 1.

After the notification of the substance evaluation draft decision, the registrant updated the registration dossier and CSR, not including the exposure scenario "Formulation of pastilles". This use is therefore not supported anymore by the active registrations.

7.13. References

- European Commission, 2002. European Union Risk Assessment Report:Dimethyldioctadecylammonium Chloride (DODMAC) vol. 14 (EUR 20397 EN. https://echa.europa.eu/documents/10162/6434698/orats_summary_dimethyldioctadecylammoniumchl_en.pdf)
- European Commission – Joint Research Centre Institute for Health and Consumer Protection European Chemicals Bureau, Technical Guidance Document on Risk assessment (2003)
- OECD Guideline 193 (*OECD guidance for characterising oleochemical substances for assessment purposes*) ENV/JM/MONO(2014)6
- Guidance on Assessment Factors to Derive a DNEL Technical Report No. 110 Brussels, October 2010.
- Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health Version: 2.1 November 2012 (HTTP:// https://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf).
- Registration dossier for Quaternary ammonium compounds, di-C16-18-alkyldimethyl, chlorides: European Chemicals Agency, http://echa.europa.eu/

- Document I- Draft Evaluation reports in the frame of the directive 98/8/EC concerning the placing of biocidal products on the market - DDAC CAS 7173 -51 -5- Product type 8 - RMS Italy, June 2015 https://echa.europa.eu/documents/10162/81fb9122-9b96-d284-cbdd-f3e28ba67632

7.14. Abbreviations

AF Assessment factor
BW Body weight
CAS Chemical abstracts service
C&L Classification and labelling
CLP Classification, labelling and packaging (Regulation (EC) No 1272/2008)
CSR Chemical Safety Report
DNEL Derived no effect level
eMSCA Evaluating Member State Competent Authority
NOAEL No Observed Adverse Effect Level
NOEC No Observed Effect Concentration
PBT Persistent, Bioaccumulative, Toxic
PEC Predicted Environmental Concentration
PNEC Predicted No Effect Concentration
RCR Risk characterization ratio
vPvB Very Persistent and very Bioaccumulative