SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Fatty acids C18 unsat, reaction products with Pentaethylenehexamine

EC No 629-732-4

CAS No 1224966-13-5

Evaluating Member State(s): Lithuania

Dated: November 2016

Evaluating Member State Competent Authority

Environmental Protection Agency
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Year of evaluation in CoRAP: 2015

Lithuania concluded the evaluation in March 2016 without any further need to ask more information from the Registrant(s) under Article 46(1) decision.

Further information on registered substances here:

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

DISCLAIMER

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

Fatty acids C18 unsat, reaction products with Pentaethylenehexamine was originally selected for substance evaluation in order to clarify concerns about:

- Human health/Sensitiser;
- Exposure/Exposure of workers, exposure of sensitive populations.

During the evaluation also other concerns were identified. The additional concerns were:

- Environmental hazards (aquatic acute hazard, aquatic chronic hazard).

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

There are no other ongoing processes.

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	
Harmonised Classification and Labelling	X
Identification as SVHC (authorisation)	-
Restrictions	-
Other EU-wide measures	-
No need for regulatory follow-up action at EU level	-

4. FOLLOW-UP AT EU LEVEL

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

Not applicable.

4.1.1. Harmonised Classification and Labelling

According to the evaluation of the eMSCA, the registered substance fulfills the criteria for classification as skin sensitizer and is hazardous for the aquatic environment. The eMSCA

therefore suggests the harmonised classification and labelling as a further action, as specified below.

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

5.2. Other actions

Not applicable.

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

Indication of a tentative plan is not a formal commitment by the evaluating Member State. A commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier should be made via the Registry of Intentions.

Table 2

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**

CLH dossier for inclusion the substance in Annex VI of the CLP.
 	
Hazards classes to be dealt with:
• Skin corrosiveness
• Skin sensitisation
• Hazardous to the aquatic environment:
  ○ Aquatic Chronic
  ○ Aquatic Acute
	Not decided yet. In consideration of resource constraints, not prioritised for action by the evaluating MS for the time being.	To be defined

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Fatty acids C18 unsat, reaction products with Pentaethylenehexamine was originally selected for substance evaluation in order to clarify concerns about:

- Human health/Sensitiser;

- Exposure/Exposure of workers, exposure of sensitive populations

During the evaluation also other concerns were identified. The additional concerns were:

- Environmental hazards (aquatic acute hazard, aquatic chronic hazard).

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Skin Corr. 1C Causes severe skin burns and eye damage.	Skin Corrosivity properties confirmed. Harmonised C&L process to be initiated for the human health hazards.
Skin Sens. 1A May cause an allergic skin reaction.	Skin Sensitisation properties confirmed. Harmonised C&L process to be initiated for the human health hazards.
Aquatic Acute 1 Very toxic to aquatic life. M=1	Aquatic Acute properties confirmed. Harmonised C&L process to be initiated for environmental hazards.
Aquatic Chronic 1 Very toxic to aquatic life with long lasting effects. M=1	Aquatic Chronic properties confirmed. Harmonised C&L process to be initiated for environmental hazards.
Exposure of workers, exposure of sensitive populations	Adequately controlled. No additional risk management measures required at the moment.

7.2. Procedure

Pursuant to Article 44(2) of the REACH Regulation, Fatty acids C18 unsat, reaction products with Pentaethylenehexamine was included on the Community rolling action plan (CoRAP) for evaluation in 2015. The Competent Authority of Lithuania was appointed to carry out the evaluation. The substance evaluation commenced on 17 March 2015.

The evaluation was targeted to human health hazards and exposure. Although not the main focus of the evaluation, an assessment of the environmental hazard was also undertaken and concerns were identified.

The main source of information for the evaluation was the original data/information submitted within REACH registration (IUCLID dossiers, Chemical Safety Reports (CSRs).

The Lead Registrant updated the registration dossier on 19 March 2015. This update was taken into account during the evaluation.

During the evaluation process the eMSCA experts found some discrepancies in the Lead Registrant's Chemical Safety Reoprt (CSR) regarding the environmental hazards. In October 2015 eMSCA experts contacted the Lead Registrants' contact point and during the informal consultation via e-mails these discrepancies were clarified.

The evaluation was based on the information available in the registration dossier. The information in the registration dossier was largely based on studies conducted with substances belonging to a category Fatty acid amidoamine/imidazolines (AAI), defined by the Registrant(s).

Based on the evaluation of the available data and informal consultation with the Lead Registrant, the eMSCA conluded that there was no need to request futher information in order to clarify initial and additional concerns.

The results of the evaluation are documented in this report.

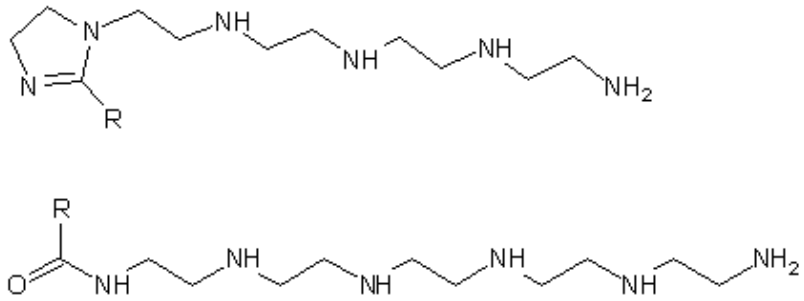
7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	Fatty acids C18 unsat, reaction products with Pentaethylenehexamine
EC number:	629-732-4
CAS number:	1224966-13-5
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	UVCB substance
Molecular weight range:	>392; ca. 897
Synonyms:	-

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

Structural formula:



R is fatty alkyl with chain lengths C 18 unsaturated chainlengths

UVCB substance

Table 5

Constituent		
Constituents	**Typical concentration**	**Concentration range**
N-(2-aminoethyl)-N'-{2-[(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)amino]ethyl}ethane-1,2-diamine	Confidential	Confidential
(9Z)-N-(14-amino-3,6,9,12-tetraazatetradec-1-yl)octadec-9-enamide	Confidential	Confidential
Unidentified reaction product(s) / Unknown	Confidential	Confidential
N-{2-[4-(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)piperazin-1-yl]ethyl}ethane-1,2-diamine	Confidential	Confidential
(9Z)-N-(2-{4-[2-({2-[(2-aminoethyl)amino]ethyl}amino)ethyl]piperazin-1-yl}ethyl)octadec-9-enamide	Confidential	Confidential
(9Z)-N-[2-({2-[4-(2-{2-[(9Z)-heptadec-9-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)piperazin-1-yl]ethyl}amino)ethyl]octadec-9-enamide	Confidential	Confidential
N,N'-bis(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)ethane-1,2-diamine	Confidential	Confidential
N-(2-aminoethyl)-N'-{2-[4-(2-{2-[(9Z)-heptadec-9-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)piperazin-1-yl]ethyl}ethane-1,2-diamine	Confidential	Confidential

(9Z)-N-(2-{[2-({2-[(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)amino]ethyl}amino)ethyl]amino}ethyl)octadec-9-enamide	Confidential	Confidential
(9Z)-N-{2-[4-(2-{[2-({2-[(9Z)-octadec-9-enoylamino]ethyl}amino)ethyl]amino}ethyl)piperazin-1-yl]ethyl}octadec-9-enamide	Confidential	Confidential
2-[4-(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)piperazin-1-yl]ethanamine	Confidential	Confidential
(9Z)-N-{2-[4-(2-{[2-({2-[(2-aminoethyl)amino]ethyl}amino)ethyl]amino}ethyl)piperazin-1-yl]ethyl}octadec-9-enamide	Confidential	Confidential
(9Z)-N-(2-{[2-({2-[4-(2-{2-[(9Z)-heptadec-9-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)piperazin-1-yl]ethyl}amino)ethyl]amino}ethyl)octadec-9-enamide	Confidential	Confidential
N-(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)ethane-1,2-diamine	Confidential	Confidential
1,4-bis(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)piperazine	Confidential	Confidential
(9Z)-N-[2-({2-[(2-{[2-(4-{2-[(9Z)-octadec-9-enoylamino]ethyl}piperazin-1-yl)ethyl]amino}ethyl)amino]ethyl}amino)ethyl]octadec-9-enamide	Confidential	Confidential
(9Z)-N-(17-amino-3,6,9,12,15-pentaazaheptadec-1-yl)octadec-9-enamide	Confidential	Confidential
3,6,9,12-tetraazatetradecane-1,14-diamine	Confidential	Confidential
(9Z)-N-[(28Z)-19-oxo-3,6,9,12,15,18-hexaazahexatriacont-28-en-1-yl]octadec-9-enamide	Confidential	Confidential
(9Z)-N-(2-{[2-({2-[(2-aminoethyl)amino]ethyl}amino)ethyl]amino}ethyl)octadec-9-enamide	Confidential	Confidential
(9Z)-N-[(24Z)-16-oxo-3,6,9,12,15-pentaazatritriacont-24-en-1-yl]octadec-9-enamide	Confidential	Confidential
N-(2-aminoethyl)-N'-{2-[(2-aminoethyl)amino]ethyl}ethane-1,2-diamine	Confidential	Confidential
N,N'-bis(2-aminoethyl)ethane-1,2-diamine	Confidential	Confidential
N-(2-aminoethyl)ethane-1,2-diamine	Confidential	Confidential
2-[(2-aminoethyl)amino]ethanol	Confidential	Confidential
2-piperazin-1-ylethanamine	Confidential	Confidential
Undefined, group of substances	Confidential	Confidential

7.4. Physico-chemical properties

Table 6

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES		
Property	**Value**	**Test material identity (in case of read-across)**
Physical state at 20°C and 101.3 kPa	The appearance is read across from a substance with structural similarities within the AAI category. The test substance is a viscous liquid at 22 °C at atmospheric pressure.	EC number: 270-500-3; CAS number: 68442-97-7.
Vapour pressure	The vapour pressure is read across from a substance with structural similarities within the AAI category. The vapour pressure of the test substance has been determined to be 0.000079 mPa at 20°C and 0.00017 mPa at 25°C.	EC number: 270-500-3; CAS number: 68442-97-7.
Water solubility	The water solubility is read across from a substance with structural similarities within the AAI category. Since the substance forms micelles in water, the water solubility is expressed as the critical micelle concentration (CMC), in this case 19 mg/L (pH 7, 23°C).	EC number: 271-417-5; CAS number: 68555-22-6.
Partition coefficient n-octanol/water (Log Kow)	The partition coefficient is read across from a substance with structural similarities within the AAI category. The partition coefficient of the test substance is 2.2 (log Pow).	EC number: 270-500-3; CAS number: 68442-97-7.
Flammability	Based on structure no pyrophoric properties are expected. Not flammable in contact with water.	-
Explosive properties	No explosive properties.	-
Oxidising properties	Based on structure, the substance is not oxidising.	-
Granulometry	Not applicable. According to ECHA'sGuidance on information requirements and chemical safety assessment Chapter R.7a: Endpoint specific guidance: "The study does not need to be conducted if the substance is marketed or used in a non solid or non granular form"	-
Stability in organic solvents and identity of relevant degradation products	Stability in organic solvent is not considered critical for this substance.	-
Dissociation constant	The dissociation constant is read across from a substance with structural similarities the AAI category. Based on QSAR predictions by SPARC on-line.	EC number: 271-417-5; CAS number: 68555-22-6.
Flash point	The flash point is read across from a substance with structural similarities within the AAI category. The flash point is	EC number: 271-417-5; CAS number: 68555-22-6.

	determined to be 181 ºC.	
Boiling point	The boiling point is read across from a substance with structural similarities within the AAI category. Boiling point is >300ºC.	EC number: 271-417-5; CAS number: 68555-22-6.

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

Table 8

USES Use(s)	
Uses as intermediate	**-**
Formulation	Formulation; Formulation: injection of the additive in warm asphalt; Formulation of emulsifier blends; Formulation of asphalt emulsion, formulation of asphlat adhesion agents; Formulation of building and construction additives.
Uses at industrial sites	Use in oilfield applications / Corrosion inhibitors; Use as an intermediate; Mixing of formulations for building and construction; Formulation of asphalt emulsion, formulation of asphalt adhesion agents.
Uses by professional workers	Professional use of building and construction formulations; Use in the laboratory; Use by professional worker: roadworks.
Consumer Uses	-
Article service life	Service life (consumers) (ERC 10a: Wide dispersive outdoor use of long-life articles and materials with low release).

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Currently no harmonised classification available.

7.6.2. Self-classification

- In the registrations:

Table 9

SELF CLASSIFICATION				
International Chemical Identification	**EC No**	**CAS No**	**Classification**	
			Hazard Class and Category Code(s)	**Hazard statement code(s)**
Fatty acids C18 unsat, reaction products with Pentaethylenehexamine	629-732-4	1224966-13-5	Skin Corr. 1C	H314: Causes severe skin burns and eye damage.
			Skin Sens. 1A	H317: May cause an allergic skin reaction.
			Aquatic Acute 1	H400: Very toxic to aquatic life. M=10
			Aquatic Chronic 1	H410: Very toxic to aquatic life with long lasting effects. M=1.

Signal words	**Pictograms**		
Danger			
	Exclamation mark	Environment	Corrosion

7.7. Environmental fate properties

7.7.1. Degradation

Based on the available information in the registration dossier, the eMSCA concludes that the substance can be considered as ultimately biodegradable and not persistent but does not meet rapidly degradable criteria of CLP.

7.7.2. Environmental distribution

Based on adsorption/desorption key studies (Using a Batch Equilibrium Method) eMSCA concluded that due to the cationic surface-active properties of Fatty acids C18 unsaturated poly ethyleneamine based imidazolines, these substances will adsorb strongly to the solid phase of soil and sediments. Because there is no principal difference between soil and sediments considering the sorption properties and because for cationic

surfactants the degree of sorption is not related to the organic carbon content, the Koc value for soil also can be used for sediment and suspended particles. Based on available information the eMSCA also considers that these substances are mainly protonated under environmental conditions. This means that the protonated fraction will behave as a salt in water and will have a very low vapour pressure. The solubility of this cationic surface active substance will be influenced by the pH and would be difficult to determine because of the surface active properties. Also eMSCA supports the Registrants' opinion that evaporation from water is very unlikely based on the low vapour pressure and the observed critical micelle concentrations values. The actual dissolved concentration in water will be extremely low due to strong absorption to sorbents both based on hydrophobicity and ionic interactions where the ionic interaction will govern the partitioning process.

7.7.3. Bioaccumulation

Based on available information eMSCA supports the Registrants' opinion that this substance has a low bioaccumulation potential and it is unlikely that the substance will accumulate in the food chain.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

Based on available information on short-term toxicity to fish the most sensitive organism appears to be is *Brachydanio rerio* (new name: *Danio rerio*) with lowest LC_{50}(96 h) = 0.19 mg/L. No long term toxicity test is available. However, fish are in general less sensitive to the alkyl amidoamines/imidazolines compared to algae and daphnia. Based on available information on short-term toxicity to invertebrates the most sensitive organism appears to be Daphnia magna with lowest EC_{50}(48 h) = 0.18 mg/L. For the long-term toxicity to the invertebrates eMSCA concluded that the value, which should be used is NOEC(21 d) = 0.320 mg/L based on the nomimal test substance concentration (corrected for active ingredient which is 96%, the NOEC is reduced to 0.307 mg/L). Based on the algae and aquatic plants toxicity eMSCA concluded that the most relevant and realiable value is *Pseudokirchnerella subcapitata* EC_{50} (72 h) = 0.638 mg/L and EC10(72h) = 0.395 mg/L based on growth rate and related to the nomimal test substance concentration (corrected for active ingredient which is 96%, the EC_{50} is reduced to 0.612 mg/L and EC_{10} is reduced to 0.379 mg/L).

7.8.2. Terrestrial compartment

Based on available information on toxicity to soil macro/micro-organisms and terrestrial plants the eMSCA concluded that alkyl amidoamines/imidazolines sorb strongly to soil but they hydrolyse quickly and the intermediates are biodegraded to CO_2 and H_2O and a polyethylene amine. The shortest polyamine diethylenetriamine (DETA) is also biodegraded. One chronic earthworm test with TEPA based imidazoline has been performed to assess the long-term risk for terrestrial species with a NOEC of 944 mg/kg dw. Based on that the eMSCA does not see a concern for terrestrial toxicity.

7.8.3. Conclusions for classification and labelling

The eMSCA concluded that reliable aquatic acute toxicity data are available for the three trophic levels: fish, invertebrates and algae. Reliable aquatic chronic toxicity data is available for two trophic levels: invertebrates and algae. The most sensitive ecotoxicological test results from the key (reliable without restrictions) acute and chronic studies are summarised in the following table and sections.

Table 10

Test organism / guideline, test method	Short-term result (endpoint)	Long-term result (endpoint)
Fish (*Danio rerio*) / OECD 203	96-h LC_{50} = 0.19 mg/L (mortality)	-
Invertebrates *(Daphnia magna)* / OECD 202	48-h EC_{50} = **0.18** mg/L (mobility)	
Invertebrates *(Daphnia magna)* / OECD 211		*21-d NOEC = 0.32 (**0.307**) mg/L (reproduction)
Algae (*Pseudokirchnerella subcapitata*) / OECD 201	72-h EC_{50} = 0.638 mg/L (growth rate)	*72-h EC_{10} = 0.395 (0.379) mg/L (growth rate)

*The 21-d NOEC for reproduction in *Daphnia magna* study is 0.320 mg/L based on the nomimal test substance concentration. Corrected for active ingredient which is 96% the NOEC is reduced to 0.307 mg/L.
*The 72-h EC_{10} based on growth rate in Algae study is 0.395 mg/L related to the nomimal test substance concentration. Corrected for active ingredient which is 96%, the EC_{10} is reduced to 0.379 mg/L.

Based on the available data eMSCA concludes that the substance is not rapidly degradable and non-bioaccumulative. Thus eMSCA propose the following classification for the environment:
Aquatic acute 1 based on a **48-hour EC_{50} = 0.18 mg/L for *Daphnia magna* *(mobility)***. As this value is in range **0.1 < L(E)C_{50} ≤ 1** that lead us to the **M factor of 1**.
The lowest Aquatic Chronic value is **21-day NOEC = 0.307 mg/L for Daphnia Magna** (reproduction).

As there are no chronic data available for all three trophic levels, classification should be made using the trophic level with chronic data and compared with the classification made using the acute toxicity data, combined with degradation and/or bioaccumulation data. The classification shall be made on the most stringent outcome.
Therefore eMSCA propose classify as **Aquatic Chronic 1** based on a **48-hour EC50 = 0,18 mg/L for Daphnia magna** (mobility). As this value is in range **0.1 < L(E)C50 ≤ 1** the **chronic M-factor is 1**.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

Alkyl amidoamine/imidazolines (AAI) are mainly protonated under environmental conditions. The protonated fraction will behave as a salt in water. AAI are surface active and have a low solubility in the form of CMC. For diethylenetriamine (DETA), N-(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)ethane-1,2-diamine (TETA) based AAI, the observed CMC were resp. 99, 19 and 15 mg/L. The actual dissolved concentration in water will be extremely low as alkyl amidoamines/imidazolines will sorb strongly to sorbents. As a consequence, absorption from gastro-intestinal system is likely to be slow.

The AAI are all corrosive to skin, and toxicity following dermal exposure is characterised by local tissue damage, rather than the result of percutaneously absorbed material.

The physicochemical properties of AAI indicate a low likelihood for exposure via inhalation, with a boiling point >300 °C and very low vapour pressure (0.00017 mPa at 25°C for DETA based AAI).

7.9.2. Acute toxicity and Corrosion/Irritation

Summary and discussion on acute toxicity

Based on the available information, the eMSCA considers that no classification is required for acute toxicity.

Summary and discussion on skin corrosion

One key study of high reliability was performed with another substance belonging to the AAI category, Tall oil, reaction products with tetraethylene-pentamine, according to OECD guideline No 404 "Acute Dermal Irritation/Corrosion" and under GLP. In total nine New Zealand white rabbits were dermally exposed to 0.5 mL of the undiluted test substance. Test material was applied as an semiocclusive coverage on a shaved skin for 3 minutes (7 days), 1 hour (7 days), and 4 hours (14 days). Skin reactions were scored at 1, 24, 48, 72 hours and 7 days after the exposure. After 3 minutes exposure slight effects, reversible after 7 days, were observed. After the 1 hour exposure irritation was observed and this effect was not reversible within 7 days. Visible necrosis were observed following an exposure period of up to 4 hours and no recovery was observed within 14 days.

According to CLP criteria (where responses (destruction of skin tissue) occur in at least one animal after exposure > 1 hour - ≤ 4 hours and observations up to 14 days) the substance shall be classified as Skin Corr. subcategory 1C, H314: Causes severe skin burns and eye damage. The eMSCA agrees with the Registrant(s) that also the registered substance should have the same classification

7.9.3. Sensitisation

Skin sensitisation

Data for skin sensitisation of Fatty acids C16-18, C18 unsat reaction products with tetraethylenepentamine was obtained from animal testing according to existing testing guidelines. One reliable key study (the guinea pig maximisation test (GPMT)) of high reliability was performed according to OECD Guideline 406 "Skin Sensitisation" and in compliance with GLP. The total number of animals included in the test was equal to the requirements following the OECD Guideline 406 i.e. 30 Hartley guinea pigs. They were intradermal (0.1 %) and epicutaneous (5 %) exposed. According to GPMT 15 % of guinea pigs must show a reaction for the test to be considered positive. Reactions (delayed contact hypersensitivity) were observed in all animals (in 19/19 (100%) guinea pigs) of treatment group and none in the control. Cutaneous effects were attributed to delayed contact hypersenisitivity.

Based on the available data, Fatty acids C16-18, C18 unsat reaction products with tetraethylenepentamine is classified as skin sensitizer 1A. The available results from animal testing are sufficient for a refined evaluation allowing the subcategorization of Fatty acids C16-18, C18 unsat reaction products with tetraethylenepentamine.

In comparison to the given criteria for the hazard category and sub-category for skin sensitisation according to CLP regulation Fatty acids C16-18, C18 unsat reaction products with tetraethylenepentamine fulfils the criteria for classification in the hazard class as skin sensitizer subcategory 1A, H317: May cause an allergic skin reaction, because a skin

sensitisation response of ≥ 60 % positive at 0.1 % i.d. induction dose was observed in the GPMT.

Based on the available data, the eMSCA can support the Registrant(s)' proposal to classify also the registered substance as skin sensitizer subcategory 1A.

Respiratory sensitisation

No information was available on respiratory sensitisation from the registration dossiers, but AAI products are sensitising to skin. Likelihood of exposures via inhalation is low considering the high boiling point (> 300 °C) and very low vapour pressure (0.00017 mPa at 25°C for DETA based AAI). The potential for inhalation is not significant to justify further studies. Furthermore, as the substance is classified as corrosive, such testing should normally not be conducted. Based on the available information, eMSCA does not see a concern for respiratory sensitisation.

7.9.4. Repeated dose toxicity

Consistent results are provided from all studies within the whole group of Amidoamine/imidazolines (AAI), indicating a low level of toxicity. The eMSCA does not see a concern for repeated-dose toxicity.

7.9.5. Mutagenicity

The data for mutagenicity of AAI substances were obtained from in vitro testing.

Different AAI substances were tested negative in a bacterial mutagenicity study (Ames test), in a study in human lymphocytes and a mammalian mutagenicity study in mouse lymphoma cells.

7.9.6. Carcinogenicity

Not evaluated.

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

No developmental toxicity was observed in an OECD 422 screening study with fatty acids C18 unsat, reaction products with pentaethylenehexamine (Amidoamine/Imidazoline). Similar OECD 422 studies have been performed on AAI based on DETA and TEPA, and have also shown no indication of concern for reproductive or developmental toxicity.

Based on the available data, the eMSCA does not see a concern for reproductive toxicity.

7.9.8. Hazard assessment of physico-chemical properties

No explosive properties. Based on the structure, the substance is not oxidising. Based on the structure no pyrophoric properties are expected. Not flammable in contact with water.

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

The evaluating MSCA concludes, that substance should be classified in accordance with CLP criteria for human health as:

- Skin Corr. hazard category 1C, H314: causes severe skin burns and eye damage;
- Skin Sens. Category 1A, H317: may cause an allergic skin reaction.

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.11. PBT and VPVB assessment

Not evaluated.

7.12. Exposure assessment

The Registrant(s) generated exposure scenarios and made exposure estimations for manufacture and for all the identified uses (see Table 8) of substance using ECETOC TRA v2 and ECETOC TRA Worker v3.0 models. In the eMSCA's opinion the Registrant(s) adequately described the operational conditions and the risk management measures for all the generated scenarios.

7.12.1. Human health

Worker

Since the substance is corrosive (systemic uptake via skin is likely to be very limited) and also a skin sensitiser the workers shall be using Personal Protective Equipment (PPE), such as goggles, chemical resistant gloves and protective clothing in order to protect eyes and skin. Local exhaust ventilations should be placed at the potential emission sources.

Consumer

Not applicable.

7.12.2. Environment

Aquatic compartment (incl. sediment)

The eMSCA considers that the level of exposure is at an acceptable level for all the exposure scenarios presented in the registration dossier and there is no need to perform additional modelling. It should be mentioned that eMSCA did not have any additional information from other sources on exposure.

Terrestrial compartment

The eMSCA considers that the level of exposure is at an acceptable level for all the exposure scenarios presented in the registration dossier and does not see the need to request further information. It should be mentioned that eMSCA did not have any additional information from other sources on exposure.

Atmospheric compartment

The eMSCA considers that the level of exposure is at an acceptable level for all the exposure scenarios presented in the registration dossier and does not see the need to request further information.

7.12.3. Combined exposure assessment

Not evaluated.

7.13. Risk characterisation

The risk for workers, industrial and professional users appears to be controlled for the indentified uses of substance taking into account RMM an OCs proposed by the registrants. Moreover eMSCA concludes that for combined environmental exposures (taking into account all possible routes of exposures) risk characterisation ratio values are way below 1. Ultimately, the eMSCA does not see a concern.

7.14. References

ECHA (2015). Guidance on the Application of the CLP Criteria. Version: 4.1 June 2015.

ECHA (2015). Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7a: Endpoint specific guidance. Version: 4.1 October 2015.

ECHA (2012). Guidance on information requirements and chemical safety assessment. Chapter R.8: Characterisation of dose [concentration]-response for human health. Version: 2.1 November 2012.

Guidance on the Application of the CLP Criteria, 2013

Chemical safety report, Fatty acids C18 unsat, reaction products with Pentaethylenehexamine, 2013-02-16

7.15. Abbreviations

a.i.	active ingridient
AAI	Alkyl amidoamine/imidazolines
ATP	Adaptation to Technical and Scientific Progress
BCF	Bioconcentration Factor
CMC	Critical Micelle Concentration
CSA	Chemical safety assessment
CSRs	Chemical Safety Reports
DETA	Diethylenetriamine
DNEL	Derived No-Effect Levels
dw	dry weight
EC50	Half maximal Effective Concentration
eMSCA	evaluating Member State Competent Authority
EPM	Equilibrium Partitioning Method
GLP	Good Laboratory Practice
GPMT	the Guinea Pig Maximisation Test
i.d.	intradermal induction
Kd	Soil/solution distribution coefficients

Koc	Estimation of Adsorption Coefficient
Kow	Octanol-water partition coefficient
LC50	Lethal concentration, 50%
LD50	Lethal dose. The dose causing 50 % lethality
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
OECD	Organisation for Economic Cooperation and Development
PBT	Persistent, Bioaccumulative and Toxic
PEC	Predicted Environmental Concentration
PEHA	N-(2-aminoethyl)-N'-{2-[(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)amino]ethyl}ethane-1,2-diamine
PNEC	Predicted No Effect Concentration
QSAR	Quantitative Structure–Activity Relationship models
STP	Sewage Treatment Plants
TEPA	2-[4-(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)piperazin-1-yl]ethanamine
TETA	N-(2-{2-[(8Z)-heptadec-8-en-1-yl]-4,5-dihydro-1H-imidazol-1-yl}ethyl)ethane-1,2-diamine
vPvB	very Persistent, very Bioaccumulative