baua:
Bundesanstalt für Arbeitsschutz
und Arbeitsmedizin
Federal Institute for Occupational
Safety and Health

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

amides, C18-unsatd., N-[3-(dimethylamine) propyl]

EC/List No 800-353-8

CAS No 1379524-06-7

Evaluating Member State(s): Germany

Dated: 31 July 2017

Evaluating Member State Competent Authority

BAuA
Federal Institute for Occupational Safety and Health
Division 5 - Federal Office for Chemicals
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D-44149 Dortmund, Germany

Year of evaluation in CoRAP: 2016

Member State concluded the evaluation without any further need to ask more information from the registrants under Article 46(1) decision.

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

Amides, C18-unsatd., N-[3-(dimethylamine) propyl] was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB
- Wide dispersive use
- Exposure of environment
- High RCR

During the evaluation no other concerns were identified.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

There are no completed or ongoing processes for this substance.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State Competent Authority (eMSCA) 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	
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	X

4. FOLLOW-UP AT EU LEVEL

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

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

4.1.1. Harmonised Classification and Labelling

The aquatic ecotoxicological properties of the registered substance (List number 800-353-8; CAS 1379524-06-7) indicate that the substance is hazardous to the aquatic environment (Category Acute 1 and Category Chronic 1). This is reflected in the current self-classification implemented by the registrants and so not considered a priority for further follow-up regulatory action at EU level, at this time.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

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

Table 2

REASON FOR REMOVED CONCERN **The concern could be removed because**	**Tick box**
Clarification of hazard properties/exposure *This conclusion can be reached e.g. if the outcome of a test on hazardous properties clarified that substance is not hazardous or the exposure data shows no risk. This can be due to the fact that the data was originally available in the registration dossiers or was obtained due to a substance evaluation decision.*	x
Actions by the registrants to ensure safety, as reflected in the registration dossiers (e.g. change in supported uses, applied risk management measures, etc.) *This conclusion can be reached if registrants changed their registrations e.g. the supported uses, applied risk management measures, reduction of the aggregated tonnage, cease of manufacture etc.*	

On the basis of the available information, the evaluating MSCA considers that the amide constituents of Amides, C18-unsatd., N-[3-(dimethylamine) propyl] are potentially bioaccumulative and potentially toxic. However, the constituents are not persistent and hence, they are not PBT or vPvB according to REACH Annex XIII. Overall, Amides, C18-unsatd., N-[3-(dimethylamine) propyl] is not a PBT/vPvB substance according to the criteria of REACH Annex XIII. Therefore, the PBT/vPvB concern could be removed.

The entire annual tonnage of Amides, C18-unsatd., N-[3-(dimethylamine) propyl] is used for the purpose as emulsifier in asphalt. The proposed exposure scenarios are based on the expected aggregated tonnage and are therefore acceptable.

The amount of amides, C18-unsatd., N-[3-(dimethylamine) propyl] (Emulsamine) released to the environment is considered to be small. Therefore, the exposure concern was clarified.

Risk Characterisation Ratios (RCR = PEC/PNEC) were altogether found to be below 1, indicating no unacceptable risk for the local or regional environment.

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

Not applicable.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Amides, C18-unsatd., N-[3-(dimethylamine) propyl] was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB
- Wide dispersive use
- Exposure of environment
- High RCR

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Persistence	Not persistent.
Bioaccumulation	Potentially bioaccumulative.
Toxicity	Potentially toxic; contains toxic constituents.
Exposure	The amount released to the environment is considered to be small. Based on PECs and PNECs, RCR are below 1, indicating no unacceptable risk.

7.2. Procedure

This Substance Evaluation is targeted to the assessment of persistence, bioaccumulation, ecotoxicity and exposure.

Unless stated otherwise, the information discussed in this report is taken from the registration dossiers for Amides, C18-unsatd., N-[3-(dimethylamine)propyl] (hereafter named Emulsamine) (ECHA 2016a). The additional information includes data on analogue substances or constituents (e.g. ECHA 2016b, ECHA 2016c, ECHA 2016c) as well as scientific literature and modelling. Detailed references are given in the respective sections.

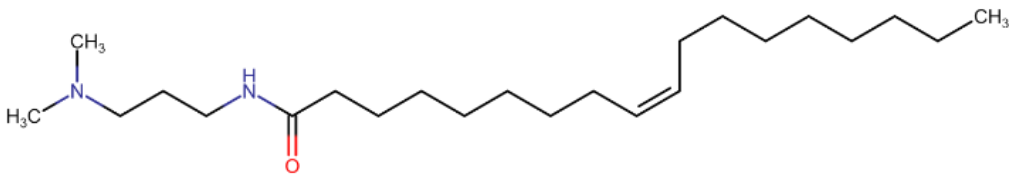
7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	Amides, C18-unsatd., N-[3-(dimethylamine)propyl]
EC/List number:	800-353-8
CAS number:	1379524-06-7
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	
Molecular weight range:	
Synonyms:	Emulsamine

Type of substance: UVCB

Structural formula:



Structural example of one constituent of the UVCB substance with one double bond

UVCB substance

Detailed information is provided in the confidential Annex.

Emulsamine is a substance of unknown or variable composition, complex reaction products or biological materials (UVCB), and therefore its constituents must be considered separately. According to the available information from the registration dossiers, C18 unsaturated fatty acids and N-[3-(dimethylamino)propyl]amine are heated at elevated temperatures and react to form amidoamines. Consequently, Emulsamine mainly contains N-[3-(dimethylamino)propyl]amides that differ by number, position and stereochemistry of the double bonds.

Further information in the registration dossiers indicate that preferably tall-oil fatty acids or rape oil fatty acids are used for the manufacture of Emulsamine. These fatty acid mixtures contain oleic acid and linoleic acid as main constituents, as well as further fatty acids, among them α-linolenic acid. Naturally occurring unsaturated fatty acids usually have a *cis* configuration, and so do the abovementioned fatty acids. The Registrants confirmed that the N-[3-(dimethylamino)propyl]amides formed from reaction of these fatty acids have a *cis* configuration, too.

It should be noted that tall-oil and rape oil are natural products and that the proportions of the fatty acids used as starting material may vary, resulting in a variable composition of the UVCB product. This may result in a higher variation of experimental results observed when tests with the UVCB substance are conducted.

The registration dossiers state that the abovementioned fatty acids as well as N-[3-(dimethylamino)propyl amine are minor constituents of the UVCB substance, indicating that the chemical reaction does not proceed completely and some starting material is still part of the substance.

For the unsaturated amides that are listed as constituents the chain length of the fatty acid residues is 18 carbon atoms. While the position of the double bonds seems to be variable, the following amides are explicitly mentioned as constituents in the registration dossiers:[2]

- (9Z)-N-[3-(dimethylamino)propyl]octadeca-9-enamide (oleamide),
- (9Z,12Z)-N-[3-(dimethylamino)propyl]octadeca-9,12-dienamide (linoleamide),
- (9Z,12Z,15Z)-N-[3-(dimethylamino)propyl]octadeca-9,12,15-trienamide (linolenamide).

Therefore, these structures appear adequate to represent the mono-, di- and triunsaturated amide constituents, respectively. The first two structures are supposed to be main constituents of the substance. This is in line with expectations based on the composition of tall-oil fatty acids and rape oil (Römpp 2016).

The following saturated constituents are given by the registrants:

- N-[3-(dimethylamino)propyl]hexadecanamide,
- N-[3-(dimethylamino)propyl]octadecanamide (stearamide) and
- N-[3-(dimethylamino)propyl]icosanamide.

Among these, the stearamide appears to be the constituent with the highest concentration. Furthermore, it has the same chain length as the unsaturated main constituents. A comparison of data for amides of a constant chain length but differing degree of saturation appears to be helpful for assessing the results in an overall read across assessment.

[2] The current dossiers (October 2016) lists these structures with a wrong stereochemistry (*trans* instead of *cis*). However, personal communication with the lead registrant confirmed that the configuration is *cis*.

7.4. Physico-chemical properties

Table 5

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Brown liquid
Melting/freezing point	-10.5°C
Boiling point	Decomposition, decomposition temperature >313°C
Density	0.895 g/cm3 at 25°C
Vapour pressure	1,78x 10-7 Pa at 25°C
Water solubility	26 mg/L at 23°C and pH 7.0 (Critical micelle concentration CMC))
Partition coefficient n-octanol/water (log K_{ow})	6.1 at 25°C for C18 carbon chain component with one double bond; 5.3 at 25°C for C18 carbon chain component with two double bonds; 4.6 at 25°C for C18 carbon chain component with three double bonds;
Flammability	idem
Explosive properties	idem
Oxidising properties	idem
Granulometry	Data waiving; In accordance with column 2 of REACH Annex IX, the test on stability in organic solvents and identity of relevant degradation products (required in section 7.15) does not need to be conducted as the stability of benzyl alcohol is not considered to be critical.
Stability in organic solvents and identity of relevant degradation products	idem
Dissociation constant	pKa 8.5 at 20°C
Surface tension	29 mN/m at 20°C and 500 mg/L At this concentration micelles are present in solution
Viscosity	122 mPa/s at 25°C.

7.5. Manufacture and uses

7.5.1. Quantities

Table 6

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

The registrants report that Emulsamine is mainly used as surface active agent in the road building industry where it is used as an emulsifier to produce bitumen emulsions in water. For further details on the use of Emulsamine, see Section 7.12.2 Exposure Assessment Environment.

Table 7

USES	Use(s)
Uses as intermediate	Not applicable
Formulation	ERC 2: Formulation of preparations in (closed) batch processes with transfer of the preparation into containers; ERC 3: Formulation of an asphalt emulsion with transfer of the mixture into containers.
Uses at industrial sites	Not applicable
Uses by professional workers	ERC 8f (wide dispersive outdoor use; inclusion into matrix); Spreading of the asphalt emulsion or the mixture with stones on the road surface.
Consumer Uses	Not applicable
Article service life	Not relevant

The entire annual tonnage of the substance Emulsamine is used as emulsifier in asphalt. The proposed exposure scenarios are based on the expected aggregated tonnage and are therefore acceptable. Registrants have specified the general ERCs further in the exposure assessment (cf. Section 7.12.2).

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

The substance is not listed in Annex VI, CLP.

7.6.2. Self-classification

- In the registration(s):

Table 8

NOTIFIED CLASSIFICATION ACCORDING TO CLP CRITERIA			
Classification		**Spec. Conc. Limits, M-factors**	**Joint Entries**
Hazard Class and Category Code(s)	**Hazard statement code(s)**		
Skin Corr. 1B	H314	M = 1 M(Chronic) = 1	yes
Skin Sens. 1B	H317		
Eye Dam. 1	H318		
Aquatic Acute 1	H400		
Aquatic Chronic 1	H410		

7.7. Environmental fate properties

Emulsamine is a UVCB substance and therefore, an adequate assessment approach needs to be chosen. The respective guidance document describes several assessment approaches and the possibility to combine these.[3] This section describes the general strategy applied while a detailed description and discussion of the relevant information can be found in sections 7.7.1 and 7.7.3, respectively. Based on the available information a combination of the "known constituents" and the "fraction profiling" approach has been chosen. These approaches are preferred to the "whole substance approach" as they account for the PBT/vPvB properties of individual fractions or constituents that may differ from each other. As only some constituents of Emulsamine are explicitly known and discrete chemical structures are used for modelling purposes, the "known constituents" and the "fraction profiling" approach are combined in order to allow best use of the available information.

[3] https://echa.europa.eu/documents/10162/13632/information_requirements_r11_en.pdf/a8cce23f-a65a-46d2-ac68-92fee1f9e54f (accessed on July 6th 2017)

UVCB Assessment Step 1: Choice of constituents relevant for PBT assessment

In a first step, the relevant constituents for the PBT assessment are chosen. In order to be relevant for PBT assessment, a constituent should be present at concentrations ≥ 0.1 % w/w in the substance and it should screen as potentially PBT.
Emulsamine consists of various N-[3-(dimethylamino)propyl] fatty acid amides, 3-aminopropyldimethylamine and several fatty acids. Not all constituents of Emulsamine are explicitly known, nor is it known whether the unknown constituents are present at ≥ 0.1 % w/w in the substance. However, it is known that the unknown constituents are very similar to the constituents explicitly known in chemical structure. Actually, they are isomers that differ only by the position of their double bonds in the alkyl chain; eventually structures with a slightly longer or slightly shorter alkyl chain might as well be contained. Due to this high degree of structural similarity, similar physico-chemical properties and similar fate properties are likely. Hence, the assessment will focus on the defined constituents that are explicitly known. Therefore, the following unsaturated N-[3-(dimethylamino)propyl] fatty acid amides have been chosen for further assessment:

- (9Z)-N-[3-(dimethylamino)propyl]octadeca-9-enamide (oleamide) as representative for monounsaturated N-[3-(dimethylamino)propyl] fatty acid amides,
- (9Z,12Z)-N-[3-(dimethylamino)propyl]octadeca-9,12-dienamide (linoleamide) as representative for diunsaturated N-[3-(dimethylamino)propyl] fatty acid amides,
- (9Z,12Z,15Z)-N-[3-(dimethylamino)propyl]octadeca-9,12,15-trienamide (linolenamide) as representative for triunsaturated N-[3-(dimethylamino)propyl] fatty acid amides.

With respect to saturated N-[3-(dimethylamino)propyl] fatty acid amides, three compounds are explicitly known (see 7.3). These are part of a homologous series and they are evaluated together. Their properties are expected to be highly similar. The stearamide appears to be the saturated amide constituent with the highest concentration. Furthermore, it has the same chain length as the unsaturated main constituents. A comparison of data for amides of a constant chain length but differing degree of saturation appears to be helpful for assessing the results in an overall read across assessment. Consequently, N-[3-(dimethylamino)propyl]octadecanamide (stearamide) has been chosen as representative for saturated N-[3-(dimethylamino)propyl] fatty acid amides. The differing chain length might however influence lipophilicity and hence bioaccumulation potential. This aspect should be noted in case an in-depth assessment of bioaccumulation becomes necessary.

In summary, the following N-[3-(dimethylamino)propyl]amide constituents are chosen for further assessment:

- N-[3-(dimethylamino)propyl]octadecanamide (stearamide)
- (9Z)-N-[3-(dimethylamino)propyl]octadeca-9-enamide (oleamide),
- (9Z,12Z)-N-[3-(dimethylamino)propyl]octadeca-9,12-dienamide (linoleamide),
- (9Z,12Z,15Z)-N-[3-(dimethylamino)propyl]octadeca-9,12,15-trienamide (linolenamide).

3-aminopropyldimethylamine and the various fatty acids do not screen as P and are not considered to be persistent as justified further under section 7.7.1. Therefore, these constituents are not considered in the following assessment steps.

UVCB Assessment Step 2: Screening in order to identify worst case constituents

In a second step, a screening assessment was done for the selected constituents based on QSAR and physico-chemical properties in order to identify one or more possible worst case constituents. The substance is a cationic surfactant and hence, the available data on octanol-water partitioning (details given in sections 7.4 and 7.7.3) are of limited evidence for bioaccumulation assessment. Therefore, the screening mainly focused on a QSAR screening of ready biodegradability. The results are described in section 7.7.1.2.1.1. The QSAR models gave conflicting results; there was no clear indication whether or not the

substances are persistent and no worst case could be identified. Therefore, all selected N-[3-(dimethylamino)propyl]amide constituents were subject to further assessment.

UVCB Assessment Step 3: Further assessment of selected constituents & conclusion

Subsequently, a further in-depth assessment was carried out on the selected constituents, using the available information. Considering all available information in a weight-of-evidence approach it was concluded that none of these constituents is persistent. Details on the available information and the assessment are given in section 7.7.1. As the constituents are not persistent they are not PBT/vPvB and the PBT assessment is finished.

For the unsaturated amide structures further information relevant for partitioning into membranes became available. This is discussed in section 7.7.3. Based on the available information the selected constituents were concluded to be potentially bioaccumulative; however, as they are not persistent no further information is required.

7.7.1. Degradation

7.7.1.1. **Abiotic degradation**

7.7.1.1.1. Hydrolysis

No hydrolysis study is available. The only functional group that might be susceptible to hydrolysis is the amide group. However, abiotic hydrolysis of amides is generally extremely slow.

7.7.1.1.2. Phototransformation/photolysis

Not relevant.

7.7.1.2. **Biodegradation**

7.7.1.2.1. Biodegradation in water

7.7.1.2.1.1. Estimated data

QSAR Screening

In order to estimate the influence of saturation on biodegradability, a QSAR screening was carried out using the BIOWIN program (U.S. Environmental Protection Agency 2010) for the following selected amide structures:

- N-[3-(dimethylamino)propyl]octadecanamide (stearamide, EC 231-609-1, CAS 7651-02-7)
- (9Z)-N-[3-(dimethylamino)propyl]octadeca-9-enamide (oleamide, EC 203-661-5, CAS 109-28-4),
- (9Z,12Z)-N-[3-(dimethylamino)propyl]octadeca-9,12-dienamide (linoleamide, CAS 81613-56-1),
- (9Z,12Z,15Z)-N-[3-(dimethylamino)propyl]octadeca-9,12,15-trienamide (linolenamide).

The SMILES codes are given in Table 9 and the results are given in Table 10. No clear trend could be derived from the results as the different estimation methods yield contradicting results.

Table 9

SMILES CODES FOR THE SELECTED COMPONENTS	
Name	**SMILES**
N-[3-(dimethylamino)propyl]-octadecanamide (stearamide)	CCCCCCCCCCCCCCCCCC(=O)NCCCN(C)C
(9Z)-N-[3-(dimethylamino)propyl]-octadeca-9-enamide (oleamide)	CCCCCCCC/C=C\CCCCCCCC(=O)NCCCN(C)C
(9Z,12Z)-N-[3-(dimethylamino)propyl] octadeca-9,12-dienamide (linoleamide)	CCCCC/C=C\C/C=C\CCCCCCCC(=O)NCCCN(C)C
(9Z,12Z,15Z)-N-[3-(dimethylamino)-propyl]octadeca-9,12,15-trienamide (linolenamide)	CC/C=C\C/C=C\C/C=C\CCCCCCCC(=O)NCCCN(C)C

Table 10

BIOWIN RESULTS FOR THE SELECTED COMPONENTS							
Name	**BIOWIN Model No.**						
	1	**2**	**3**	**4**	**5**	**6**	**7**
N-[3-(dimethylamino)-propyl]octadecanamide	0.6854	0.5215	2.3738	3.5024	0.5973	0.5369	-0.8693
(9Z)-N-[3-(dimethyl-amino) propyl]octadeca-9-enamide	0.6863	0.5286	2.3783	3.5053	0.5169	0.3553	-1.0683
(9Z,12Z)-N-[3-(dimethyl-amino)propyl]octadeca-9, 12-dienamide	0.6873	0.5357	2.3827	3.5082	0.4364	0.2076	-1.2673
(9Z,12Z,15Z)-N-[3-(di-methylamino)propyl]-octadeca-9,12,15-trien-amide	1.0540	0.9760	2.6974	3.8626	0.5154	0.2418	-0.1346

The BIOWIN 1-4 models predict the saturated stearamide structure as a worst case and the triunsaturated amide structure as a best case. However, the BIOWIN 5 and 6 models do not yield a steady relationship between degree of saturation and biodegradability: They predict the diunsaturated amide structure as a worst case and the saturated stearamide structure as a best case. Regarding estimation of ready biodegradability, the QSAR estimations do neither allow a clear conclusion on the persistence of the constituents nor do they support the identification of a worst case constituent.

Estimation of Biodegradation Pathways using the EAWAG-BBD

The EAWAG Biocatalysis /Biodegradation Database (EAWAG-BBD 2016, http://eawag-bbd.ethz.ch/index.html) corresponds to the former University of Minnesota Biocatalysis /Biodegradation Database; both are based on a large collection of data on microbial reactions (Gao et al, 2010) which are used to derive transformation rules. These rules are used in a Pathway Prediction System (PPS) to predict the biodegradation pathways of organic compounds. It should be noted that it is not possible to predict rate constants with this system and therefore it is uncertain if the mechanism proposed by PPS is relevant in the environment. However, the EAWAG-BBD is considered as state-of-the-art for the prediction of biotransformation pathways.

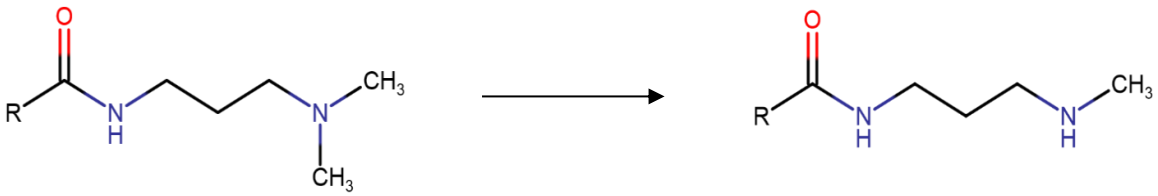
Biodegradation pathways have been estimated for the following selected amide structures, with the aim to identify possible differences in biodegradation behaviour:

- N-[3-(dimethylamino)propyl]octadecanamide (stearamide)
- (9Z)-N-[3-(dimethylamino)propyl]octadeca-9-enamide (oleamide),
- (9Z,12Z)-N-[3-(dimethylamino)propyl]octadeca-9,12-dienamide (linoleamide),
- (9Z,12Z,15Z)-N-[3-(dimethylamino)propyl]octadeca-9,12,15-trienamide (linolenamide).

The Pathway Prediction System (PPS) of the EAWAG-BBD predicts the same general biodegradation pattern for all structures under consideration. Of special interest are the main metabolites containing the alkyl chain moiety (R), as these might show differing results due to the variation of saturation and/or chain length of the moiety. The other metabolites formed in these reactions may differ between pathways. However, these metabolites do not contain the moiety denoted as R and therefore, they are not subject to the variation caused by its differing chain length and saturation degree. The proposed initial biodegradation steps are the following:

1) Demethylation of the tertiary amine moiety

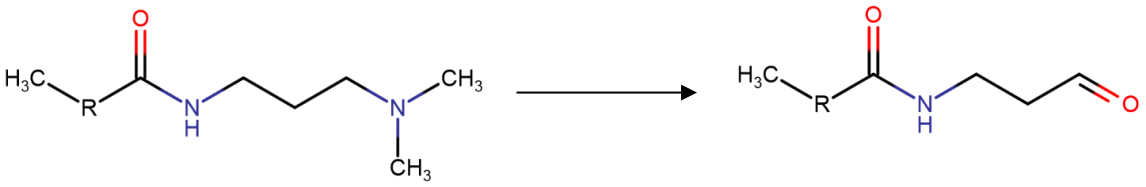
This transformation is based on biotransformation rule 0063 and the aerobic likelihood of rule 0063 is rated as "likely" in the Pathway Prediction System.



This initial step is followed by repeated transformations according to rule 0063 (oxidative attack on amine moiety) and then by transformations according to biotransformation rules 0063 (rated "likely), 0067 or 0243 (both rated "neutral"). These result in the same main metabolites as the below-mentioned reactions 2), 3) and 4), respectively. Therefore, the products of this reaction correspond to the products of the reactions mentioned below.

2) Transformation to an aldehyde by oxidative attack on the tertiary amine moiety

This transformation is also based on biotransformation rule 0063 and the aerobic likelihood of rule 0063 is rated as "likely" in the Pathway Prediction System.



This initial step is followed by oxidation of the aldehyde group to a carboxylic acid group (rated "likely"). Subsequently, three possible transformations are proposed, two of them according to biotransformation rules 0067 and 0243 (both rated "neutral"), which lead to the main metabolites described below for reactions 3) and 4). The third proposed reaction follows biotransformation rule 0334 (rated "neutral") and is a terminal hydroxylation of the alkyl chain which is either followed by step-wise oxidation to the aldehyde and then the carboxylic acid (rules 001 & 003, "likely") or biotransformation according to rules 0067 and 0243 (both rated "neutral"). These would result in hydroxylated fatty acids or hydroxylated primary amides of fatty acids. These are expected and predicted to biodegrade ultimately to the same metabolites as the corresponding non-hydroxylated fatty acids or primary amides of fatty acids. Therefore, only the pathway leading to the carboxylation is considered further. It is depicted in figure 1.

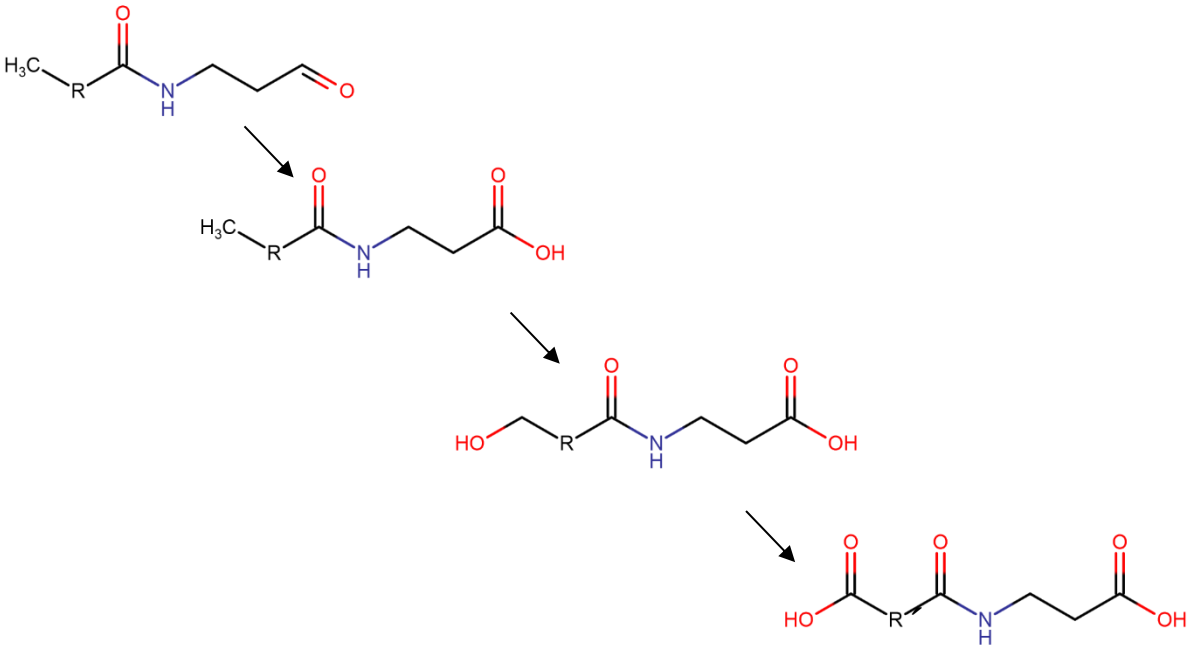
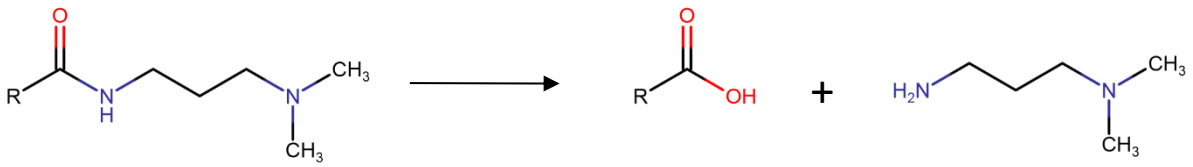


Figure 1: Biodegradation pathway leading to terminal carboxylation of the alkyl residue R.

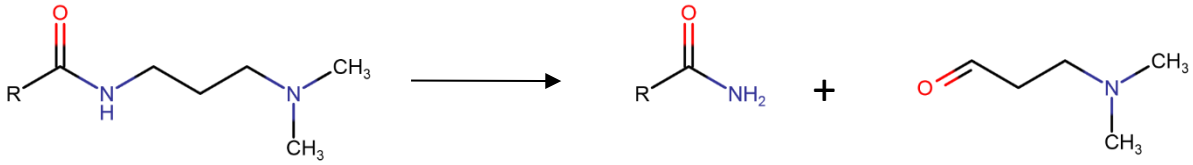
For this carboxylated metabolite, biotransformation according to rules 0067 and 0243 is proposed by the system, which would lead to fatty acids or primary amides of fatty acids with a terminal carboxyl group. The same considerations are applied for them as for the hydroxylated species. Furthermore, for the saturated R, biotransformation rule 0337 (beta-oxidation, rated "likely") is also proposed. This rule leads to a shortening of the alkyl chain by two carbon units. The subsequent pathway consists of further beta-oxidation steps (and/or biotransformation according to rules 0067 and 0243), and ultimately to biotransformation according to rules 0067 and 0243, i.e. transformation to fatty acids or primary amides of fatty acids with a terminal carboxyl group. These substances are expected to be readily biodegradable. The influence of chain length and saturation of the R moiety mainly concerns the proposed steps of beta-oxidation: As *cis* double bonds cannot undergo beta-oxidation, they are transformed to single bonds by reductases (rule 0021, rated "neutral") or to *trans* double bonds by isomerases. Therefore, the proposed pathway for the unsaturated structures includes hydration of the double bonds. However, while this might result in a slightly delayed transformation of the unsaturated structures, it ultimately leads to analogous results as for the saturated component. Furthermore, naturally occurring unsaturated fatty acids are readily degraded by this pathway and it is therefore assumed that micro-organisms are capable of conducting it.

3) Enzymatic hydrolysis to fatty acid and amine
This transformation is based on biotransformation rule 0067 and the aerobic likelihood of rule 0067 is rated as "neutral" in the Pathway Prediction System.



If the degradation pattern of the UVCB substance followed reaction path 3), it would result in the starting materials used for manufacturing it. These are naturally occurring fatty acids which are assumed to be readily biodegradable and 3-aminopropyldimethylamine. 3-aminopropyldimethylamine is also considered readily biodegradable (see section on screening tests above). Therefore, reaction pathway 3) is expected to result in mineralization of the substance. With regard to differences concerning the saturation degree, the remarks made above on the beta-oxidation of fatty acids should apply. However, all fatty acids are considered to be readily biodegradable.

4) Oxidative cleavage of the amidic C-N bond
This transformation is based on biotransformation rule 0243 and the aerobic likelihood of rule 0243 is rated as "neutral" in the Pathway Prediction System.



Reaction pathway 4) results in the primary amides of fatty acids and in 3-(dimethylamino)-propanal. The primary amides of fatty acids are naturally occurring signaling molecules that are rapidly hydrolyzed in mammals by an enzyme called fatty acid amide hydrolase (FAAH) (Ezzili et al, 2010). Particularly, the primary amides of oleic acid, linoleic acid and stearic acid have been observed in this context (Ezzili et al, 2010). Another relevant substance is Arachidonamide, which has a chain length of 20 and four double bonds and which is hydrolyzed by FAAH even faster than the primary acid amide of oleic acid (Ezzili et al, 2010). Therefore, it is expected that linolenamide would be susceptible to FAAH as well. Generally, micro-organisms are even more capable of metabolizing organic substances and therefore, it is assumed that the primary amides of oleic acid, linoleic acid, stearic acid and linolenic acid are not only metabolized by mammals, but that they are also biodegradable by micro-organisms. 3-(dimethylamino)propanal is not registered and no data on biodegradation are available. However, it is predicted to "likely" degrade further to readily biodegradable compounds. If it was persistent, this should have become obvious in the screening test on the stearamide structure that is discussed below. With regard to differences concerning the saturation degree of R, the remarks made above on the beta-oxidation of fatty acids should apply for the primary amides, too.

Summing up the results, it can be concluded that all structures follow the same degradation pathways. The only difference is that the beta-oxidation of the *cis* unsaturated fatty acid alkyl chains requires enzymatic transformation of the double bonds. While this may delay biodegradation of the unsaturated compounds as compared to the saturated compounds, it is generally expected that this transformation occurs and that it is environmentally relevant. Furthermore, it is expected that the general biodegradability of the unsaturated compounds is similar.

7.7.1.2.1.2. Screening tests

The registration dossiers contain three screening tests on the ready biodegradability of Emulsamine. As these tests were conducted with the UVCB substance itself, no clear conclusions can be drawn regarding the individual constituents. In addition, confirmation of validity of all tests is not possible because important information, i.e. the difference of replicate values, is missing in the dossiers. However, the results can be used as supporting information in a weight-of-evidence approach. All tests show some shortcomings, which are explained below.

One study was performed according to the EU method C.4-C, which is compliant with OECD Guideline 301 B (CO2 Evolution Test / Modified Sturm Test). This test was conducted with AT-O Emulsifier (No CAS or EC number is provided), which appears to be a former tradename of Emulsamine (EC 800-353-8). The study meets GLP requirements. Apart from the mentioned missing information, approx. 20 % abiotic elimination was found in a sterile control, which might indicate that the reliability of the test is limited. After 28 days, 20 % biodegradation was observed. The registrant states that the lack of degradation might be caused by toxicity towards microorganisms. This assumption is not confirmed by the inhibition control; however, a slight inhibition of the reference substance was observed. The test on microbial toxicity discussed below in section 7.8.3 yields an EC_{50} of 192 mg/L which is well above the concentration used in this screening test. Nevertheless, the test concentration of 26.7 mg/L used in this study does not correspond to the recommendation given in the OECD 301 testing guideline, which suggests testing at concentrations less than 1/10 of the EC50 values to avoid inhibition due to toxicity (OECD 1992). The eMSCA considers that there are different possibilities for explaining the lack of degradation in this test: First, variation of ready biodegradability test results is quite common and often caused by differing inocula. Second, the amount of abiotic elimination observed leaves some doubt about the reliability of this test. Third, there might indeed have been some inhibition due to toxicity towards microorganisms.

A second study was performed according to OECD guideline 301 D (Closed Bottle Test) in compliance with GLP requirements. The test was conducted with EC 272-047-7 which corresponds to Emulsamine (EC 800-353-8). The test concentration was 2 mg/L and thus low enough to avoid potential inhibition of microorganisms. After 28 days, 75 % ThOD was reached, and the 10-day window criterion was passed.

A third study was performed according to OECD guideline 301 D (Closed Bottle Test) in compliance with GLP requirements. The test concentration was 2 mg/L and thus low enough to avoid potential inhibition of microorganisms. The test was conducted with EC 281-990-3 (Amides, C8-22, N-[3-(dimethylamino)propyl]) which is not listed as a corresponding EC number for Emulsamine (EC 800-353-8) in the CSR. However, the eMSCA expects that the test substance contains the main constituents of Emulsamine , and additionally further constituents. Therefore, the eMSCA considers that the experimental results for EC 281-990-3 are relevant for the assessment of Emulsamine, although they might be confounded by the influence of the additional constituents. After 28 days 60 % ThOD was reached, but the 10-day window criterion was not passed.

The registrants explain this by the substance properties (UVCB, ionic, surface-active). Inoculum concentration related to suspended solids per litre corresponded to the test guideline but exceeded it related to colony forming units (CFU) per litre by a factor of 10^1-10^4.

The registrants argue that the differing results on ready biodegradability might be caused by toxicity towards microorganisms. However, all tests used inhibition control and none of these confirm this assumption. Furthermore, the test on microbial toxicity discussed below in section 7.8.3 yields an EC_{50} of 192 mg/L which is well above the concentration used in the screening tests. Nonetheless, the highest test concentration of 26.7 mg/L was used in the study according to C.4-C, while the OECD 301 testing guideline recommends testing

at concentrations less than 1/10 of the EC50 values to avoid inhibition due to toxicity. A lower concentration of 2 mg/L was used in the OECD 301 D tests.

The eMSCA considers that there may have been some inhibition of microorganisms in the first test, but that the differing results in the conducted screening tests may also be explained by the inherent variability of results from the applied experimental methods. Furthermore, the variable composition of the test substances results in an even larger variability of experimental results. In the view of the eMSCA the high amount of elimination in the sterile control also indicates that the first test might not be reliable.

Further supporting information is also available in the registration dossiers (https://echa.europa.eu) for 2 of the constituents of Emulsamine that were selected for further assessment:

N-[3-(dimethylamino)propyl]octadecanamide (stearamide, EC 231-609-1) is registered as a mono-constituent substance (ECHA 2016c) and thus, the data in the respective registration dossiers can be used directly for the assessment of the N-[3-(dimethylamino)propyl]stearamide constituent. An OECD 301 B study was conducted for this substance (ECHA 2016c). 88 % biodegradation were observed after 28 days. According to the dossiers, some validity criteria were fulfilled, however, as mentioned above some information on validity is missing. The substance is considered to be readily biodegradable (ECHA 2016c). The registration dossiers do not contain sufficient data to enable a thorough evaluation of this study. Nevertheless, based on the available information, the eMSCA considers that it is reasonable and plausible to assume that N-[3-(dimethylamino)propyl]stearamide is readily biodegradable.

N-[3-(dimethylamino)propyl]oleamide (EC 203-661-5) is registered as an UVCB substance (ECHA 2016b). Beside the N-[3-(dimethylamine)¬propyl]-oleamide it contains other N-[3-(dimethylamine)propyl] amides. However, the overall composition of this UVCB differs significantly from Emulsamine (see Confidential Annex). Therefore, the eMSCA considers that the result of the OECD 301 B test for this substance can only be used as supporting information. 91% biodegradation were observed after 28 days and the registrants state that the validity criteria were fulfilled (ECHA 2016b).

Furthermore, a registration dossier for 3-aminopropyldimethylamine (EC 203-680-9, mono-constituent substance) is available. 3-aminopropyldimethylamine was observed to be readily biodegradable in an OECD 301 D study (ECHA 2016d). This result is supported by read-across to a structurally related substance. Based on the available information the eMSCA considers that it is reasonable and plausible to assume that 3-aminopropyldimethylamine is readily biodegradable. It should be noted, however, that information on the study with 3-aminopropyldimethylamine is scarce and conclusions have to consider this. No further evaluation of the PBT properties of 3-aminopropyldimethylamine has been carried out, as it does not appear to fulfil the screening criterion on persistence. Hence, the eMSCA considers that it is not a PBT/vPvB substance, based on the currently available information.

The eMSCA considers that the naturally occurring fatty acids contained within Emulsamine are expected to be biodegradable. Consequently, they are not considered further in this substance evaluation.

7.7.1.2.1.3. Simulation tests (water and sediments)

A study according to OECD 303A was carried out on amides, rape-oil, N-[3-(dimethylamino)propyl] in compliance with GLP. An immediate high removal was observed that can be explained by adsorption and possibly also by biodegradation. The mean removal percentage was 105 %. This test is not considered as relevant for PBT assessment as it represents waste water treatment plants and not the environment.

7.7.1.2.1.4. Summary and discussion of biodegradation in water and sediment

In summary, although all individual screening tests have same shortcomings they can be used together in a weight-of-evidence approach. It can be concluded that mineralisation occurs. However, it is not possible to conclude this for all constituents from the screening tests alone. Despite some shortcomings the biodegradability test on stearamide indicates that this constituent is indeed readily biodegradable.

Furthermore, the analysis of degradation mechanisms using EAWAG-BBD (EAWAG-BBD, Gao et al, 2010) shows a common degradation pattern for all amide constituents, resulting in corresponding metabolites. The only difference occurs with respect to the saturation of the alky chain which is degraded by beta-oxidation. For the unsaturated structures, transformation of the *cis* double bonds is required to proceed with beta-oxidation and therefore, the selected structures undergo reduction to single bonds. However, degradation of unsaturated fatty acids is a common biochemical process and it is therefore assumed that this additional reaction step will not hinder the biodegradation of these compounds. While the predicted pathways do not allow a conclusion on reaction rates, they strongly indicate that the reaction rates of the examined structures will be similar. Particularly, there might be faster degradation of the stearamide, while biodegradation of the unsaturated structures might proceed slightly slower.

This mechanistic finding can be combined with the results of the screening tests on biodegradability. The pass level was reached in two out of three tests. The eMSCA considers that the differing results may be caused by the inherent variability of the ready biodegradability tests, but also by a slight inhibition of microorganisms in the failed test. Furthermore, the result of the sterile control indicates that the reliability of the failed test might be limited. In summary, the eMSCA considers that the results of the two tests showing mineralisation outweigh the negative result of the failed test.

While the stearamide constituent, the fatty acids and 3-aminopropyldimethylamine show to be readily biodegradable, the sum of their contents is still not high enough to explain the biodegradation observed in the screening tests on the UVCB substances. Since the unsaturated amides show a common degradation mechanism (and finally, common degradation products) it is not plausible that one of these amides should be persistent while the others would be readily biodegradable. It can rather be concluded that the unsaturated amides are inherently biodegradable and thus not persistent.

7.7.1.2.2. Biodegradation in soil

No experimental data on degradation in soil are available. However, the conclusions drawn above on data for the water compartment indicate that the constituents of Emulsamine are not persistent in soil.

7.7.1.3. **Summary and discussion of degradation**

3-aminopropyldimethylamine is assumed to be not persistent. It is expected that the fatty acids contained in N-[3-(dimethylamine)propyl] C18-unsatd. amides are not persistent, too.

The amides structures examined above are concluded to be not persistent based on a weight-of-evidence approach that combines information on biodegradation pathways and the results of screening tests. The screening tests show that the saturated amide is readily biodegradable. The biodegradation observed in the screening tests on the UVCB substances cannot be explained alone by the mineralisation of the saturated amide, the fatty acids and 3-aminopropyldimethylamine. It can be concluded that the unsaturated amides biodegrade, too. As all unsaturated amides show a common degradation pattern, they are

expected to show a similar biodegradability. Based on this assumption, the unsaturated constituents can be concluded to be inherently biodegradable and thus not persistent.

7.7.2. Environmental distribution

7.7.2.1. **Adsorption/desorption**

The adsorption/desorption behaviour of the substance was examined in an OECD 106 study conducted in accordance with GLP. Depending on the different soils tested, the observed adsorption coefficients K_d range from 2500 L/kg to 4500 L/kg with an average K_d of 3300 L/kg. Therefore, the substance is considered to be strongly sorptive to soil/sediment particles.

7.7.2.2. **Volatilisation**

No information available.

7.7.2.3. **Distribution modelling**

No information available.

7.7.2.4. **Summary and discussion of environmental distribution**

Based on high measured adsorption coefficients, the substance is considered to be strongly sorptive to soil/sediment particles.

7.7.3. Bioaccumulation

The amide constituents of Emulsamine are largely protonated under environmental conditions. The protonated part of the molecule is hydrophilic while the long-chained fatty acid residue is lipophilic and hence, these constituents are surfactants. The measured dissociation constant (pKa) is 8.5 at 20 °C, indicating that a small percentage of neutral species exists under environmentally relevant conditions. Dissociation and the amphiphilic nature of the substance have to be taken into account when assessing bioaccumulation.

Octanol-Water Partition Coefficient K_{OW}

The log K_{OW} of the main constituents was measured in a study according to OECD 123. The observed log K_{OW} values are 6.1 for the monounsaturated amide, 5.3 for the diunsaturated amide and 4.6 for the triunsaturated amide. Based on the log K_{OW} values, these constituents are potentially bioaccumulative. However, the log K_{OW} yields only limited evidence on the bioaccumulation of ionic compounds.

Distribution Coefficient D

A property generally used for the assessment of ionic substances is the log D value. Table 11 shows calculated log D values for the stearamide, oleamide, linoleamide and linoleneamide constituents, respectively. The respective graphs are given in figures 2, 3, 4 and 5. Calculations show the following tendency:

log D (Stearamide) > log D (Oleamide) > log D (Linoleamide) > log D (Linolenamide).

This trend is in agreement with the experimentally determined log K_{OW} values for the monounsaturated amide, the diunsaturated amide and for the triunsaturated amide. The estimated log D values at pH 7 range from 4.5 (stearamide) to 3.4 (linolenamide) and are lower than the corresponding log K_{OW} values.

Table 11

LOG D VALUES FOR THE RELEVANT CONSTITUENTS, READ OFF THE CALCULATED LOG D (PH) GRAPHS (Chemicalize 2016)				
Constituent	**SMILES Code**	**Log D**		
		pH = 6	pH = 7	pH = 8
Stearamide	CCCCCCCCCCCCCCCCCC(=O)NCCCN(C)C	3.9	4.5	5.4
Oleamide	CCCCCCCC/C=C\CCCCCCCC(=O)NCCCN(C)C	3.5	4.1	5.0
Linoleamide	CCCCC/C=C\C/C=C\CCCCCCCC(=O)NCCCN(C)C	3.1	3.8	4.6
Linolenamide	CC/C=C\C/C=C\C/C=C\CCCCCCCC(=O)NCCCN(C)C	2.7	3.4	4.2

Figure 2: Calculated log D for the stearamide constituent (Chemicalize 2016).

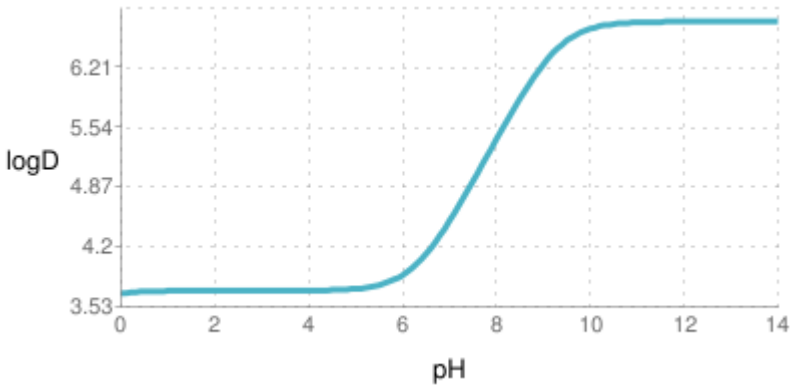


Figure 3: Calculated log D for the oleamide constituent (Chemicalize 2016).

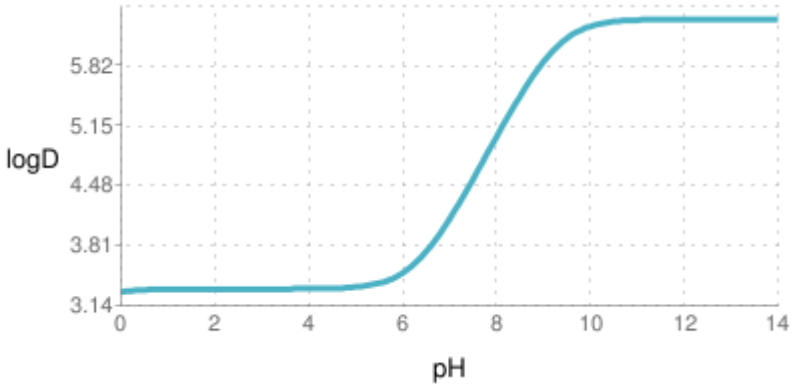


Figure 4: Calculated log D for the linoleamide constituent (Chemicalize 2016).

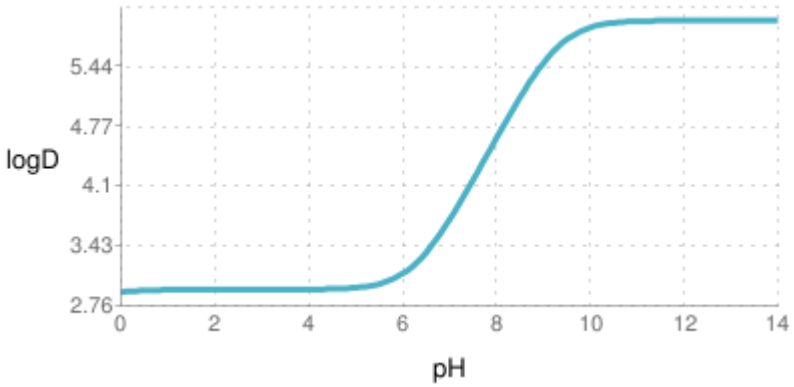
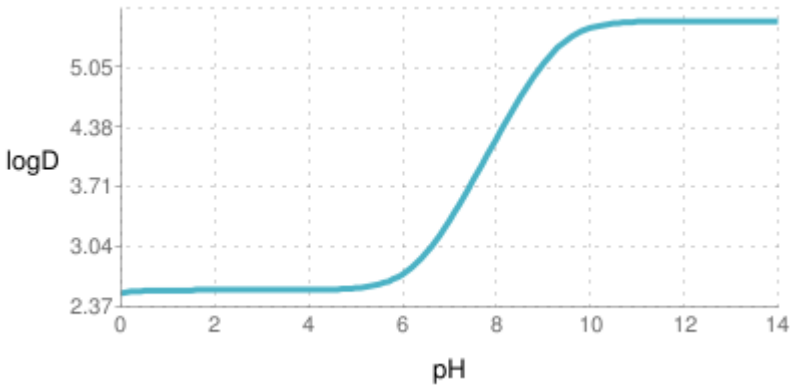


Figure 5: Calculated log D for the linoleneamide constituent (Chemicalize 2016).



Membrane-Water Partition Coefficient K_{lipw}

However, bioaccumulation of ionic substances should rather be assessed using a membrane-water partition coefficient K_{lipw}. Calculations by Bittermann and Goss using the program COSMOmic (COSMOmic 16-01; Eckert and Klamt 2002; Klamt et al 2008; Ingram et al 2013) yield log K_{lipw} values of 6.92, 5.91 and 5.15 for the oleamide, the linoleamide and the linoleneamide, respectively (Bittermann and Goss 2016). Currently, COSMOmic has been validated with experimental values up to a log K_{lipw} of 5.2 (Bittermann and Goss 2016). Furthermore, according to the authors, the length of the substances is higher than that of the structures used for validation (Bittermann and Goss 2016). However, the authors still consider the molecules to fit into a lipid bilayer (Bittermann and Goss 2016). The molecular mass of the structures is within the range of the validation data (Bittermann and Goss 2016).

In contrast to many QSARs that are solely based on correlations, the COSMOmic method is an essentially mechanistic approach based on quantum chemical calculations and the COSMO-RS theory and it contains only few calibrated parameters (COSMOmic 16-01; Eckert and Klamt 2002; Klamt et al 2008; Ingram et al 2013). Therefore, the program is expected to give meaningful results for these substances despite their high K_{lipw} values and their length. However, the prediction accuracy is probably slightly reduced. In summary, it can be concluded that the three constituents under consideration show very high K_{lipw} values and are thus potentially bioaccumulative. Furthermore, the observed trend is in agreement with the log K_{OW} and log D values.

Metabolism

The amide structures might be susceptible to metabolism, following similar reaction pathways as described above in the section about biodegradation. However, further information would be required to conclude on this aspect.

7.7.3.1. **Aquatic bioaccumulation**

No information available.

7.7.3.2. **Terrestrial bioaccumulation**

No information available.

7.7.3.3. **Summary and discussion of bioaccumulation**

The amide structures are ionic and amphiphilic. The structures might be susceptible to metabolic reactions; however, further information would be required to conclude on metabolism. Based on the examined partition coefficients K_{ow}, D and K_{lipw}, they are considered to be potentially bioaccumulative.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

7.8.1.1. **Fish**

There are three short-term (96 h) toxicity studies on fish (*Danio rerio*) available for Emulsamine. Recently, a study performed in 2012 according to OECD Test Guideline 203 used a bulk approach in freshwater under semi-static conditions. Due to strong adsorption of the test substance (amides rape-oil, CAS: 8540-42-3) initial concentrations have been measured and were used to calculate an EC_{50} (96 h) of 0.94 mg/L. A supporting study (2004) was conducted according to EU Method C.1. No certificate was available for the substance used in this test and no analysis was done during the test procedure. The study resulted in a nominal LC_{50} (96 h) of 0.3904 mg/L. A weight-of-evidence study (1995) according to OECD Test Guideline 203 used Redicote E-85 as test substance. No analyses have been performed. The test substance was insoluble in water but dispersible. This study resulted in a nominal NOEC of 0.1 mg/L and an LC_{50} (96 h) of 0.22 mg/L was calculated.

No long-term toxicity test on fish is available.

7.8.1.2. **Aquatic Invertebrates**

A 48-h acute toxicity test with *Daphnia magna* was conducted according to OECD Guideline 202. Therein, Amides, rape-oil, N-[3-(dimethylamino)propyl] (CAS 85408-42-0, EC 287-003-2) was used as test substance. Test item concentration was not determined as the values were lower than limit of quantification of the analytical method used. The EC_{50} (48 h) was 0.28 mg/L.

A long-term toxicity test on aquatic invertebrates (*Daphnia magna, 21 d*) was conducted according to OECD Guideline 211 with Amides rape-oil, N-[3-(dimethylamino) propyl] as test substance. Natural surface water was used to allow a more environmentally realistic test (OECD guideline 211 recommends fully defined media). A calculated NOEC (21 d) of 0.048 mg/L is reported and the EC_{10} (21 d) based on reproduction was calculated as 0.07 mg/L. Physical adhesion of the test substance to *Daphnia* was visible and caused considerable mortality in early stages of test.

7.8.1.3. **Algae and aquatic plants**

In 2013 a 72-hour toxicity test on green algae (*Pseudokirchneriella subcapitata*) was conducted according OECD Guideline 201 (with deviations). The study used Amides, rape-oil, N-[3-(dimethylamino)propyl] (CAS 85408-42-0) and was flagged as key study by the registrants. The substance used for this test corresponds to the registered substance. The NOEC (growth), EC_{10} (growth), LOEC (growth) and EC_{50} (growth) were calculated as 0.103 mg/L, 0.32 mg/L, 0.316 mg/L, and > 0.96mg/L, measured initial concentrations, respectively. The registrants informed about following deviation from OECD Guideline 201.

The mean coefficient of variation for section by section specific growth rate in the control exceeded 35 %. The registrants explained this deviation by the presence of suspended matter. However, according to OECD Guideline 201 the test should be considered as invalid. Therefore, the eMSCA assessed the study as not reliable.

A second study conducted in 2005 is marked as "disregarded study" by the registrants. This study was performed according to OECD guideline 201 and used modified tall oil fatty acids, reaction compounds with dialkylsubstituted diamines (CAS 84082-43-9) for a 74 h toxicity test to green algae (*Pseudokirchneriella subcapitata*). This substance is a UVCB but no detailed information on constituents is available. The registered substance and the test substance used in this study were compared to justify the read-across. Further, the study was used to evaluate ecotoxicology to aquatic algae not only for Emulsamine but also for the substance N-[3-(dimethylamino)propyl]oleamide (CAS 109-28-4) by independent registrants. N-[3-(dimethylamino)propyl]oleamide is similar to Emulsamine. This instance is used to support the read-across from modified tall oil fatty acids, reaction compounds with dialkylsubstituted diamines (CAS 84082-43-9) to Emulsamine.

The toxicity to aquatic algae of related N-[3-(dimethylamino)propyl] alkyl-amides was compared to the toxicity of Emulsamine. Between these substances, the alkyl chains differed in length and saturation.

The physico-chemical properties and toxicological effects on aquatic algae are summarised in Table 12. For the registration of amides, C16-C18 N-[3-(dimethylamino)propyl] (CAS: 940-123-5) either stearic acid 3-(dimethylaminopropyl) amide with a C18 alkyl chain or C20/C22 ATQ trocken were used for the read-across of the algae tests. The NOEC obtained from tests with stearic acid 3-(dimethylaminopropyl) amide is 10-fold lower than EC_{10} obtained with tests using C20/C22 ATQ trocken. Further algae toxicity tests done for Amides, coco N-[3-(dimethylamino)propyl] (CAS: 68140-01-2) resulted in a low EC_{10} for saturated and unsaturated alkyl chains with a length between C8 and C18. Findings from Yamane et al. (2008) support these results. The comparison of toxicity to aquatic algae supports the results from the study done in 2005. Therefore, the testing results for modified tall oil fatty acids, reaction compounds with dialkylsubstituted diamines (CAS: 84082-43-9) can be used to assess ecotoxicological properties of Emulsamine and the study needs to be considered.

This study done in 2005 used following nominal test concentrations of test substance: 0.02 mg/L, 0.04 mg/L, 0.09 mg/L, 0.21 mg/L, 0.45 mg/L and 1 mg/L. The test resulted in an EC_{10} (biomass and growth rate) of 0.002 mg/L, and an EC_{50} (biomass) = 0.003 mg/L and EC_{50} (growth) = 0.005 mg/L. No deviations of validity criteria were reported, but the registrants informed that the concentration of the substance being tested has not been

maintained within ± 20 % of the nominal and measured initial concentration. Further, no test substance could be measured in the test systems for the nominal concentration 0.02 and 0.04 mg/L. The amount of test substance was below the detection limit. Therefore, authors used half the value of the detection limit (i.e. 0.0015 mg/L) for calculation of the mean of these concentrations. For the nominal concentration 0.09 mg/L, the amount of substance was below the quantification limit. Therefore, half the value of the quantification limit (0.045 mg/L) was used for calculation of mean.

The authors used geometric mean concentrations for subsequent calculations of desired ecotoxicological parameters in accordance with OECD Guideline 201. However, the calculations of four geometric mean concentrations are based on defined (but not measured) values.

Taking the available information into account, the evaluating MSCA assessed the study as reliable with restrictions. The study is therefore considered suitable for ecotoxicological characterisation of Emulsamine.

Table 12

PHYSICO-CHEMICAL AND EXOTOXICOLOGICAL PROPERTIES OF N-[(DIMETHYLAMINO)PROPYL]-ALKYLAMIDES								
COMMON NAME	**CAS**	**ALKYL-CHAIN CHARCTERISTICS**	**APPEARANCE**	**WATER SOLUBILITY**	**SOLUBILITY IN ORGANIC SOLVENTS**	**SUBSTANCE USED FOR ALGAE TEST**	**RESULT ALGAE TOXICITY TEST**	**COMMENT**
Amides, C16-18 (even numbered), N-[(dimethylamino)propyl]	940-123-5	C16 - C18, saturated	Solid white flakes	3.65 mg/L at 23 °C	woE: 19.7 – 180 g/L @ RT	a) Stearic acid 3-(dimethylaminopropyl)amide) (C18); b) C20/22 ATQ trocken	a) NOEC (72 h) 0.0316 mg/L b) EyC_{10} [mean] 0.412 mg/L	
Amides, coco, N-[3-(dimethylamino)propyl]	68140-01-2	C8 - C18, saturated and unsaturated	pasty (waxy), yellow (off-white) substance	0.03 [C18] – 257 [C8] mg/L (calculated values)	no data	constituent	E_bC_{10} 0.05 mg/L, E_rC_{10} 0.1 mg/L	
Emulsamine	1379524-06-7	C18 unsaturated	Brown liquid	26 mg/L at 23 °C	No data	Modified tall oil fatty acids, reaction compounds with dialkylsubstituted diamines (84082-43-9)	NOEC 0.002 - 0.003 mg/L	

7.8.1.4. **Sediment organisms**

No data available.

7.8.1.5. **Other aquatic organisms**

No data available.

7.8.2. Terrestrial compartment

An 8-week long-term toxicity test on earthworms (*Eisenia fetida*) was conducted according to OECD guideline 222 showing no toxic effects on earthworm (NOEC (mortality/reproduction) 1000/910 mg test item/kg soil dry weight, respectively).

Annex IX 9.4.2 and 9.4.3 of REACH regulation lists effects on soil micro-organisms and on plants as required information. Further, due to the adhesive nature of the test substance, it is possible that the test substance influences processes of soil micro-organisms and plants. However, no data have been provided for these groups.

7.8.3. Microbiological activity in sewage treatment systems

A study according to OECD 209 with activated sludge was conducted with Amides, rape-oil (CAS: 85408-42-02) as test substance in 2010. The test showed effects at nominal concentrations of 20, 40, 80, 160, 320 and 640 mg/L. However, oxygen uptake in blank control was 15.6 $mg_{O2}/(g_{[sludge]} \times h)$. Therefore, the OECD guideline validity criterion of blank control oxygen uptake was not met. However this deviation was not reported by the registrants. Nevertheless, the test estimated an EC_{50} of 192 mg/L of total respiration for the substance tested. The registrants concluded that test substance is not harmful to micro-organisms of active sludge in sewage treatment plants.

However, OECD guideline 209 recommends copper(II) sulphate pentahydrate as a reference substance for inhibition of total respiration. It should yield an EC_{50} in the range of 53-155 mg/L to consider the test as valid. The substance used for the test from 2010 revealed an EC_{50} of 192 mg/L and is therefore roughly as low as for the reference substance copper(II) sulphate pentahydrate. In opinion of the evaluating MSCA, the tested substance is therefore likely to impair microbiological activity in sewage treatment systems.

7.8.4. PNEC derivation and other hazard conclusions

PNEC values in the registration dossiers are acceptable with the exception of the $PNEC_{aquatic}$ which was revised by the eMSCA using a different study than by the registrants (cf. Section 7.8.1).

The $PNEC_{aquatic}$ of 0.0004 mg/L was derived in accordance to ECHA Document R.10 (2008) with an assessment factor of 50, since two long term studies covering two trophic levels covering the tropic level with lowest EC_{50} value are available for assessment.

7.8.5. Conclusions for classification and labelling

The aquatic ecotoxicological properties of the registered substance (List number 800-353-8; CAS 1379524-06-7) indicate that the substance is hazardous to the aquatic environment

(Category Acute 1 and Category Chronic 1). This is reflected in the current self-classification implemented by the registrants and so not considered a priority for further follow-up regulatory action at EU level at the moment.

7.9. Human Health hazard assessment

Not assessed.

7.10. Assessment of endocrine disrupting (ED) properties

Not assessed.

7.11. PBT and vPvB assessment

Persistence

The biodegradability of Emulsamine (CAS: 1379524-06-7) was tested in several screening tests on ready biodegradability using the registered UVCB and closely related UVCB as test substance resulting values of 20 to 75 % of the respective theoretical degradation indicators. A screening test on the stearamide (saturated constituent) alone achieved 88 % $ThCO_2$-evolution. Simulation tests are not available, neither for the UVCB nor for individual constituents.

The biodegradation pathways of selected amide constituents were predicted and compared with each other. It became apparent that all amide constituents share a common degradation pattern, with the unsaturated constituents undergoing an additional transformation: As the alkyl chains of all amide structures are degraded via beta-oxidation, the double bonds are transformed to single bonds in order to proceed with beta-oxidation. However, this transformation is a common pathway in the biodegradation of unsaturated fatty acids and is therefore expected to occur in this case, too. Consequently, while biodegradation of the unsaturated components might be delayed as compared to the stearamide, it is expected that the unsaturated constituents show a similar biodegradation behaviour.

Combining both information from screening tests and information on mechanistic pathways, the high biodegradation observed in the tests on UVCB cannot be explained by biodegradation of the stearamide and the remaining educts (i.e. fatty acids and 3-aminopropyldimethylamine). It is apparent that the unsaturated amides biodegrade, too. As – based on the mechanistic information – it is not plausible to assume significant differences in biodegradability of the unsaturated constituents, it is concluded that all unsaturated constituents are at least inherently biodegradable and probably also readily biodegradable.

Consequently, the constituents of the UVCB substance (and hence the UVCB) are not considered to be persistent (not P/vP) according to the criteria of REACH Annex XIII. Further testing is not deemed necessary.

Bioaccumulation

The amide constituents of this UVCB substance are largely protonated under environmental conditions. The log K_{OW} of the main constituents of Emulsamine (CAS 1379524-06-7) was measured in a study according to OECD 123. The observed log K_{OW} values are 6.1 for the monounsaturated amide, 5.3 for the diunsaturated amide and 4.6 for the triunsaturated amide.

A property generally used for the assessment of ionic substances is the log D value. Calculated log D values for the stearamide, oleamide, linoleamide and linoleneamide

constituents range from 4.5 (stearamide) to 3.4 (linoleamide). They show a trend which is in agreement with the experimentally determined log K_{OW} values for the monounsaturated amide, the diunsaturated amide and for the triunsaturated amide:

log D (Stearamide) > log D (Oleamide) > log D (Linoleamide) > log D (Linolenamide).

The bioaccumulation of ionic Emulsamine constituents was also assessed using a membrane-water partition coefficient K_{lipw}. Calculations using the program COSMOmic yield log K_{lipw} values of 6.92, 5.91 and 5.15 for the oleamide, the linoleamide and the linoleneamide, respectively. The K_{lipw} values and the chain length exceed the range given in the validation data set, which may result in a lower accuracy of the results. However, it is concluded that the considered structures show high K_{lipw} values.

No experimental information is available on aquatic or terrestrial bioaccumulation. The structures might be susceptible to metabolic transformations. However, further information on this endpoint is not available.

Consequently, Emulsamine is considered potentially bioaccumulative based on screening information, i.e. on high log K_{ow} , log D and log K_{lipw} values. Therefore, Emulsamine is potentially B/vB according to the screening criteria of REACH Annex XIII. Because of the expected low persistence, further testing of bioaccumulation is not deemed necessary.

(Eco-)Toxicity

The ecotoxicity of Emulsamine (CAS 1379524-06-7) was tested in several studies and has been assessed in Section 7.8.1.

Short-term data are available for fish and aquatic invertebrates. The lowest short-term ecotoxicity value is a 48 hour EC_{50} for *Daphnia* at 0.28 mg/L (nominal).

Long-term toxicity data are available for *Daphnia*, algae and earthworm as a terrestrial model organism. The lowest long-term exotoxicity value is a 72-hour EC_{10} (biomass and growth rate) for green algae at 0.002 mg/L (geometric mean measured/defined concentrations).

Consequently, Emulsamine as UVCB is considered toxic to aquatic organisms. Emulsamine contains one or more constituents that fulfil the T-criterion according to the criteria of REACH Annex XIII. However, a conclusion on the single constituents cannot be drawn. Because of the expected low persistence, further testing of toxicity to environment is not deemed necessary.

Overall conclusion of the PBT assessment

The amide constituents of Emulsamine are considered as potentially bioaccumulative and potentially toxic. However, the constituents of the UVCB substance are not persistent and hence, they are not PBT or vPvB according to REACH Annex XIII.

Overall, Emulsamine is not a PBT/vPvB substance according to the criteria of REACH Annex XIII.

7.12. Exposure assessment

7.12.1. Human health

Not assessed.

7.12.2. Environment

The eMSCA has assessed the exposure scenarios provided by the registrants, but did not perform its own calculations; some estimations on the fate and behaviour of Emulsamine were conducted. The characterisation of the general exposure scenarios (ES), as well as the description of the activities and technical processes covered in the exposure scenarios were found plausible and acceptable. The spERCs for the exposure scenarios manufacture (ES 1), formulation of Emulsamine (ES 2) and formulation of the asphalt emulsion (ES 3) were found acceptable. Nevertheless, within ES 4 (use by professional workers – use in asphalt emulsion application; ERC 8f), the spERC ESVOC 8.15.v1 is considered not appropriate due to assumed release to air of 95 %. However, a more appropriate spERC is not known to the eMSCA; the registrants may consider an update. The PEC values from calculations of the registrants were found sufficiently conservative.

Environmental emissions of Emulsamine and releases to waste may be expected to be extremely limited at the stage of manufacture and formulation.

As mentioned before, the major use of Emulsamine is in road building industry where it is used as an emulsifier to produce bitumen emulsions in water. When the emulsion is mixed with stone filler, Emulsamine will rapidly adsorb onto the surface of the stones and the emulsion will break. The substance will be immobilised in the bitumen-stone mixture. The concentration of Emulsamine in the final bitumen mix is below 1.5 % (Holl & Rüttgers, 1985).

The application scenario which is considered worst-case with regard to environmental exposure is the asphalt emulsion distribution where liquid bitumen emulsion is spread on the road surface (e.g. spraying at 80 °C), after which the stone aggregate is spread into the emulsion. Typically surface dressing emulsions do have emulsifier contents ranging from 0.15 % to 0.25 %. This content may be higher in more specific applications (e.g. impregnation) but should never exceed 1 % (Holl & Rüttgers, 1985).

The registrants assume that the use in road and construction products results in 100 % release to the environment with the majority being transferred to air, although vapour pressure was estimated to be low (< 0.00005 Pa at 60 °C) which results in a very low fugacity coefficient of 8.5 $x10^{-10}$ (compared to the coefficients for water 0.04 or fuel oil 0.001); 1 % reaches waste water through disposal or wash off. However, in the opinion of the eMSCA the chosen spERC does not fit the application scenario. Release into the air is very unlikely; even the release of 15 % to air, as assumed in ERC 8F is considered to be too high. Consequently, any released Emulsamine is expected to be washed off from the newly paved road to neighbouring ditches and soil on the shoulder of the road. The further fate of Emulsamine would be adsorption to particles and possibly degradation.

Therefore, remainders of Emulsamine on road pavements will result in local releases over a short period of time to neighbouring surfaces. Nevertheless, the amount of Emulsamine released from the stone/bitumen mix (after breaking of the emulsion) is considered to be small.

7.12.3. Combined exposure assessment

7.13. Risk characterisation

Based on PECs and PNECs provided by the registrants and assessed in Sections 7.12.2 and 7.8, Risk Characterisation Ratios (RCR = PEC/PNEC) were altogether found to be below 1, indicating no unacceptable risk for the local as well as the regional environment.

7.14. References

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7.15. Abbreviations

B/vB	Bioaccumulative /very Bioaccumulative
CFU	Colony Forming Units
CLP	Classification, Labelling and Packaging
CMC	Critical Micelle Concentration
D	Distribution Coefficient
EAWAG	Swiss Federal Institute of Aquatic Science and Technology (Eidgenössische Anstalt für Wasserversorgung, Abwasserreinigung und Gewässerschutz)
EAWAG-BBD	EAWAG Biocatalysis /Biodegradation Database
EC_{10}	Effective Concentration, 10%
EC_{50}	Median Effective Concentration
ECHA	European Chemicals Agency
eMSCA	evaluating Member State Competent Authority
Emulsamine	amides, C18-unsatd., N-[3-(dimethylamine) propyl]
ERC	Environmental Release Category
ES	Exposure Scenario
FAAH	Fatty Acid Amide Hydrolase
GLP	Good Laboratory Practice
K_a	Dissociation constant
K_d	Adsorption coefficient
K_{lipw}	Membrane-water partition coefficient
K_{ow}	Partition coefficient n-octanol / water

LC_{50}	Median Lethal Concentration
Linoleamide	(9Z,12Z)-N-[3-(dimethylamino)propyl]octadeca-9,12-dienamide
Linolenamide	(9Z,12Z,15Z)-N-[3-(dimethylamino)propyl]octadeca-9,12,15-trienamide
LOEC	Lowest Observed Effect Concentration
NOEC	No Observed Effect Concentration
Oleamide	(9Z)-N-[3-(dimethylamino)propyl]octadeca-9-enamide
P/vP	Persistent /very Persistent
PBT	Persistent, Bioaccumulative and Toxic
PEC	Predicted Environmental Concentration
pK_a	pK_a = - log K_a (dissociation constant, see K_a)
PNEC	Predicted No Effect Concentration
PPS	Pathway Prediction System
QSAR	Quantitative Structure Activity Relationship
RCR	Risk Characterisation Ratio
SIP	Substance Identity Profile
SMILES	Simplified Molecular Input Line Entry Specification
spERC	Specific Environmental Release Category
spERC ESVOC	spERC by the European Solvents Volatile Organic Compounds Committee
Stearamide	N-[3-(dimethylamino)propyl]octadecanamide
SVHC	Substance of Very High Concern
T	Toxic
$ThCO_2$	Theoretical Carbon Dioxide
ThOD	Theoretical Oxygen Demand
UVCB	Substances of Unknown or Variable composition, Complex reaction products or Biological materials
vPvB	very Persistent and very Bioaccumulative