SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Polyethylene polyamine, pentaethylenehexamine fraction

EC No 701-266-7

CAS No –

Previously registered as
3,6,9,12-Tetraazatetradecamethylenediamine
EC No 223-775-9
CAS No 4067-16-7

Evaluating Member State: Czech Republic

Dated: 05 March 2019

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2019

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

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

Polyethylene polyamine, pentaethylenehexamine fraction was originally selected for substance evaluation in order to clarify concerns about:

- respiratory sensitisation,

- exposure assessment.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Decision on a compliance check of a registration pursuant to article 41(3) of Regulation (EC) No 1907/2006 (CCH-D-2114292247-43-01/F)

- The standard information requirements of Annex VI, section 2 of the REACH regulation – the identity of the substance

The identity of the substance was changed based on the compliance check as follows:

- the original identity: 3,6,9,1-tetraazatetradecamethylenediamine (EC: 223-775-9, CAS: 4067-16-7)

- the new identity: Polyethylene polyamine, pentaethylenehexamine fraction (List No. 701-266-7)

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	
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

4.1.1. Harmonised Classification and Labelling

There were no grounds for classification of the substance as respiratory sensitiser in accordance with Regulation (EC) No. 1272/2008 (CLP).

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

All available information (registration dossier, Chemical Safety Report and literature data and review) was used to clarify the concerns. The available information is sufficient to conclude the substance evaluation.

Table 2

REASON FOR REMOVED CONCERN The concern could be removed because	Tick box
Clarification of hazard properties/exposure	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.)	

The following conclusions were reached:

Respiratory sensitisation
According to information from the lead registrant, there are no signs of respiratory problems during the production or processing of the evaluated substance. No relevant information on the possibility of respiratory sensitisation has been found in the literature. Based on this, the Polyethylene polyamine, pentaethylenehexamine fraction is not considered to be a respiratory sensitiser.

Exposure assessment
Exposure scenarios were processed using CHESAR software. The structure of exposure scenarios including descriptors and conditions of use was taken from the registration dossier and the CSR for polyethylene polyamine, pentaethylenehexamine fraction.

Estimated exposure to the substance seems to be under control. Based on the available data it appears that all the exposure values are below the derived DNEL(s) and all the RCRs (including those for combined exposures) are below 1. Therefore the eMSCA considers that the risks are controlled.

5.2. Other actions

Not applicable.

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

Not applicable, see section 5.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Polyethylene polyamine, pentaethylenehexamine fraction was originally selected for substance evaluation in order to clarify concerns about:

- respiratory sensitisation,

- exposure assessment.

No further concerns were identified during the evaluation. For exposure assessment, the dermal exposure was added via route-to-route extrapolation.

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Respiratory sensitisation	Concern not substantiated. No further action. See section 7.9.3.
Exposure and RMM	RCRs are below 1

7.2. Procedure

Relevant data available in the CSR and the registration dossier were evaluated in relation to specified concerns. For further information the eMSCA performed also its own literature search.

The Lead Registrant updated the registration dossier on 20 Nov 2018. This update included, among other things, a change in substance identification. The update was taken into account during the evaluation.

Additional data were gathered to assess the potential of the evaluated substance for respiratory sensitisation, or to propose appropriate test to clarify the uncertainty.

The exposure of industrial uses were estimated using CHESAR software in connection with the IUCLID dataset. The structure of exposure scenarios including descriptors and main conditions of use was taken from the registration dossier and the CSR for Polyethylene polyamine, pentaethylenehexamine fraction.

7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	Polyethylene polyamine, pentaethylenehexamine fraction
IUPAC name:	Polyethylene polyamine, pentaethylenehexamine fraction
EC number:	701-266-7
CAS number:	-

SUBSTANCE IDENTITY	
CAS name:	-
Molecular formula:	n/a
Molecular weight range:	232 – 258
Synonyms:	-

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

Structural formula:

not applicable

Multiconstituent/UVCB substance/others

See Part C, Confidential Annex.

7.4. Physico-chemical properties

Table 5

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	clear yellowish viscous odourless liquid
Melting / freezing point	freezing point < —70°C
Boiling point	426°C (calculated)
Density	1.003 g/cm^3 (20°C)
Vapour pressure	0.002 Pa (20°C)
Water solubility	> 500 g/l (20°C, pH = 12.6)
Partition coefficient n-octanol/water	log Kow = —3.67 (calculated)
Flash point	183°C (101.3 kPa)
Autoflammability / self-ignition temperature	335°C (101.3 kPa)
Flammability	non flammable
Explosive properties	non explosive
Oxidising properties	non oxidising
Viscosity	203.1 mm^2/s (20°C)
Dissociation constant	pKa = 9.40 (20°C) pKa = 6.18 (20°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

Polyethylene polyamine, pentaethylenehexamine fraction is used as detergent and cleaner, epoxy curing agent, diesel and gasoline additive or wood preservative.

The list of exposure scenarios is given in the Table 9 in Part C – Confidential Annex.

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Polyethylene polyamine, pentaethylenehexamine fraction does not have harmonized classification.

7.6.2. Self-classification

Acute Tox. 4; H302+H312
Skin Corr. 1B; H314
Eye Damage 1; H318
Skin Sens. 1; H317
STOT RE 2; H373 (lungs, oral)
Aquatic Acute 1; H400
Aquatic Chronic 1; H410

7.7. Environmental fate properties

Not relevant for this evaluation.

7.8. Environmental hazard assessment

Not relevant for this evaluation.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

The toxicokinetics of the evaluated substance was assessed based on structurally similar triethylenetetramine (CAS: 112-24-3) in the form of its hydrochloride salts as there are no studies available on the evaluated substance.

According to information provided in CSR, triethylenetetramine is absorbed only in limited quantities after oral administration (approx. 20 % of the administered dose). The substance is metabolised most likely by acylation. It appears that the substance does not pass through another transformation as the metabolites were converted to the original substance by acid hydrolysis. The metabolised substance is excreted from the body via urine or bile.

Dermal absorption of triethylenetetramine is negligible. It can be assumed that the properties of the evaluated substance are similar. On the other hand, the evaluated substance is classified as corrosive to skin, and its penetration through etched skin can be higher.

Inhalation exposure appears to be insignificant due to the low vapour pressure of the evaluated substance, but must be considered for aerosol-generated applications (e.g. spraying).

7.9.2. Acute toxicity and Corrosion/Irritation

Not relevant for this evaluation.

7.9.3. Sensitisation

Polyethylene polyamine, pentaethylenehexamine fraction is classified by the registrant as skin sensitiser (Skin Sens. 1; H317).

This evaluation is focused on respiratory sensitisation. The main reason for concern is due to the two basic ethyleneamines (1,2-ethanediamine and piperazine), which have a harmonised classification - respiratory sensitisers.

Noteworthy, respiratory sensitisation is not part of the standard information requirements under REACH (Annex VII – XI). On the other hand, respiratory sensitisation is a serious classification.

The legal rules for classification of substances or mixtures as respiratory sensitisers according to Regulation (EC) No. 1272/2008 provide two criteria:

- if there is evidence in humans that the substance can lead to specific respiratory hypersensitivity;

- if there are positive results from an appropriate animal test.

It is also mentioned that, at present, recognised and validated animal models for the testing of respiratory hypersensitivity are not available. Under certain circumstances, data from animal studies may provide valuable information in a weight of evidence assessment. Therefore, the classification should be primarily be based on human data (epidemiological studies, case studies), on their frequency and severity. Other data from animal studies may provide valuable information in a weight of evidence assessment.

For the purposes of classification, respiratory sensitisation is assessed as "asthma, but other hypersensitivity reactions such as rhinitis/conjunctivitis and alveolitis are also considered. The condition will have the clinical character of an allergic reaction. However, immunological mechanisms do not have to be demonstrated"[1]. In general, allergy is characterised by the fact that the disease develops in two phases. The first phase is induction (sensitisation), in which the undefined organism is exposed to the allergen. The immune system evaluates the allergen as a foreign substance and learns to respond to it. This phase is usually without clinical symptoms. Following subsequent exposure (elicitation), an immune response can be provoked that results in inflammation and the signs and symptoms of allergic disease[7]. The situation is all the more complicated that respiratory irritants may provoke allergy-like symptoms in susceptible individuals, which are hard to distinguish from respiratory allergy due to the similarity in clinical symptoms[19].

According to information from the lead registrant, there are no signs of respiratory problems during production or handling of the evaluated substance. Further information, related to respiratory sensitisation, are provided in the text below. They were gathered to assess the potential of the evaluated substance for respiratory sensitisation, or to attempt to propose an appropriate test to clarify the uncertainty.

Respiratory allergens are generally divided into two categories according to their molecular mass and specific immune mechanisms. The evaluated substance belongs to the low molecular weight (LMW) allergens. There is a widely accepted theory that LMW allergens do not cause allergies on their own as their molecules are too small to be analysed as foreign by the immune system. These allergens are capable of reacting with amino acids in proteins and form macromolecules known as hapten-protein conjugates, which can initiate the immune response[7].

The nature of the cellular and molecular immunological processes that lead to allergic sensitisation of the respiratory tract to chemicals was not yet completely clarified. There is quite a broad consensus in that respiratory sensitisation is associated with IgE antibody. However, there are cases with evidence of respiratory sensitisation in which the IgE could not be ascertained. This is true especially with respect to the diisocyanates[2,5,14,15]. This may signal that other cell-mediated, IgE independent, immunological mechanisms promote sensitisation of the respiratory tract to some chemicals[16,22].

It is also important to note that exposure performs a considerable role in the development of respiratory allergy. It was found that the induction phase may be initiated not only by inhalation but also by dermal exposure[5,17,18]. On the other hand, the elicitation phase, apparently, can be activated only by inhalation[5,17]. Sensitisation potential may, therefore, be tested using a dermal exposure assay (for example LLNA). However, there are some substances that do not pass through a skin barrier[20] and there is not yet clear whether such a test is applicable to them. The toxicokinetics assay given in the CSR suggests that the evaluated substance is probably negligibly absorbed through intact skin.

Cytokine profiling (or cytokine fingerprinting) is apparently the most promising method to distinguish skin and respiratory sensitisers. It is assumed that, irrespective of occurrence IgE antibody, the development of T helper 2 type (Th2) lymphocyte immune response in the form of production of specific cytokines (especially IL-4, IL-5, IL-10 and IL-13)[5,16]. In contrast to respiratory allergens, skin sensitisers evoke Th1-type immune response mainly associated with IL-2 and IFN-γ production[5,17]. Theoretically, it should be appropriate to combine the established LLNA method with the cytokine profile. Unfortunately, the problem is more complicated. Not yet clarified doses selection for this assay. Doses for cytokine profile measurement usually elicit a positive response in the LLNA assay. This is a paradox if respiratory sensitisers and skin sensitisers are to be distinguished[17,21]. A noticeable change in cytokine levels is thus found at a significantly higher value of the stimulation index[19] (SI≥10). A cytokine profile can change over time[19.27], there is still no consensus at which time the sample is to be evaluated. Moreover, interlaboratory results are somewhat variable[22]. Specificity and sensitivity of the assay are not known, as well as standard workflows and interpretation of results including limit values.

Cytokine profile assay is a part of registration dossier of diethylenetriamine (lower member of the homologous series). After dermal application of the diethylenetriamine (10 %), very low or no IL-4 or IL-10 levels were detected[3] thus diethylenetriamine failed in the cytokine profile assay.

In the last years, considerable attention was paid to both the prediction of respiratory sensitisers and development of a suitable assay for their reliable identification. Prediction of this end-point is usually based on the presence of the certain structural alerts in the molecule (e.g. isocyanates or cyclic anhydrides) or expected reactivity to proteins (expected haptenation).

The overwhelming majority of prediction methods for respiratory allergens are mainly focused on conventional alerts (e.g. isocyanates or cyclic anhydrides); ethyleneamines or similar fragments are mentioned only marginally. For this reason, it is worth mentioning the article Jarvis et al.[8], where the authors assessed respiration allergy hazard not only according to the presence of alerts but also with regard to the number of alerts in a molecule. The result of the calculation is the normalized hazard index that represents a quantitative estimate of asthmagenic potential of the substance. The results of this approach, at least in respect of ethylenediamine derivatives, are not in accordance with the facts and implemented classification. For example, ethylenediamine and piperazine are evaluated as negative herein, although they are proven respiratory sensitisers.

Another SAR model attempts to determine the potential of substances to form a covalent bond to an amino group of the proteins[10,11], i.e. the first step in triggering the allergic reactions. It is assumed that the molecule should be an electrophile to be able to react with nucleophilic centres of amino acids. On the other hand, ethylenediamine is not electrophile but the authors expect its metabolisation into glyoxal by oxidative deamination[10]. The resulting aldehyde can already react with a protein amino group to form a Schiff base. This mechanism of action may work for some aliphatic amines or diamines but in the case of the evaluated substance and structurally similar amines, such method of metabolisation was not confirmed.

Comparison of several SAR models has been made in the article Dik et al.[9] The authors concluded that no single SAR method is sufficiently reliable to determine respiratory sensitisers. They recommend using a tiered approach consisting of the sequential use of several different SAR models.

The Direct Peptide Reactivity Assay (DPRA) is trying to distinguish skin sensitisers from respiratory sensitisers on the basis of different reactivity of the test substance with two different peptides containing, respectively, lysine and cysteine amino acids[12,13, 23]. Due to the nucleophilic nature of the evaluated substance (and, in general, aliphatic amines), this assay cannot be directly applied to it without metabolic or abiotic activation to form protein reactive intermediates[12].

Several decision trees provide a useful tool for assessing respiratory sensitisation and evaluating the potential for classification[24,25,26]. The advantage of this approach is the stepwise evaluation of available information in closed sets. Use of these decision trees leads in one case to decision on non-classification as respiratory sensitiser[24], in other cases to subsequent consideration[25,26] (exposition routes, risk assessment etc.).

An important question is whether the 1,2-ethylenediamine group can be considered a structural alert for respiratory sensitisation. Ethylenediamine and piperazine, two basic members of the homologous series, are proven respiratory sensitisers. Higher members of the homologous series are not classified as respiratory sensitisers, although they are harmonised classified as skin sensitisers. Diethylenetriamine has been registered according to the Regulation REACH and part of its registration dossier is cytokine profile assay, the result of which is negative. It is the fact that diethylenetriamine and higher homologues of 1,2-ethylenediamine are sometimes considered to be suspected respiratory sensitisers (for example[9,11]) but this statement has not yet been credibly proven. For example, QSAR Toolbox (version 4.2) does not consider ethylamino group (or diethylamino group) as a structural alert for respiratory sensitisation.

In conclusion: Basic ethyleneamines (1,2-ethanediamine and piperazine) are classified as respiratory sensitisers. On the other hand, for the higher members of the homologous series, no conclusive and unambiguous evidence for this classification is available. Other supporting evidence for the classification was not found using literature search, *in chemico* methods or (Q)SAR. Currently, no test can be proposed that would unambiguously or at least very likely decide whether the evaluated substance has respiratory sensitising properties.

Justification for classification or non-classification

An increased frequency of respiratory distress in workers was not observed in production or processing of polyethylene polyamine, pentaethylenehexamine fraction, nor is there enough conclusive evidence to this effect. Based on current knowledge and pursuant to the rules for classification under CLP, the eMSCA concludes that the polyethylene polyamine, pentaethylenehexamine fraction **cannot be classified** as a respiratory sensitiser.

7.9.4. Repeated dose toxicity

Not relevant for this evaluation.

7.9.5. Mutagenicity

Not relevant for this evaluation.

7.9.6. Carcinogenicity

Not relevant for this evaluation.

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

Not relevant for this evaluation.

7.9.8. Hazard assessment of physico-chemical properties

Not relevant for this evaluation.

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

The eMSCA concluded that DNEL(s) provided by the registrants for the exposure assessment are acceptable. In addition, for substance evaluation purposes the DNEL for dermal long-term systemic effects was used for exposure assessment. Its value was derived from oral exposure DNEL via route-to-route extrapolation according to ECHA guidance (Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health, ECHA, 2012).

DNEL (dermal) = 1.667 mg/kg/day

$LOAEL_{corrected\ dermal} = LOAEL_{oral} \times ABS_{rat,oral} / ABS_{human,dermal}$
$ABS_{rat,oral}$ = 20 % (from toxicokinetic data)
$ABS_{human,dermal}$ = 5 % (estimate based on toxicokinetic behaviour)
$LOAEL_{oral}$ = 50 mg/kg/day (rat, oral)

AF (interspecies) = 4 (allometric scalling)
AF (dose-response relationship) = 3 (starting value is LOAEL)
AF (duration) = 2 (sub-chronic to chronic exposure)
AF (intraspecies) = 5 (for workers)

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

The eMSCA does not propose classification of polyethylene polyamine, pentaethylenehexamine fraction as a respiratory sensitiser because the classification criteria are not met.

7.10. Assessment of endocrine disrupting (ED) properties

Not in the scope of this evaluation.

7.11. PBT and VPVB assessment

Not in the scope of this evaluation.

7.12. Exposure assessment

The eMSCA has carried out an exposure assessment based on the information provided in the registration dossier and agrees with the Registrants' assessment and concludes that there is no concern for occupational exposure.

The exposure scenarios are designed for manufacture, formulation and industrial use; consumer exposure is not expected. Polyethylene polyamine, pentaethylenehexamine fraction is classified as Acute Tox. 4 (H302+H312), Skin Corr. 1B (H314), Eye Damage 1 (H318), Skin Sens. 1 (H317), STOT RE 2 (H373 lungs, oral), Aquatic Acute 1 (H400), Aquatic Chronic 1 (H410). The exposure assessment is focused on the effects on human health. Dermal and inhalation exposure is anticipated. Workers exposure can be effectively reduced via operational conditions (ventilation, closed processes, etc.) or using personal protection equipment (goggles, gloves, etc.). The long-term systemic effects are quantified, short-term and acute effects are evaluated only qualitatively as DNELs could not be determined.

Exposure scenarios were processed using CHESAR software (version 3.4.1). The structure of exposure scenarios including descriptors was taken from registration dossier and CSR for polyethylene polyamine, pentaethylenehexamine fraction.

Human exposure estimates are based on ECETOC TRA3; environmental exposure estimates are based on EUSES (version 2.1.2).

Polyethylene polyamine, pentaethylenehexamine fraction is negligible volatile liquid, excellently soluble in water.

7.12.1. Human health

7.12.1.1. Worker

Industrial workers come into contact with polyethylene polyamine, pentaethylenehexamine fraction in the manufacture, formulation and industrial use of the substance. Dermal and inhalation exposure is anticipated.

Workers who are exposed to polyethylene polyamine, pentaethylenehexamine fraction should wear chemically resistant gloves (tested to EN374) and use suitable eye protection due to corrosive properties of the substance. The workplace should be equipped with local exhaust ventilation or workers should use a respirator with APF of 10 for respiratory protection. Assumes a good basic standard of occupational hygiene is implemented. Employees should pass through specific training on safe working with respect to the substance hazards.

7.12.1.2. Consumer

Consumer exposure is not expected.

7.12.2. Environment

Not in the scope of this evaluation.

7.13. Risk characterisation

Human Health

Workers

The risks from exposure scenarios can be effectively reduced via operational conditions (ventilation, closed processes, etc.) or using standard personal protective equipment (goggles, gloves, etc.). The highest exposure values were estimated for workers for industrial spraying (PROC 7). In this exposure scenario, the workplace must be equipped with effective local exhaust ventilation and workers must use a respirator with APF of 20 for respiratory protection. It is recommended to use full-body protective working clothes to protect the body surface. Duration of activity must be limited in order to reduce the exposure of workers.

Nevertheless, the level of exposure is at an acceptable level. In eMSCA's opinion no additional risk management measures are required at the moment.

Consumers

Consumer exposure is not expected.

Indirect exposure of humans via the environment

For all exposure scenarios and for all eligible routes of exposure including combined exposure, RCRs are below 1.

Environment

Not relevant for this evaluation.

7.14. References

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7.15. Abbreviations

CAS	Chemical Abstract Services
CLP	Regulation (EC) No. 1272/2008
CSR	chemical safety report
DNEL	derived no effect level
eMSCA	evaluating Member State Competent Authority
ES	exposure scenario
IFN	interferon
IL	interleukin
IUPAC	International Union of Pure and Applied Chemistry
LMW	low molecular weight (substaces)
LOAEL	the lowest observed adverse effect level
PBT	persistent, bioaccumulative and toxic (substances)
REACH	Regulation (EC) No. 1907/2006
QSAR	quantitative structure–activity relationship
SAR	structure–activity relationship
SVHC	substances of very high concern
UVCB	unknown or variable composition (substances)
vPvB	very persistent and very bioaccumulative (substances)