SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

S-(tricyclo[5.2.1.0^{2,6}]deca-3-en-8(or 9)-yl) O-(isopropyl or isobutyl or 2-ethylhexyl) O-(isopropyl or isobutyl or 2-ethylhexyl) phosphorodithioate

aka "Hi-TEC 511"

EC No 401-850-9

CAS RN 255881-94-8

Evaluating Member State : Belgium

Dated: 02 September 2021

Evaluating Member State Competent Authority

Belgian CA

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Year of evaluation in CoRAP : 2014

Before concluding the substance evaluation a Decision to request further information was issued on 19 December 2016.

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

Table of Contents

1. CONCERN(S) SUBJECT TO EVALUATION 7
2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION 7
3. CONCLUSION OF SUBSTANCE EVALUATION 7
4. FOLLOW-UP AT EU LEVEL 7
4.1. Need for follow-up regulatory action at EU level 7
4.1.1. Harmonised Classification and Labelling 7
4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation) 8
4.1.3. Restriction 8
4.1.4. Other EU-wide regulatory risk management measures 8
5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL 8
5.1. No need for regulatory follow-up at EU level 8
5.2. Other actions 8
6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS 8
Part B. SUBSTANCE EVALUATION 9
7. EVALUATION REPORT 9
7.1. Overview of the substance evaluation performed 9
7.2. Procedure 9
7.3. Identity of the substance 10
7.4. Physico-chemical properties 11
7.5. Manufacture and uses 13
7.5.1. Quantities 13
7.5.2. Overview of uses 13
7.6. Classification and Labelling 13
7.6.1. Harmonised Classification (Annex VI of CLP) 13
7.6.2. Self-classification 14
7.7. Environmental fate properties 14
7.7.1. Degradation 14
7.7.2. Environmental distribution 21
7.7.3. Bioaccumulation 21
7.8. Environmental hazard assessment 23
7.8.1. Aquatic compartment (including sediment) 23
7.8.2. Terrestrial compartment 25
7.8.3. Microbiological activity in sewage treatment systems 25
7.8.4. PNEC derivation and other hazard conclusions 25
7.8.5. Conclusions for classification and labelling 26
7.9. Human Health hazard assessment 26
7.10. Assessment of endocrine disrupting (ED) properties 26
7.11. PBT and vPvB assessment 26
7.11.1. Persistence 26

7.11.2. Bioaccumulation 26
7.11.3. Toxicity 27
7.11.4. Overall conclusion 27
7.12. Exposure assessment 27
7.13. Risk characterisation.....27
7.14. References 27
7.15. Abbreviations.....27

Part A. CONCLUSION

1. CONCERN(S) SUBJECT TO EVALUATION

S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-(isopropyl or isobutyl or 2-ethylhexyl) O-(isopropyl or isobutyl or 2-ethylhexyl) phosphorodithioate, also known under its trade name Hi-TEC 511, was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT / vPvB properties;
- Exposure of the environment;
- Wide dispersive use.

No additional concerns were identified during this evaluation. The assessment under substance evaluation was targeted on the environmental and ecotoxicological properties of the substance.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Not applicable.

3. CONCLUSION OF SUBSTANCE EVALUATION

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

Table 1: Conclusion of Substance Evaluation

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

4. FOLLOW-UP AT EU LEVEL

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

4.1.1. Harmonised Classification and Labelling

Currently the Substance is listed in annex VI of the CLP Regulation and is classified as Aquatic Acute 1 (H400) and Aquatic Chronic 1 (H410).

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

The (v)P, B and T criteria according to annex XIII or REACH are considered fulfilled. The eMSCA plans to proceed with the identification of the Substance as an SVHC according to article 57(d) of REACH.

4.1.3. Restriction

Not applicable.

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

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

Not applicable, see section 4.

5.2. Other actions

Not applicable, see section 4.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS

Indication of a tentative plan is not a formal commitment by the evaluating Member State.

A commitment to prepare a REACH Annex XV (SVHC, restrictions) and/or CLP Annex VI dossier is to be made via the Registry of Intentions.

Table 2: Tentative plan for follow-up actions

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**
RMOA	March 2021	BE CA
SVHC identification	August 2021	BE CA

Part B. SUBSTANCE EVALUATION

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

The Substance, S-(tricyclo[5.2.1.02,6]deca-3-en-8(or 9)-yl) O-(isopropyl or isobutyl or 2-ethylhexyl) O-(isopropyl or isobutyl or 2-ethylhexyl) phosphorodithioate, also known under its trade name Hi-TEC 511, was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT / vPvB properties;
- Exposure of the environment;
- Wide dispersive use.

No additional concerns were identified during the evaluation. The assessment under substance evaluation was targeted on the environmental and ecotoxicological properties of the substance.

Table 3: Evaluated endpoints

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
PBT / vPvB properties	Confirmed: Based on the currently available information, it is concluded that the group of the ip-ip constituents of the Substance meet the PBT criteria as set out in annex XIII of REACH. These constituents form a relevant part (>0,1%) of the Substance, which is as a whole is identified as a PBT substance.
Exposure of the environment Wide dispersive use	Confirmed: Considering the uses, exposure of the environment cannot be avoided, and because of the high number of point sources the use is considered as wide dispersive.

7.2. Procedure

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to suspected PBT/vPvB, exposure of the environment and wide dispersive use, the Substance (EC No 401-850-9) was included in the Community rolling action plan (CoRAP) for substance evaluation pursuant to Article 44(2) of REACH, and was foreseen to be evaluated in 2014. The updated CoRAP was published on the ECHA website on 26 March 2014. The Competent Authority of Belgium was appointed to carry out the evaluation.

Pursuant to Article 45(4) of REACH, the Competent Authority of Belgium has initiated the substance evaluation for the Substance, based on registration(s) submitted by the Registrant(s) and other relevant and available information.

The evaluating MSCA considered that further information was required to clarify the suspected PBT/vPvB concern. Therefore, it prepared a draft decision pursuant to Article 46(1) of REACH to request further information. It submitted a draft decision to ECHA on 19 March 2015.

A unanimous agreement of the Member State Committee on the draft decision was reached on 29 August 2016 in a written procedure. ECHA notified the Registrant(s) of the decision pursuant to Article 51(6) of REACH on 19 December 2016 requesting two studies on the

S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isopropyl O'-isopropyl phosphorodithioate constituents: 1. a water solubility study (EU A.6) and 2. an aerobic mineralisation study in surface water (EU C.25 at 12 °C). Moreover, it was requested that a soil simulation study was to be conducted if the aerobic mineralisation study in surface water could not be conducted in the requested manner.

In accordance with Article 46(2) of REACH the Registrant(s) updated their dossier on 25 March 2019 with the requested water solubility study and an aerobic mineralisation study in surface water. In accordance with Article 46(3) of REACH, the evaluating Member State started the second round of the evaluation without undue delay.

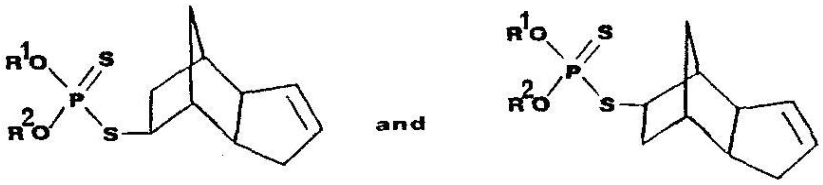
In accordance with Article 46(4) of REACH, the evaluating Member State finished its evaluation activities within 12 months of the information being submitted.

7.3. Identity of the substance

Table 4: Substance identity

SUBSTANCE IDENTITY	
Public name :	S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-(isopropyl or isobutyl or 2-ethylhexyl) O-(isopropyl or isobutyl or 2-ethylhexyl) phosphorodithioate
EC number :	401-850-9
CAS number :	255881-94-8
Index number in Annex VI of the CLP Regulation :	015-146-00-0
Molecular formula :	The various constituents have the following molecular formula: - ip-ip constituents : $C_{16}H_{27}O_2PS_2$ - ip-ib constituents : $C_{17}H_{29}O_2PS_2$ - ib-ib constituents : $C_{18}H_{31}O_2PS_2$ - ip-eh constituents : $C_{21}H_{37}O_2PS_2$ - ib-eh constituents : $C_{22}H_{39}O_2PS_2$ - eh-eh constituents : $C_{26}H_{47}O_2PS_2$
Molecular weight range :	346.5 – 486.8 g/mol
Synonyms :	Phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and isobutyl and isopropyl) S-[3a,4,5,6,7,7a-hexahydro-4,7-methano-1H-inden-5(or 6)-yl]esters Hi-TEC 511 Hi-TEC 511 Performance additive X-4261

Structural formula :



where R = isopropyl/isobutyl/2-ethylhexyl

Multiconstituent/UVCB substance/others

Table 5: Overview of constituents

See confidential annex

Constituent			
Constituents	**Typical concentration**	**Concentration range**	**Remarks**
S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isopropyl O'-isopropyl phosphorodithioate	confidential	confidential	ip-ip constituents
S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isopropyl O'-isobutyl phosphorodithioate	confidential	confidential	ip-ib constituents
S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isobutyl O'-isobutyl phosphorodithioate	confidential	confidential	ib-ib constituents
S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isopropyl O'-2-ethylhexyl phosphorodithioate	confidential	confidential	ip-eh constituents
S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isobutyl O'-2-ethylhexyl phosphorodithioate	confidential	confidential	ib-eh constituents
S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-2-ethylhexyl O'-2-ethylhexyl phosphorodithioate	confidential	confidential	eh-eh constituents

7.4. Physico-chemical properties

In the registration dossier(s) the following values are presented.

Table 6: Summary of physicochemical properties

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES		
Property	**Value**	**Remarks**
Physical state at 20°C and 101.3 kPa	Pale yellow liquid	
melting point	Indeterminable	method : OECD TG 102
boiling point	not determined	
density @ 20°C	1.075 g/cm^3	method : OECD TG 109
vapour pressure	11 Pa @ 20°C 16 Pa @ 25°C	method : OECD TG 104 values in registration dossier(s), considered to be unreliable
water solubility @ 20°C	1.4 mg/L	method : OECD TG 105 value in registration dossier(s), considered to be unreliable
partition coefficient n-octanol/water (log K_{ow})	>6.6	ISO HPLC method value in registration dossiers(s)
surface tension @ 20°C	68 mN/m	method : OECD TG 115
flash point	102 °C	method : EU A.9
self ignition temperature	450 °C	method : EU A.15

The eMSCA considers that the values given for crucial properties like the vapour pressure and the water solubility do not reflect at all the real values for the relevant constituents of the Substance. Indeed, the values presented in the registration dossier(s) differ by 3 to 7 orders of magnitude compared to the EPI Suite estimated values. The result of the water solubility study that was required in the SEv decision on the most soluble constituents (ip-ip constituents show a water solubility of 50 µg/L) confirms that the QSAR values are much more reliable.

Table 7: EPI Suite estimations

EPI SUITE ESTIMATED PHYSICOCHEMICAL PROPERTIES FOR SPECIFIC CONSTITUENTS						
Property	**ip-ip**	**ip-ib**	**ib-ib**	**ip-eh**	**ib-eh**	**eh-eh**
molecular weight (g/mole)	346	361	375	417	431	487
vapour pressure (mPa)	3.4	1.6	0.7	0.05	0.019	0.003
water solubility (µg/L) (WATERNT)	17	5	1.5	0.04	0.012	0.00035
Water solubility (µg/L) (WSKOW)	40	13	3.9	0.12	0.037	0.00049
Henry's law constant (Pa.m^3/mol)	19	26	34	79	105	327
log Kow (KOWWIN)	6.1	6.6	7.1	8.6	9.0	11.0
log Koa (KOAWIN)	8.2	8.6	9.0	10.1	10.4	11.9
log Koc (MCI method)	4.6	4.9	5.1	5.9	6.2	7.3

7.5. Manufacture and uses

7.5.1. Quantities

Table 8: Quantities *

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

*Dissemination website checked on 6 April 2021

7.5.2. Overview of uses

Table 9: Overview of uses

USES	Use(s)
Uses as intermediate	/
Formulation	– Industrial formulation of lubricant additives, lubricants and greases ○ Formulation into mixture
Uses at industrial sites	– General industrial use of lubricants and greases in vehicles or machinery ○ Use of non-reactive processing aid at industrial site (no inclusion into or onto article) ○ Use of functional fluid at industrial site – Industrial use of lubricants and greases in open systems ○ Use of non-reactive processing aid at industrial site (no inclusion into or onto article) – Industrial use of lubricants and greases in high energy open processes ○ Use of non-reactive processing aid at industrial site (no inclusion into or onto article)
Uses by professional workers	– Professional use of lubricants and greases in open systems ○ Widespread use of non-reactive processing aid (no inclusion into or onto article, indoor) ○ Widespread use of non-reactive processing aid (no inclusion into or onto article, outdoor) – General professional use of lubricants and greases in vehicles or machinery ○ Widespread use of functional fluid (indoor) ○ Widespread use of functional fluid (outdoor)
Consumer Uses	/
Article service life	/

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

The Substance is listed in annex VI of the CLP Regulation under entry 015-146-00-0. The harmonised classification is Aquatic Acute 1, H400 and Aquatic Chronic 1, H410.

Table 10: Harmonised Classification

HARMONISED CLASSIFICATION ACCORDING TO ANNEX VI OF CLP REGULATION (REGULATION (EC) 1272/2008)							
Index No	**International Chemical Identification**	**EC No**	**CAS No**	**Classification**		**Spec. Conc. Limits, M-factors**	**Notes**
				Hazard Class and Category Code(s)	**Hazard statement code(s)**		
015-146-00-0	*S*-(tricyclo(5.2.1.$0^{2,6}$)deca-3-en-8(or 9)-yl *O*-(isopropyl or isobutyl or 2-ethylhexyl) *O*-(isopropyl or isobutyl or 2-ethylhexyl) phosphorodithioate	401-850-9	255881-94-8	Aquatic Acute 1 Aquatic Chronic 1	H400 H410		

7.6.2. Self-classification

The self-classification in the registration dossier(s) is the same as the harmonised classification published in annex VI of the CLP Regulation.

7.7. Environmental fate properties

7.7.1. Degradation

7.7.1.1. Abiotic degradation

Hydrolysis

A preliminary test to assess the hydrolysis potential of the substance according to OECD Guideline 111 is available. At pH 9 the half-life for hydrolysis is greater than 1 year.

The definitive tests carried out under GLP conditions, at pH 4 and 7 and at a temperature ranging from 50 to 70 °C, showed that the test material is hydrolytically stable at all studied pH values. Estimated half-lives at pH 4 for tests at 50-70 °C range from 33 to 243 days and at pH 7 measured values for the same temperature interval range from 107 to 326 days. The substance is also stable at the physiologically significant pH value of 1.2 at a temperature of 37 °C, conditions considered in an additional test. It was not possible to derive a reliable hydrolysis rate constant from the trials due to divergent experimental results. Nevertheless, from these results, it can be concluded that it is unlikely that the substance will hydrolyse to a relevant extent; this study indicates that half-lives at 12 °C and at various pH values are in the order of magnitude of 1 year.

This conclusion is supported by the observation that for none of the zinc salts of O,O'-dialkyldithiophosphates that are registered under REACH, hydrolysis is mentioned as a potentially relevant degradation process under environmental conditions.

Phototransformation & photolysis

No experimental data regarding these potential degradation processes are presented in the registration dossier. Considering the very low vapour pressure of the substance, phototransformation or photolysis are not considered as relevant degradation pathways.

Using the QSAR program AOP v1.92 from EPI Suite an overall hydroxyl radicals reaction rate constant of 2.36 x 10^{-10} cm^3/molecule.sec is calculated for the ip-ip constituents resulting in an estimated half-life in air of 0.544 hours.

7.7.1.2. Biotic degradation

Estimated data

The degradation pattern of the constituents of the Substance can be evaluated by various QSAR estimation programs. It should be noted that all these estimation methods predict whether organic compounds can be classified as readily biodegradable or not. They do not predict half-lives in environmental compartments and so they do not provide a direct method to assess whether the persistence criterion is met or not.

A first model and one that is also used by the registrant(s) is the Catalogic 301C model developed by the Laboratory of Mathematical Chemistry in Bulgaria. This QSAR predicts that the primary degradation of the constituents of the Substance occurs by a chemical reaction called oxidative desulfuration, i.e. the substitution of the double bonded sulfur atom with an oxygen atom. Catalogic modelling shows that all 12 constituents of the Substance can undergo this type of reaction with a predicted half-life of 1 to 2 days. On the contrary, further biodegradation of the formed monothiophosphates is estimated to be quite slow and these degradation products can be persistent. This conclusion remains to a certain extent uncertain as the rate of oxidative desulfuration is not well established and it is not clear whether the predicted degradation products could react further. (e.g. by hydrolysis or ring opening).

It is noted that the Catalogic model consists of a metabolism simulator and an endpoint model. Microbial metabolism is simulated by the rule-based approach. However, a good understanding on how the prediction of oxidative desulfurisation is established is not included in the QSAR Model Reporting Format, and it is not clear on which literature and what rules the QSAR prediction is based. This makes it difficult to evaluate the reliability of the prediction for this specific case.

Further, it should be noted that none of the twelve constituents the Substance are fully in the applicability domain of the Catalogic model because they are out of the structural domain due to the fact that they contain 16 to 24 % of unknown fragments, i.e. fragments not recognised by the model. This observation adds more uncertainty to the prediction presented here.

Another useful source of information on the potential metabolic pathways of the constituents of Hi-TEC 511 is the EAWAG-BBD Pathway Prediction System (formally from the University of Minnesota). This program estimates that three types of biodegradation can be relevant for the various constituents, namely 1) bt0103, which is the oxidative desulfurization of the dithiophosphate functionality, 2) bt0241, which is the hydroxylation of a tertiary carbon atom and 3) bt0242, which is the hydroxylation of a secondary carbon atom. It should also be noted that the probability that these biotransformation reactions takes place is categorized by the program as "neutral" and not as (very) likely. That means that according to this estimation program the likelihood that these reactions occur in aerobic conditions is rather low.

Another QSAR method and one that, in contrast to Catalogic, is publicly available is Biowin v.4.10 which is integrated in EPI Suite. Biowin estimates aerobic and anaerobic biodegradability of organic chemicals using seven different submodels. As indicated in the Reach Guidance chapter 11 the results of three submodels can be used to screen the potential of biodegradation. Based on the combination of the results for Biowin 2 (all

constituents show a value of 1.00) and Biowin 3 (values ranging from 2.53 to 2.87), all the constituents would be readily biodegradable. In contrast with this result, the combination of Biowin 6 (values varying between 0.0017 and 0.02) and Biowin 3 (values ranging from 2.53 to 2.87) indicates that none of the constituents do readily biodegrade and are thus potentially persistent. Further, it is observed that the S=P functionality is not included in the fragments in Biowin models 2, 3 and 6. Considering the conflicting predictions with Biowin, and taking into account that a crucial functionality is not recognized as a fragment, the eMSCA is of the opinion that it is not possible to come to a definitive conclusion in this way regarding the biodegradability of the constituents of the Substance.

A third method that evaluates ready biodegradability of substances is the VEGA model. The VEGA model reports that only moderately similar compounds with known experimental values have been found in the training set. Some atom-centered fragments of the Substance's constituents have not been found in the compounds of the training set or are rare fragments. In the VEGA dataset two trialkyldithiophosphates are found (substances with CAS numbers 121-75-5 & 2597-03-7). Based on these results, it can be concluded that all constituents of the Substance are likely non-biodegradable.

Based on the above analysis, the eMSCA is of the opinion that QSAR data are not sufficiently reliable to conclude on the potential persistence of the Substance and that other information must be considered.

Read-across

In theory, a read-across approach is a potential method to assess the biodegradation behaviour of the Substance. It should be noted that a series of coordination compounds that contain zinc as the central atom belong to the class of dithiophosphates. The substance with public name phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and iso-bu and iso-pr) esters, zinc salts (EC number 288-917-4) is registered in the >1000 t/y band and can be considered as an analogous substance. Experimental studies relating to the biodegradation potential of this substance could not be found. For a similar substance in this class of compounds, i.e. phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and iso-Pr) esters, zinc salts (EC number 283-392-8), a ready test according to OECD TG 301B (CO_2 evolution test) is available. After 28 days 1.5 % degradation is observed, clearly indicating that this type of compounds are not readily biodegradable. In the Chemical Safety Reports of both substances it is stated that the substance is likely to meet the P criterion in order to fulfil its technical specifications.

The OECD toolbox was used to identify dithiophosphates that do not contain a central zinc atom. More specifically the "protein binding by OASIS profile" is used to search for these molecules. The following three analogous substances including their experimental biodegradation results as obtained in an OECD TG 301C study are found in the OECD toolbox: CAS RN 121-75-5, 22 % degradation after 28 days; CAS RN 2597-03-7, 2 % after 28 days; CAS RN 60-51-5, 0 % after 28 days.

Based on the read-across to these substances, it is noted that the various constituents of the Substance are not readily biodegradable. It can be argued that some methods of enhancement should have been used in the test design in order to improve bioavailability. However, even in this case, it is still unclear whether this biodegradation pathway is likely to happen.

Data from biodegradation screening studies

Several tests that screen the biodegradation potential of the Substance are available. In some of these tests, techniques that enhance the bioavailability are not utilized; one test dating from 2011 was carried out with the use of enhancement techniques.

In two older biodegradation screening tests the ready biodegradability of the Substance was examined. In 1987 a closed bottle test was performed according to OECD TG 301D and in 1996 a modified MITI test was carried out according to OECD TG 301C. Both studies are performed at test substance concentrations substantially above the water solubility. Maximum 4 % of the substance is biodegraded after 28 days in both tests. As the pass level for ready biodegradation is not reached, based on these tests the Substance is considered to be not readily biodegradable. However, because of the high test substance concentrations, these studies are considered to be of low reliability.

In 2011 Roberts and Daniel conducted an enhanced biodegradability study using the modified OECD TG 301D. The used enhancements included the use of silicone oil as a solvent and Synperonic PE 105 as a surfactant. The modifications also included increasing the test volume and extending the test duration up to 63 days. The study used a test substance concentration of 1 mg/L and an activated sludge concentration of 2 mg/L. A positive (sodium benzoate) and a negative (2,4-di-tert-butylphenol) control substance were also added to the test systems. The level of biodegradation is measured as O_2 consumption. After 28 days 12% degradation is found after direct addition of the Substance, 7 % degradation is found when added in combination with silicone oil and 41% degradation is found when added with silicone oil and surfactant. A maximum degradation level of 46% is found after 35 days and at the end of the test after 63 days degradation amounted to 35%. Unfortunately, the negative control 2,4-di-tert-butylphenol when added in combination with silicone oil and surfactant also showed substantial O_2 consumption (up to 30%!). Therefore, this study probably overestimates the real degradation of the Substance.

As the pass level in these screening biodegradation tests is never reached, independent of the fact whether enhancements are applied or not, the eMSCA concludes that the substance is not readily biodegradable.

Data from a simulation study in surface water

An aerobic mineralisation study in surface water according to OECD TG 309 is available with the isopropyl-isopropyl constituents (ip-ip) of the Substance.

In a preliminary study the water solubility of the ip-ip constiteunts was verified. This study demonstrated that the actual solubility of the ip-ip constituents is 50 µg/L, while the limit of quantification (LoQ) is found to be 0.5 µg/L. As the LoQ is about 2 orders of magnitude lower than the water solubility, a simulation study in surface water can be monitored using test item concentrations below the water solubility. So reduced bioavailability of the test substance can be avoided in this simulation test does not jeopardize the reliability or the relevance of the results.

Main study according to GLP

The main GLP study for aerobic mineralization in surface water was conducted in 2018 with non-adapted surface water over a period of 91 days according to OECD TG 309. Besides the main study three supporting non-GLP tests were performed in order to be able to come to a more reliable interpretation of the results of the main study. It is noted that the main study is executed with non-radiolabelled test item which hampered the establishment of a mass balance. The eMSCA carefully examined the data resulting from specific chemical analysis of the parent compound and its metabolite(s) and has concluded that under the circumstances of this study the ip-ip constituents of the Substance do not biodegrade to a relevant extent.

Summary of the relevant characteristics of the main study:

- test guideline: OECD TG 309 with some adaptations
- study type: laboratory shake flask test determining aerobic primary degradation
- mineralization is not monitored

- surface water from the river Örtze (Saxony, Germany) @ 15.7 °C
- surface water characteristics: pH = 7.23, DOC = 4.07 mg/L, TIC = 8.01 mg/L
- colony forming units: 8.85 x 10^7 CFU/L
- handling: suspended coarse particles were removed prior to use by sieving
- test duration: 91 days
- temperature: 12 °C ± 2 °C
- test item: ip-ip constituents of the Substance
- test item concentrations: 10 µg/L and 50 µg/L
- reference item: sodium benzoate
- reference item concentration: 18 mg/L (while 10 µg/L is advised in § 31 of TG 309)
- sterile control: performed with surface water that is autoclaved twice
- blank control: performed with surface water without test and/or reference item
- test volumes: 100 mL in 250 mL headspace flasks
- oxygen concentration during study: 9.3 – 11.2 mg/L
- pH during study: 6.82 – 7.28
- sampling schedule: day 0, 1, 3, 5, 7, 14, 21, 31, 91
- analytical evaluation with UPLC-HRMS

The degradation of the test item is monitored by specific chemical analysis of the parent compound and its potential metabolites. Because radiolabelling is not applied it is not possible to establish the mass balance in a reliable way.

At the end of the study at day 91 the concentration of the test item has diminished substantially: at a test item concentration of 10 µg/L the residual percentage declined to 14% and at 50 µg/L only 5% of the test item is retrieved in the reaction mixture. At the same time it is observed that only 1 metabolite is formed and this only in a very minute fraction, i.e. never more than 1.5% compared with the parent compound. The metabolite is identified as the corresponding phosphorothioate, i.e. S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O,O'-diisopropyl phosphorothioate. This observation clearly demonstrates that the disappearance of the test item in this study is not caused by (bio)degradation but nearly completely by dissipation out of the reaction mixture. As dissipation is taking place to a great extent a degradation rate cannot be determined in a direct manner. However, in the study also sterile controls are carried out and as these sterile controls are executed in the same manner as the replicates with viable microorganisms, it is appropriate to determine a biodegradation rate based on a comparison between viable and sterile set ups.

Unfortunately, the sterile controls were only sampled on day 31 and 91 and so only the results of these sampling points can be used. The percentages residual test item were as follows (cfr. table 15, p. 39) :

- @ 10 µg/L viable experiment: 31 d = 29%, 91 d = 14%
- @ 10 µg/L sterile experiment: 31 d = 32%, 91 d = 10%
- @ 50 µg/L viable experiment: 31 d = 35%, 91 d = 5%
- @ 50 µg/L sterile experiment: 31 d = 31%, 91 d = 6%

Comparing the viable with the sterile experiment at the same sampling day and the same concentrations one can see qualitatively that biodegradation is hardly taking place if not at all:

- @ 10 µg/L, 31 d : 3% extra disappearance
- @ 10 µg/L, 91 d : -4%, no extra disappearance
- @ 50 µg/L, 31 d : -4%, no extra disappearance
- @ 50 µg/L, 91 d : 1% extra disappearance

Qualitatively, it is reasonable to conclude that in this experiment biodegradation is hardly taking place. Transforming this qualitative observation in a quantified parameter cannot be done in the usual way as the mass balance is not at all fulfilled. In fact, two processes contribute simultaneously to the disappearance of the test item, i.e. dissipation out of the testing system and biodegradation. It is clear that dissipation is considerably faster than biodegradation. As we are dealing here with a kinetically biphasic system and we only dispose of a few measured data points, one can only approximatively calculate a half-life for biodegradation. In the eMSCA's view the most reliable approach to estimate a half-life is to consider the relative amounts of test item that remain in the viable and the sterile experiments. Proceeding in this way and looking at the data point with the highest extra disappearance (i.e. experiment at 10 µg/L and 31 days), a biodegradation half-life of 218 days is obtained (9.38 % biodegradation in 31 days). It should be noted that this estimation is based on the least critical data points as using the other data points would only lead to still greater half-life estimations. Because this estimated half-life of 218 days largely exceeds the vP threshold of 60 days, the eMSCA has concluded that based on this study the ip-ip constituents of the Substance meet the vP criterion in fresh water.

Another relevant issue in the interpretation of this simulation study, is the question whether the study is valid or not. According to the registrant the validity criteria relating to the reference substance sodium benzoate that is used as functional control are not fulfilled. Consequently, the activity of the inoculum used in the main study would not be sufficient, and for that reason the study would be invalid and cannot be used to assess the persistence of the Substance.

The eMSCA is of the opinion that the argumentation regarding the non-validity of the test can be further discussed. It is correct that the OECD TG 309, paragraph 51, stipulates that if the reference substance is not degraded within the expected time interval (usually less than 14 days for sodium benzoate), the validity and the relevance of the test must be further verified. In the same paragraph the guideline mentions that in surface waters usually employed the degradation rate constant for the reference substance at 20°C is on average 0.8 d^{-1} (half-life = ± 0.9 d). The guideline also explicitly states that the reference substance concentration should be 10 µg/L (paragraph 31). It is obvious that the advised values for the reference item concentration and its degradation rate constant are linked to each other. In this study the sodium benzoate concentration is 18 mg/L (i.e. 1800 (!) times higher than the concentration advised in the guideline) and so a direct comparison with the validity criteria expressed in a relative manner (e.g. >60% degradation within 14 days) is not appropriate. The relative degradation rate of the reference item is lower than expected, not because the inoculum is insufficiently active but because the inoculum is overloaded.

Another way to assess the activity of the inoculum is to consider the measured degradation rate in absolute terms and not in relative terms. Although it is not the standard approach it provides a reasonable indication of the activity of the inoculum used in the test. As mentioned in the above paragraph the inoculum in a simulation test is considered to be sufficiently active if the mineralization half-life of the reference substance is 0.9 days (at 10 µg/L). This means that on average viable microbial communities in a simulation test mineralise the reference substance at a rate of ca. 7.7 µg/L/d. In the main study one measures 8% CO_2 formation after 21 days and 59% after 89 days (without solvent). Based on the value found after 21 days, one can calculate that on average the mineralisation rate is 69 µg/L/d (18000 µg/L * 0.08/21 d). Based on the CO_2 formation after 89 days the mineralisation rate becomes 119 µg/L/d (18000 µg/L * 0.59/89 d). It is correct that the influence of the growth of the microbial population is difficult to take into account, but the fact that the absolute mineralisation rates found in this study are substantially higher than the rates found in studies performed with standard reference substance levels indicates that the inoculum in this study actually was viable.

Thus, in the view of the eMSCA the main study indicates 218 days as a relevant and reliable estimation of the biodegradation half-life of the ip-ip constituents of the Substance.

Non-GLP complementary simulation test

Because the registrant was of the opinion that the main study was not valid and could not be used in the persistence assessment of the Substance, a complementary study was executed shortly after the main simulation study. This study is equivalent to a simulation study but was not carried out according to the GLP protocol.

The relevant characteristics of the complementary study are summarized as follows:
- test type: simulation study in surface water
- GLP protocol: no
- mineralisation is not monitored
- surface water from the river Leine (Germany)
- surface water characteristics: "more" undissolved organic matter than in Örtze water
- test duration: 69 days
- temperature: 12 °C
- test item: ip-ip constituents of the Substance
- test item concentrations: 10 µg/L and 50 µg/L
- reference item: sodium benzoate
- reference item concentration: 17.14 mg/L
- sterile control: yes
- test volumes: 200 mL in 300 mL headspace flasks
- sampling schedule: day 0, 28, 36, 69

It is noted that the degradation pattern observed in this complementary test is completely in line with the pattern that is seen in the main study. Also in this test it is not possible to establish a mass balance. Disappearance from the reaction mixture occurs gradually during the whole test duration, both in the viable test item replicates and in the sterile control replicates. At the lower test concentration (10 µg/L) 14% of the test item is retrieved in the viable replicates at the end of the test, while in the sterile controls only 10% is retrieved. The same pattern is seen at the higher test concentration (50 µg/L). This proves that disappearance of the test item is caused by dissipation and that biodegradation is not taking place at all. Indeed, residual concentrations are even higher in the viable replicates than in the sterile replicates. In theory the half-life for biodegradation would be infinite.

Another similarity between this complementary test and the main study is the fact that in both tests only 1 metabolite is found in minute amounts. In both tests the metabolite is the same and is found to be S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O,O'-diisopropyl phosphorothioate. In fact, in the complementary test the concentration of the metabolite is a bit higher and the highest relative level is observed in the 10 µg/L replicate at day 36. One can estimate a degradation half-life based on the concentrations of the parent compound (9.29 nmol/L) and the metabolite (1.22 nmol/L) at day 36. Proceeding in this way a first order degradation half-life of 202 days is estimated. Because no other metabolites are formed, this calculation method provides an alternative but nevertheless reliable estimation of the degradation half-life. The value of 202 days determined in this way is also very close to the value of 218 days derived in the evaluation of the data from the main study. As both approaches lead to estimated half-lives greater than 200 days, the eMSCA has concluded that the vP criterion for fresh water is met.

It is important to note that in the complementary study, in contrast to the main study, the viability of the microorganisms is not an issue at all. The reference item is degraded for 50% after 5 days incubation, indicating that the microorganisms in this study are sufficiently active. In that respect the complementary study is even more useful and indicative as the main study. In the main study the viability of the microorganisms could be questioned, but it should be noted that the results of both tests are very much in line with each other. Therefore one must conclude that the absence of biodegradation in the main study is not triggered by the inactiveness of the microbes but by the inherent persistence of the test item.

7.7.1.3. Conclusion on degradation

Although it was not possible to derive a reliable hydrolysis rate constant due to divergent experimental results, it is appropriate to conclude that the Substance is hydrolytically stable at pH 4, 7 and 9. There are no indications that the constituents of the Substance degrade abiotically.

The results derived from screening biodegradation tests, QSAR estimations and read-across approaches did not allow to come to a robust conclusion on the biodegradation characteristics of the Substance. Therefore, a simulation test in surface water with the ip-ip constituents of the Substance was performed. Although the simulation study showed some shortcomings, the eMSCA made a quantified estimation of the biodegradation rate in the best possible way and this for both the main study and the complementary test. Both approaches led to an estimated biodegradation half-life of more than 200 days. Therefore the eMSCA concludes that the ip-ip constituents meet the vP criterion in fresh water.

7.7.2. Environmental distribution

7.7.2.1. Adsorption/desorption

In the registration dossier one study is presented that examines the adsorption capacity of the Substance. The study is executed according to EU method C.19 (HPLC method). The log K_{oc} value varies from 5.57 to >5.63 depending on the constituent that is measured.

The KOCWIN program (v2.00) in EPI Suite estimates log K_{oc} values for the ip-ip constituent as follows: MCI method 4.59 and log K_{ow} method 4.21. The estimated log K_{oc} values for all other constituents are consistently higher. Therefore, all constituents of the Substance are expected to adsorb significantly to suspended solids, sediments and soils.

7.7.2.2. Distribution

The Substance consists of 6 groups of constituents whose physical properties like water solubility, vapour pressure and log K_{ow} vary to some extent. Consequently, the estimated distribution after release of the Substance over the various environmental compartments will also depend on the constituents that are considered. Because our evaluation of the PBT properties pointed out that the ip-ip constituents are the ones that most likely meet the PBT criteria, the current assessment of the environmental distribution is based on these constituents.

The environmental distribution of the ip-ip constituents is assessed via the level III fugacity model that is incorporated in EPI Suite. The available values for various key physical properties are nearly always obtained via experiments on the whole substance and therefore these experimental values are less accurate for the ip-ip constituents. In stead the values estimated by the submodels in EPI Suite are used to evaluate the environmental distribution. (v.p. = 3.38 mPa; Henry's law ct = 19 Pa.m³/mol; log K_{ow} = 6.1; log K_{oc} = 4.59).

The following distributions can be predicted for the Substance in EPI Suite (given equal release, emissions to water only and emissions to soil only).

Table 11: Distribution modelling for the ip-ip constituents (Level III Fugacity Model; EPIWEB v4.1)

Release (%)	Air	Water	Soil	Sediment
Equal	0.03	9.3	71.5	19.2
Only to water	0.03	32.6	0.07	67.3
Only to soil	0	0.01	99.96	0.03

Based on this analysis, the ip-ip constituents will mainly distribute to soil and sediment and to a lesser extent to water.

7.7.3. Bioaccumulation

7.7.3.1. Bioaccumulation in aquatic organisms

The bioaccumulation potential of the Substance in aquatic species was examined in a bioconcentration study from 1997. The study was carried out according to the OECD 305C protocol that was valid at that time and that protocol shows some deviations from the current OECD 305 guideline. Consequently, some elements cannot be evaluated as it is done nowadays, but in general the study is well conducted and follows GLP principles. Therefore, the eMSCA considers that this study is valid and can be used to evaluate the bioaccumulation potential of the Substance.

The study is carried out with a mixture of 3 constituents of the Substance, namely with the O,O'-diisopropyl constituent (ip-ip or C3), the O,O'-diisobutyl constituent (ib-ib or C4) and the O,O'-di-2-ethylhexyl constituent (eh-eh or C8) in a 1:1:1 ratio. The main characteristics of the study are the following :

- study protocol: OECD 305C (v1981)
- set up: continuous flow-through system
- test item: mixture of C3, C4 and C8 (ratio 1:1:1)
- test item concentrations: 50 µg/L & 500 µg/L
- dispersant: Hydrogenated Castor Oil (HCO-30)
- dispersant concentration: 20 x test item concentration
- test fish: Cyprinus carpio
- body weight: 22-37 g
- fat content fish: 4.4 %
- sampling points uptake period: 2, 4, 6, 8 weeks
- elimination period: 13 days

The results of the study indicate that steady state is reached after 6 weeks of exposure, both in the high and the low exposure experiment. In order to determine the BCF_{ss} the average of the measured test item concentrations in the sampled fish after 6 and 8 weeks is used.

Proceeding in this way, the following non-normalized steady-state BCFs were obtained for the various homologues:

- diisopropyl, high exposure: 2059 L/kg
- diisopropyl, low exposure: 3339 L/kg
- diisobutyl, high exposure: 718 L/kg
- diisobutyl, low exposure: 2115 L/kg
- di-2-ethylhexyl, high exposure: < 5 L/kg (below LoQ in fish)
- di-2-ethylhexyl, low exposure: < 49 L/kg (below LoQ in fish)

After lipid normalisation (fish fat content = 4.4 %) the steady-state BCFs are:

- diisopropyl, high exposure: 2340 L/kg
- diisopropyl, low exposure: 3794 L/kg
- diisobutyl, high exposure: 816 L/kg
- diisobutyl, low exposure: 2403 L/kg

Although HCO-30 is used as a dispersant, it is not clear whether the constituents at the high exposure level are fully solubilized and that is probably the reason why the measured BCFs for the higher exposure level are systematically less than those for the lower exposure level. It is further noted that in the older version of the OECD TG 305 dispersants are

allowed if the concentration is below the toxicity of the dispersant and not above 100 mg/L. The concentrations of HCO-30 used in this test were 10 and 1 mg/L and hence they are below the limit indicated in the guideline. Also no mortality or sublethal effects were observed in the test. Therefore, it seems that HCO-30 did not cause toxic effects in the fish, and its use can be considered acceptable and did not affect the validity of the study.

Based on these results, the eMSCA concludes that the diisopropyl constituents of the Substance certainly meet the B criterion as the steady-state BCFs found in the high and low exposure experiment (2340 L/kg & 3794 L/kg respectively) both exceed the threshold value of 2000 L/kg. Probably also the diisobutyl constituents with a BCF_{ss} of 2403 L/kg in the low exposure experiment meet the B criterion for aquatic organisms.

7.7.3.2. Bioaccumulation in terrestrial organisms

Experimental data on the bioaccumulation potential in terrestrial organisms are not available for the Substance.

The potential for terrestrial bioaccumulation can be screened by the log K_{oa}. The estimation program KOAWIN v1.10 presents the following log K_{oa} values for the various constituents of the Substance:

- isopropyl-isopropyl 8.21
- isobutyl-isopropyl 8.58
- isobutyl-isobutyl 8.95
- 2-ethylhexyl-isopropyl 10.05
- 2-ethylhexyl-isobutyl 10.41
- 2-ethylhexyl-2-ethylhexyl 11.89

All the estimated log K_{oa} values are greater than 5 and therefore all the constituents screen as potentially bioaccumulative in air-breathing organisms.

7.7.3.3. Summary of bioaccumulation

The eMSCA performed an in-depth analysis of the results of the experimental study performed according to an older version of the OECD TG 305 (1981). In this study, the steady-state BCFs of 3 constituents of the Substance were determined. The constituents are the di-isopropyl, the di-isobutyl and the di-2-ethylhexyl constituents. From this study the eMSCA concludes that the di-isopropyl constituent meets the B criterion for aquatic organisms. The di-isobutyl constituent only meets the B criterion when tested at the lower exposure level and the di-2-ethylhexyl constituent does not meet the B criterion. Experimental data on the bioaccumulation potential in air-breathing organisms is not available. Nevertheless, all the constituents meet the screening criteria for bioaccumulation in air-breathers, and thus also the di-isopropyl constituents.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

7.8.1.1. Fish

Only one experimental fish toxicity test is available for the Substance. The test is carried out according to OECD guideline 203 with rainbow trout as test species. The animals were exposed at 15 °C for 96 hours to five concentrations of the test substance. Acetone was employed as solubilizer and the nominal test concentrations ranged from 313 mg/L to 5000 mg/L. Measured concentrations at the start of the test ranged from 5.6 mg/L to 17 mg/L and the measured end concentrations ranged from 2.3 mg/L to 4.5 mg/L.

LC_{50} values were calculated by arranging the measured start and end concentrations in ascending order. Proceeding in this way, the 96 hour LC_{50} values based on measured concentrations are estimated to lie between 2.9 mg/L and 10.9 mg/L.

It must be noted that because of the much lower real water solubility of the Substance and the reduced accuracy of the analytical determinations, this LC_{50} value has a low reliability.

7.8.1.2. Aquatic invertebrates

Short-term toxicity to aquatic invertebrates

Two acute toxicity tests on *Daphnia magna* are available for the Substance.

The oldest test dates from 1987 and is performed according to EU method C.2 or OECD guideline 202. In this test, five nominal concentrations of the Substance were employed ranging from 0.08 mg/L to 1.2 mg/L. The median effect concentration EC_{50} was found to be 0.22 mg/L based on the number of immobile daphnia and 0.12 mg/L based on the number of immobile and/or floating daphnia. Considering that during the test a maximum 4-fold decrease in concentration is observed, a reasonable worst case LC_{50} value is 0.03 mg/L.

A more recent acute toxicity test on *Daphnia magna* was conducted in 2006. The test was also carried out according to OECD TG 202. In this case the daphnia were only exposed to a saturated Substance solution with a nominal concentration of 0.13 mg/L. No immobilisation was observed in 20 daphnids exposed to this saturated solution. At the end of 48 hour test period measured concentrations dropped to 0.050 mg/L and 0.043 mg/L. Given this decline in measured test concentrations, it is considered justifiable to base the results on the geometric mean measured test concentration. In this way, it is concluded that the EC_{50} value is greater than 0.077 mg/L.

Long-term toxicity to aquatic invertebrates

A 21 days *Daphnia magna* immobilisation and reproduction test was carried out according to EU method C.20 which is equivalent to OECD TG 211. The test was performed with the following starting Substance concentrations: 0.0013, 0.0041, 0.013, 0.041 and 0.13 mg/L under semi-static conditions. Because of the low water solubility of the test material, these test concentrations were prepared by dilution of a saturated solution prepared by centrifugation of a dispersion at a concentration of 50 mg/L. The mentioned concentrations are based on chemical analysis of a saturated solution prepared during the acute toxicity to *Daphnia magna* test. There was a decline in measured concentrations over the test media renewal periods. This could be due to possible adsorption to glassware or waste material in the test vessels, adsorption to algal cells given as food and/or bioaccumulation in the test organisms. Given the variability in measured concentrations over each media renewal period, it was considered appropriate to recalculate the results based on time-weighted mean measured test concentrations. Surprisingly these time-weighted test concentrations turned out to be a bit higher than originally determined: 0.0018, 0.0059, 0.014, 0.051 and 0.18 mg/L.

The 21 day EC_{50} value based on immobilisation of the parental daphnia generation was calculated to be 0.046 mg/L, while the 21 day EC_{50} value for reproduction was determined to be 0.021 mg/L.

The LOEC and the NOEC values based on the time weighted mean measured test concentrations were 0.0059 and 0.0018 mg/L respectively. Based on the original approach to determine the concentrations the LOEC and NOEC would be 0.0041 and 0.0013 mg/L respectively.

The test item that is used in theory in this test is the Substance, but it should be noted that the real composition of the test item probably deviates from the original the Substance

composition. Indeed, at the start of the experiment the Substance is dispersed in tap water and this dispersion is stirred for 48 hours. Then the undissolved test material is removed by centrifugation and the test is continued with the saturated solution that is obtained. Although the water solubility of the various constituents is not experimentally measured, it is justifiable to assume that the solubilities will differ substantially. So, one can foresee that the real composition of the tested material is determined by the relative solubilities of the various constituents. According to the WATERNT v1.01 submodule in EPI Suite the relative solubilities vary as follows : ip-ip = 1; ip-ib = 0.30; ib-ib = 0.09; ip-eh < 0.01; ib-eh < 0.01; eh-eh < 0.01. Based on this QSAR estimation the real composition of the test item is estimated to be circa 72% ip-ip constituent, 22% ip-ib constituent and 6% ib-ib constituent. The eh constituents are not present in the tested replicates. This study does not allow to come to a definitive conclusion on the toxicological profile of the individual constituents. It should be noted however that the ECOSAR submodule in EPI Suite clearly predicts that they all meet the T criterion for aquatic organisms. For the ip-ip constituents an LC_{50} and a ChV for daphnids of respectively 0.45 µg/L and 0.04 µg/L is estimated by ECOSAR. This QSAR thus underpins the conclusion that the ip-ip constituents meet the T criterion.

7.8.1.3. Algae and aquatic plants

A growth inhibition test on the green algae *Scenedesmus subspicatus* was performed according to OECD guideline 201. The algae were exposed for 72 h to a measured test concentration at the start of 0.40 mg/L under constant illumination. As the measured test concentration declined during the test, it was considered justifiable to base the results on the geometric mean of the measured concentrations. On this basis the EC_{50} was determined to be greater than 0.23 mg/L.

7.8.1.4. Sediment organisms

Experimental data are not available.

7.8.1.5. Conclusion on toxicity towards aquatic organisms

Based on the available toxicity data it is concluded that *Daphnia magna* is the most sensitive aquatic species. It is appropriate to state that the test material in these studies consists mainly of the ip-ip constituent of the Substance. In the 21 day long-term immobilisation and reproduction test, a LOEC of 5.9 µg/L and a NOEC of 1.8 µg/L was determined. As these values are less than 10 µg/L, the eMSCA concludes that the ip-ip constituents and the Substance as a whole meet the T criterion.

7.8.2. Terrestrial compartment

Experimental data are not available.

7.8.3. Microbiological activity in sewage treatment systems

A toxicity test on microorganisms from an activated sludge was conducted in aerobic conditions according to OECD guideline 209. The bacteria were exposed during 3 hours to the Substance at a nominal concentration of 1000 mg/L which exceeds by far the water solubility of the test item. Under these conditions, no effect on respiration of the activated sewage sludge was observed.

The eMSCA concludes that at saturation the Substance does not affect activated sludge microorganisms.

7.8.4. PNEC derivation and other hazard conclusions

Table 12: PNEC derivation

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	PNEC = 18 ng/L	Assessment factor: 100 Justification : 1 long-term study for a freshwater organism NOEC for daphnia = 1.8 µg/L
Marine water	PNEC = 1.8 ng/L	Assessment factor: 1000 Justification : 1 long-term study for a freshwater organism NOEC for daphnia = 1.8 µg/L
Intermittent releases to water	PNEC = 300 ng/L	Assessment factor: 100 Justification : lowest LC_{50} for freshwater organisms = 30 µg/L
Sediments (freshwater)	PNEC = 15 µg/kg wwt	Justification : via equilibrium partitioning
Sediments (marine water)	PNEC = 1.5 µg/kg wwt	Justification : via equilibrium partitioning
Sewage treatment plant	PNEC = 5 µg/L	Assessment factor: 10 No effect at saturation Saturation is ca. 50 µg/L
Soil	PNEC = 12 µg/kg wwt	Justification : via equilibrium partitioning

7.8.5. Conclusions for classification and labelling

At the moment the Substance is listed in table 3.1. of the CLP Regulation (No 1272/2008) under entry 015-146-00-0. The harmonized classification is

- Aquatic acute 1, H400
- Aquatic chronic 1, H410

According to the available environmental toxicity data, the eMSCA considers this classification to be appropriate.

7.9. Human Health hazard assessment

Because human health endpoints did not belong to the initial grounds of concern, the eMSCA has not evaluated the available data for these endpoints.

7.10. Assessment of endocrine disrupting (ED) properties

Assessment of the endocrine disrupting properties is not in the scope of this evaluation report.

7.11. PBT and vPvB assessment

7.11.1. Persistence

The eMSCA has concluded that the Substance is hydrolytically stable and there are no indications that the constituents degrade abiotically otherwise.

The results derived from screening biodegradation tests, QSAR estimations and read-across approaches did not allow to come to a reliable definitive conclusion on the biodegradation characteristics of the Substance. Therefore, a simulation test in surface water with the ip-ip constituents was performed. After careful analysis of the obtained results, the eMSCA has estimated the biodegradation half-life of the tested constituents at more than 200 days. It is recognized there were some shortcomings in the execution of this simulation test. However, as this calculated half-life value significantly exceeds the thresholds laid down in annex XIII of REACH (40/60 days), the eMSCA has concluded that the ip-ip constituents and thus also the Substance meets at least the P criterion in fresh water.

7.11.2. Bioaccumulation

The eMSCA performed an in-depth analysis of the results of the experimental study performed according to an older version of the OECD guideline 305. The steady state BCFs found in the high and low exposure experiment were respectively 2340 L/kg and 3794 L/kg. Based on this study, it is concluded that the ip-ip constituent meets the B criterion for aquatic organisms. Experimental data on the bioaccumulation potential in air-breathing organisms are not available, but all the constituents meet the screening criteria for this endpoint.

7.11.3. Toxicity

All the experimental studies on aquatic toxicity are in principle performed with the composition of the Substance as it is marketed. However, it is reasonable to assume that in practice the test item consisted mainly of the ip-ip constituents of the Substance. In the long-term daphnia test a LOEC of 5.9 µg/L and a NOEC of 1.8 µg/L was determined. Therefore, it is concluded that the ip-ip constituents and also the Substance meet the T criterion.

7.11.4. Overall conclusion

Because the Substance is a multi-constituent substance consisting of six groups of homologous dithiophosphates, it was appropriate to focus the PBT assessment on the most suspected constituents, i.e. the isopropyl-isopropyl (ip-ip) constituents.

The simulation study in fresh water was performed with the ip-ip constituents and it is concluded that the test item meets the P criterion. The bioaccumulation study was carried out with 3 constituents and the results indicate that certainly the ip-ip constituents meet the B criterion for aquatic organisms. In the long-term toxicity test on *Daphnia magna* the test item consisted mainly of the ip-ip constituents and the result indicates that the T criterion for aquatic organisms is met.

Overall, the eMSCA concludes that the ip-ip constituents meet the P, B as well as the T criterion as set out in annex XIII. The ip-ip constituents are clearly present in concentrations higher than 0.1% and so the Substance can be identified as a PBT substance.

7.12. Exposure assessment

The Substance is not manufactured in the EU. Reported aggregated volume that is imported in the EU is in the 10-100 t/y range. The substance is mainly applied in the mineral oil and fuel industry and it is used as a lubricant and as an additive. Due to the uses of the substance exposure of the environment is expected.

7.13. Risk characterisation

Because the original concern relates to the PBT/vPvB character, a quantitative risk characterisation is not in the scope of this evaluation report.

7.14. References

See ECHA's dissemination website for the registration dossier study reports.

7.15. Abbreviations

Related to this evaluated substance

ip-ip :	S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isopropyl O'-isopropyl phosphorodithioate
ip-ib :	S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isopropyl O'-isobutyl phosphorodithioate
ib-ib :	S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isobutyl O'-isobutyl phosphorodithioate
ip-eh :	S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isopropyl O'-2-ethylhexyl phosphorodithioate
ib-eh :	S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-isobutyl O'-2-ethylhexyl phosphorodithioate
eh-eh :	S-(tricyclo[5.2.1.$0^{2,6}$]deca-3-en-8(or 9)-yl) O-2-ethylhexyl O'-2-ethylhexyl phosphorodithioate

Other abbreviations

B :	Bioaccumulative
BAF :	Bioaccumulation Factor
BCF :	Bioconcentration Factor
CA :	Competent Authority
C&L :	Classification & Labelling
CLP :	Classification, Labelling and Packaging
Conc. :	Concentration
CoRAP :	Community Rolling Action Plan
DT_{50} :	Disappearance Time-50; Time in which half of the test item disappears
EC :	Effect Concentration
ECHA :	European Chemicals Agency
eMSCA :	evaluating Member State Competent Authority
EU :	European Union
GC :	Gas Chromatography
GLP :	Good Laboratory Practice
K_{oa} :	Octanol-Air Partition Coefficient
K_{oc} :	Organic Carbon-Water Partition Coefficient
K_{ow} :	Octanol-Water Partition Coefficient
LC :	Lethal Concentration
LOEAL :	Lowest Observed Adverse Effect Level
MS :	Mass Spectrometry
NOAEL :	No Observed Adverse Effect Level
NOEC :	No Observed Effect Concentration

OECD :	Organisation for Economic Co-operation and Development
P :	Persistent
PBT :	Persistent, Bioaccumulative and Toxic
PNEC :	Predicted No Effect Concentration
QSAR :	Quantitative Structure-Activity Relationship
REACH :	Regulation No 1907/2006 concerning Registration, Evaluation, Authorisation and Restriction of Chemicals
SVHC :	Substance of Very High Concern
T :	Toxic
TG :	Test Guideline
vB :	very Bioaccumulative
vP :	very Persistent