federal public service
HEALTH, FOOD CHAIN SAFETY AND ENVIRONMENT

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Reaction mass of O,O'-diisopropyl (pentathio)dithioformate and O,O'-diisopropyl (trithio)dithioformate and O,O'-diisopropyl (tetrathio)dithioformate

aka "Robac AS100"

EC No 403-030-6

CAS No 137398-54-0

Evaluating Member State(s): Belgium (formerly United Kingdom)

Dated: December 2020

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: n/a

Transitional substance formerly notified under Dir. 67/548/EEC

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

Robac AS100 was originally assessed under the New Substances Directive in the UK (NoNS evaluation scheme). The assessment considered PBT properties. As a consequence of the UK leaving the European Union, the substance evaluation of Robac AS100 was taken over/finalised by Belgium.

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

Robac AS100 was originally selected for substance evaluation in order to clarify concerns about:

- suspected PBT/vPvB properties
- exposure of the environment

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Before the entry into force of REACH, Robac AS100 was assessed under the Notification of New Substances (NONS) Directive (92/32/EEC) in the UK.

The assessment considered PBT properties. It was noted that the substance hydrolyses primarily to DIXD (O,O-di(1-methylethyl)dithio-bisthioformate) which in turn was considered stable. Robac AS100 was therefore considered to screen as being persistent / very persistent on the basis of its transformation product. Robac AS100 was also considered to screen as bioaccumulative / very bioaccumulative on the basis of the log K_{ow} >5.9 for the substance and a log K_{ow} of 5.72 for the degradant DIXD. Based on the available data, Robac AS100 was not considered to meet the toxicity criteria although data gaps for chronic toxicity were noted and there were no toxicity data for DIXD.

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

4. FOLLOW-UP AT EU LEVEL

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

No need for follow-up actions.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

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

Table 2: Reason for removed concern

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

The UK Competent Authority reviewed the available data for Robac AS100 in 2015 and considered that there was insufficient information to conclude the PBT/vPvB assessment. Consequently, a final decision requesting further information was issued on 16 June 2017 and the registration dossier was updated on 20 March 2019 with the requested data (Unpublished, 2019 'Aerobic Mineralization of [^{14}C] Robac AS100 in Surface Water').

The Belgian Competent Authority evaluated the new information and on the basis of all the available data, Robac AS100 is considered not PBT/vPvB.

5.2. Other actions

Not applicable.

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

Not applicable.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Robac AS100 was originally selected for substance evaluation in order to clarify concerns about:

- suspected PBT/vPvB properties
- exposure of the environment

Table 3: Evaluated endpoints

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
PBT/vPvB	Concern not substantiated. Based on the results of the aerobic simulation study in surface water, it is concluded that the parent constituents of Robac AS100 and its primary transformation product (DIXD) do not meet the P criterion. However, the same simulation study also demonstrates that a further transformation product, whose chemical identity could not be determined, is probably P. Based on the interpretation of experimental data in combination with QSAR estimations, it is unlikely that this unidentified transformation product is bioaccumulative. As none of the constituents and the transformation products are both P and B, the eMSCA considers that Robac AS100 should not be identified as a PBT/vPvB substance.
Exposure of the environment	Not evaluated since the PBT/vPvB concern is not confirmed.

7.2. Procedure

Following the implementation of REACH, Robac AS100 was further evaluated as a Transitional Substance (Art. 135) formerly notified under Dir. 67/548/EEC with UK as eMSCA.

In April 2012 the UK Competent Authority requested an update from the registrant(s) regarding the completion of the fate study required under the pre-REACH new substances directive. Following this, an updated REACH Registration and CSR (dated 24 November 2012) were submitted. The UK Competent Authority reviewed the update and determined that there was insufficient information to be able to conclude whether the substance met the PBT criteria or not. Subsequently an extended ready biodegradation study was submitted by the registrant(s) in a dossier update on 11 February 2015.

The UK CA reviewed these data and considered that there remained insufficient information to conclude the PBT/vPvB assessment for Robac AS100. Therefore an environmental simulation study was required to investigate persistence.

At their 10th meeting the ECHA PBT Expert Group (September 2015) supported this view.

Following discussion at the Member State Committee meeting (MSC-53, 24-28 April 2017), the following data were requested (Decision dated 16 June 2017).

> Either:
>
> Sediment simulation testing; test method: Aerobic and anaerobic transformation in aquatic sediment systems, EU TM C.24. / OECD TG 308 using the registered substance. The simulation test should be performed at a temperature of 12 °C with the test item added directly to the sediment and include analytical measurement of the registered substance and degradants/impurities including O,O-di(1-methylethyl)dithio-bisthio-formate (DIXD), CAS: 105-65-7.
>
> Or:
>
> Simulation testing on ultimate degradation in surface water; test method: Aerobic mineralisation in surface water – simulation biodegradation test, EU C.25./OECD TG 309 using the registered substance. The simulation test should be performed at a temperature of 12 °C and include analytical measurement of the registered substance and degradants/impurities including DIXD. The study should follow the "pelagic test" option with a concentration of suspended solids in the surface water approximately 15 mg dw/L (natural surface water containing between 10 and 20 mg SPM dw/L is considered acceptable).

In accordance with Article 46(2) of REACH the registrant(s) updated their dossier on 20 March 2019 with an OECD TG 309 study. Following an initial review of these data, the UK CA requested some further clarifications regarding an unknown degradant 'unknown ~2.85 mins' identified in the OECD 309 simulation study to be able to conclude on the potential persistence of the substance.

Due to the EU withdrawel of UK on 31 January 2020, Belgium took over the substance evaluation in the conclusion stage. The evaluation of the available test results relies mainly on UK's assessment. Based on this, no regulatory actions have been proposed by the Belgium eMSCA.

In accordance with Articles 46(3) and 46(4) the Belgian Competent Authority evaluated the available information and concluded the substance evaluation in December 2020.

7.3. Identity of the substance

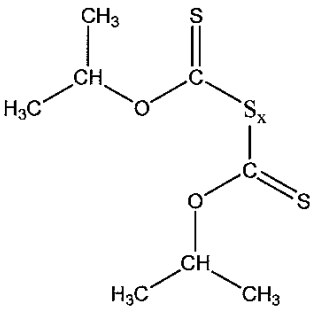
Information publicly available on ECHA's website (December 2020)

Table 4: Substance identity

SUBSTANCE IDENTITY	
Public name	A mixture of O,O-di(1-methylethyl)trithio-bis-thioformate; O,O-di(1-methylethyl)tetrathio-bis-thioformate; O,O-di(1-methylethyl)pentathio-bis-thioformate Reaction mass of O,O'-diisopropyl (trithio)dithioformate, O,O'-diisopropyl (tetrathio)dithioformate & O,O'-diisopropyl (pentathio)dithioformate
EC number:	403-030-6
CAS number:	137398-54-0
Index number in Annex VI of the CLP Regulation:	607-209-00-1
Molecular formula:	$C_8H_{14}O_2S_5$, $C_8H_{14}O_2S_6$, $C_8H_{14}O_2S_7$
Molecular weight range:	302.5 – 366.7 g/mole
Synonyms:	Di-isopropyl xanthogen polysulfide Trade name : Robac AS100 IUPAC name : mixture of 1,3-bis(propan-2-yl)trisulfanedicarbothioate, 1,4-bis(propan-2-yl)tetrasulfanedicarbothioate, 1,5-bis(propan-2-yl)pentasulfanedicarbothioate

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

Structural formula: x=3, 4, 5



The overall substance purity is stated to be ≥83 - ≤90 % (w/w).

The substance name includes the tri-, tetra- and penta-sulfurconstituents although the registration data presents the penta-sulfurconstituent as an impurity rather than a constituent.

Table 5: Constituents

Constituent			
Constituents	**Typical concentration**	**Concentration range**	**Remarks**
O,O-di(1-methylethyl)trithio-bis-thioformate CAS: 52584-27-7	Confidential information	Confidential information	**$(CH_3)_2$-CH-O-C(=S)-S_3-C(=S)-O-CH-$(CH_3)_2$**
O,O-di(1-methylethyl)tetrathio-bis-thioformate CAS: 69303-50-0	Confidential information	Confidential information	Referred to as DIXT $(CH_3)_2$-CH-O-C(=S)-S_4-C(=S)-O-CH-$(CH_3)_2$

Table 6: Impurities

Impurity			
Constituents	**Typical concentration**	**Concentration range**	**Remarks**
O,O-di(1-methylethyl)pentathio-bis-thioformate CAS: 149368-01-4	Confidential information	Confidential information	$(CH_3)_2$-CH-O-C(=S)-S_5-C(=S)-O-CH-$(CH_3)_2$
Sulfur CAS: 7704-34-9	Confidential information	Confidential information	

Table 7: Degradation (transformation) products or metabolites

Degradation (transformation) product or metabolite			
Constituents	**Typical concentration**	**Concentration range**	**Remarks**
O,O-di(1-methylethyl)dithio-bis-thioformate EC: 203-319-5 CAS: 105-65-7			$(CH_3)_2$-CH-O-C(=S)-S_2-C(=S)-O-CH-$(CH_3)_2$ Referred to as DIXD

7.4. Physico-chemical properties

Table 8: Summary of physico-chemical properties

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**

Physical state at 20 °C and 101.3 kPa	Oily viscous liquid (Anonymous (1988a)) Substance tested was main constituent DIXT (di-isopropyl xanthogen tetrasulfide (polysulfide) (CAS No.: 69303-50-0)
Vapour pressure	0.05 Pa at 20 °C GLP study dated 2013. It is unclear what substance composition was tested. An old study measuring 36,100 Pa at 25 °C is considered unreliable as based on extrapolation and likely to reflect an impurity – possibly sulfur. For the main constituents EpiSuite estimates a vapour pressure range of $5x10^{-4}$ to $2x10^{-6}$ Pa @ 25 °C.
Water solubility	1.3 mg/L at 20-23 °C Non-GLP study dated 2010 following OECD 105. It is unclear what substance composition was tested. Additional available data: 0.3 mg/L at 22 °C Non-GLP study dated 2015 equivalent or similar to EU Method A.6 (Flask method). It is unclear what substance composition was tested. 0.752 mg/L at 20 °C GLP study dated 1988 conducted with di-iso propyl xanthogen polysulfide mixture. It is unclear what the ratio of the constituents was.
Partition coefficient n-octanol/water (Log K_{ow})	≥5.9 at 21 °C GLP study according to EU Method A.8 (HPLC method). Test item was di-iso propyl xanthogen polysulfide mixture. It is unclear what the ratio of the constituents was.
Partition coefficient organic carbon/water (Log K_{oc})	Log K_{oc} ranges between 5.49 and >5.63. The determination of the log Koc was carried out using the HPLC screening method.
Dissociation constant	No data available. Substance does not contain any ionisable groups.
Surface Tension	73 mN/m at 20 °C using 90% saturated solution.

7.5. Manufacture and uses

7.5.1. Quantities

Table 9: 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

There is 1 registration for Robac AS100 under REACH.

7.5.2. Overview of uses

Robac AS100 is used as a vulcanizing agent in the manufacture of rubber.

Table 10: Overview of uses

USES	Use(s)
Uses as intermediate	Not applicable.
Formulation	Formulation into solid matrix.
Uses at industrial sites	Use in rubber goods: use of reactive process regulators in polymerisation processes at industrial site (inclusion or not into/onto article).
Uses by professional workers	No information.
Consumer Uses	No information.
Article service life	No information.

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Table 11: 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)**		
607-209-00-1	Reaction mass of O,O'-diisopropyl (pentathio)dithioformate and O,O'-diisopropyl (trithio)dithioformate and O,O'-diisopropyl (tetrathio)dithioformate	403-030-6	137398-54-0	Acute Tox. 4* Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H302 H317 H400 H410		

7.6.2. Self-classification

The Registrant considers that the Aquatic Chronic 1 classification is not required and its self-classification is:

- Acute Tox. 4, H302
- Skin Sens. 1, H317

- Aquatic Acute 1, H400

There are no other entries in the CLP inventory[2].

7.7. Environmental fate properties

7.7.1. Degradation

A summary of available valid information on the fate of Robac AS100 is presented in Table 12 below.

Table 12: Overview of studies on degradation

SUMMARY OF RELEVANT INFORMATION ON DEGRADATION OF ROBAC AS100			
Method	**Results**	**Remarks**	**Reference**
Aquatic hydrolysis EU Method C.7 GLP	Half-life at pH 4, 15 °C: 400 hours Half-life at pH 7, 15 °C: 361 hours Half-life at pH 9, 15 °C: 6.88 hours	Accepted under NONS	Anonymous (2003a)
Ready biodegradation using Robac AS100 OECD Test Guideline 301D Ready Biodegradability: Closed Bottle Test GLP	10-15 % degradation, after 28 days	Accepted under NONS	Anonymous (1988b)
Inherent biodegradation Modified MITI (II) using Robac AS100 Not GLP	9.29 % degradation (HPLC analysis)	Conducted for Chinese Chemical Notification Scheme. Supporting information	Anonymous (2014)
Extended ready biodegradation using AS100 OECD Test Guideline 301B Ready Biodegradability: CO_2 Evolution GLP	Inorganic carbon analysis: 15% degradation, after 28 days 26% degradation, after 60 days HPLC analysis: ~11 to 13% degradation by day 61 (based on analysis of the DIXT component and DIXD degradant)		Anonymous (2015)
Aerobic mineralisation in surface water OECD Test Guideline 309 GLP	Primary degradation of the parent at 12 °C: Transformation half-life - 3 days Transformation - DT_{90} 24 days 25.6 % Applied Radioactivity as CO_2 by day 28		Anonymous (2019)

Abiotic degradation

Hydrolysis study (Anonymous, 2003a)

[2] Checked 11 October 2019.

A GLP study (EU Method C.7) considered valid under NONS using Robac AS100 (unknown composition) is available. Based on HPLC-UV analysis of the tetramer component (DIXT), the test material was observed to be more hydrolytically unstable at higher pH. Test solutions were prepared with a co-solvent (0.5% tetrahydrofuran) to aid solubility and a nominal concentration of 0.35 mg/L test item. Solutions were sonicated and degassed with nitrogen to minimize dissolved oxygen content. The reaction was considered to be pseudo-first order with the following hydrolysis half-lives at 15 ±0.5 °C in the dark:

pH 4 = 400 hours (~17 days)
pH 7 = 361 hours (~15 days)
pH 9 = 6.88 hours

The eMSCA has converted these values to half-lives at 12°C:
pH 4 = 508.3 hours (~22 days)
pH 7 = 458.9 hours (~19 days)
pH 9 = 8.75 hours

The principle degradant was identified (although not quantified) by HPLC-UV to be di-isopropyl xanthogen disulfide (DIXD) with sulfur as an additional hydrolysis product. Concentrations of DIXD were observed to increase throughout the hydrolysis test with a decrease in parent DIXT indicating the rate of hydrolysis of DIXD is slower than its rate of formation from DIXT.

The study did not analyse for the tri- component or penta- impurity of the test material or consider additional degradants. The eMSCA notes that study chromatograms suggested the presence of other substances.

Biotic degradation

QSAR data

The Registrant's CSR does not include a QSAR prediction.

The eMSCA has reviewed the BIOWIN QSAR models (which are available via the Help function of the EPI Suite programme). The three sulfur fragments in the models are sulfonic acid / salt (aromatic), sulfonic acid / salt (aliphatic) and thiocarbamate. These fragments reflect the sulfur-containing chemicals in the QSAR training sets. There are no chemicals or fragments containing xanthogens or sulfides in the model, and so there are no sulfur-containing substances structurally similar to Robac AS100.

The BIOWIN predictions for Robac AS100 are either calculated from the biodegradability of the remaining fragments (for example methyl groups) and a factor for the molecular weight, or from molecular weight alone.

In the opinion of the eMSCA this results in significant uncertainty as a large proportion of the molecule is excluded from the prediction. The molecular weight of Robac AS100 is within the molecular weight domain of the model, however the eMSCA considers that this alone is insufficient to be confident of the predictions.

Overall, the chemical is not assessed by the eMSCA to be within the domain of the BIOWIN models.

Measured data

Ready biodegradation study (Anonymous, 1988b)

The biodegradation of Robac AS100 was evaluated in an OECD Test Guideline 301D (Closed Bottle) study considered valid under NONS. The study was run with ~2 mg/L test item dissolved in diethyl ether before dispersion on filter paper, then the solvent evaporated before the paper was placed in test vessels (2 replicates). The source of the inoculum was a sewage treatment plant treating predominantly domestic sewage. A toxicity control was not included. A reference control using sodium benzoate was included with 87% degradation observed by day 15. By day 28, between 10 and 15% mineralisation of Robac

AS100 occurred based on oxygen depletion, and it was concluded as not being readily biodegradable.

Inherent biodegradation study (Anonymous, 2014)

An inherent biodegradability study was conducted in China to comply with Chinese regulations. The study used di-isopropyl xanthogen polysulfide with the molecular formula $C_8H_{14}O_2(S)_n$ where n is 5, 6 or 7 reflecting either the tri-, tetra- or penta-S constituents. The 28-day study followed a Chinese guideline modified MITI (II) method using a mixture of Chinese domestic and industrial inoculum and was not performed according to GLP.

The study was conducted in the dark at 25 ± 2 °C. The reference substance, sodium benzoate, was assessed by the Registrant to meet the validity criteria. The test item was dissolved in acetone to make a stock solution resulting in test vessels containing ~30 mg/L test item which is significantly above quoted test item solubility.

BOD was measured by determining oxygen consumption. The test item was analysed by HPLC. Based on BOD, degradation was 6.26% for n=5 in the molecular formula of the test item, 6.39% for n=6 and 6.32% for n=7.

Based on HPLC analysis, 7.54 to 11.5% biodegradation was observed based on test item loss and 3 samples. The HPLC analysis did not allow separation of mixture components.

Extended ready biodegradation study (Anonymous, 2015)

The NONS assessment noted one principle component of the parent mixture (DIXT) hydrolyses to DIXD based on the OECD 111 test described above. Due to the lack of mineralisation in the original ready biodegradation test, and measured log K_{ow}, the degradant DIXD screened as vPvB. As a first step of the PBT assessment under NONS, persistence testing of the degradant DIXD was required by the eMSCA using an enhanced ready biodegradation study.

In February 2015, the REACH Registrant submitted an extended 60-day ready biodegradation study using 'AS100' to ECHA. The study was performed according to GLP and followed OECD Test Guideline 301B (CO_2 evolution). The study used inoculum from a sewage treatment works treating predominantly domestic effluent.

Degradation was followed using inorganic carbon (IC) analysis and high-performance liquid chromatography (HPLC). IC analysis was performed on samples taken on days 0, 1, 5, 8, 10, 14, 21, 28, 60 and 61. On days 0, 1, 5 and 61 high-performance liquid chromatography with UV detection (HPLC-UV) chemical analysis was also performed to determine total concentrations of the AS100 parent test item based on analysis of the principle component DIXT and DIXD. Further HPLC analysis for solely DIXD degradant concentrations was also undertaken.

The concentration of AS100 in the test was nominally 34.8 mg/L equating to 10 mg carbon/L. This is an order of magnitude above the water solubility value of 1.3 mg/L at 20 °C used in the current REACH Registration. The test item was dispersed in 30 mL silicone oil (PDMSO: polydimethylsiloxane) by ultrasonication. The Registrant has explained that the silicone oil was added to slow premature hydrolysis of the parent substance (and therefore formation of DIXD) to allow potential biodegradation of the parent to occur. They anticipated that the environmental degradation pathway does not include abiotic degradation to DIXD, although the basis for this hypothesis is unclear to the eMSCA. Observations in the study report indicated silicone oil to be present as a layer on the surface of the dispersions in the test vessels. The test item was reported to be present as globules in the dispersion.

Study conditions and validation criteria of the test guideline were met. The eMSCA notes total carbon dioxide evolution values in the inoculum control at the end of the study were 41-42 mg/L which is just above the OECD recommendation of 40 mg/L. Given values at 28 days were within the recommendation reflecting the time period for the non-extended study, the eMSCA considers that this is acceptable. The study pH was reported as being around 7.6.

On the basis of IC analysis, 15% biodegradation was observed at day 28 and 26% biodegradation by day 61 (corrected for blank). Using this method, it is unclear what proportion of the degradation represents direct biodegradation of parent test item AS100 and hydrolysis and subsequent biodegradation of the degradant DIXD. The toxicity control contained the test item and sodium benzoate. It was prepared by dispersing the test item in silicone oil with ultrasonication before dispersal in inoculated medium with an aliquot of sodium benzoate. The toxicity control achieved ≥25% degradation by IC analysis by day 14 and therefore AS100 was considered non-inhibitory.

Table 13 presents measured HPLC concentrations of 'AS100' as the principle DIXT component and the degradant DIXD. Table 13 also presents measured concentrations of the degradant DIXD. Using HPLC analysis, on day 0, 1 and 5, analysis of DIXD and DIXT together was 100% of nominal 34.8 mg/L with DIXD below the limit of quantification of 0.22 mg/L. The next analytical point was study termination at day 61 when the analysis of DIXD and DIXT together[3] was 23.0 mg/L equating to 65-67% of nominal. At day 61, the concentration[4] of DIXD was 7.6 mg/L demonstrating that some hydrolysis had occurred. The study report considered approximately 11-13% biodegradation had occurred. This assessment is based on addition of measured AS100 test item and DIXD degradant and percentage of nominal parent concentrations.

No other degradants were investigated or quantified although the eMSCA notes that small peaks were observed in the example chromatogram on day 61 which were not present in the control or day 0 sample.

Table 13: Analysis results

ANALYSIS OF AS100 AS DIXT AND DEGRADANT DIXD AND ANALYSIS OF HYDROLYSIS DEGRADANT DIXD (ANONYMOUS, 2015)					
Day	**Sample**	**AS100 (as DIXT and DIXD) concentration by HLPC (mg/L)**	**AS100 % nominal**	**DIXD concentration by HPLC (mg/L)**	**Mineralisation based on CO_2 evolution from IC analysis (%)**
0	Control *	<LOQ	-	<LOQ	0
	R1	34.6	99	<LOQ	
	R2	24.7	100	<LOQ	
1	Control *	<LOQ	-	<LOQ	7
	R1	34.8	100	<LOQ	
	R2	35.7	103	<LOQ	
5	Control *	<LOQ	-	<LOQ	15
	R1	35.6	102	<LOQ	
	R2	34.9	100	<LOQ	
61	Control *	<LOQ	-	<LOQ	26
	R1	23.5	67	7.44	
	R2	22.6	65	7.83	

*average of 2 replicates
AS100 LOQ = 0.24 mg/L
DIXD LOQ = 0.22 mg/L

[3] Average of two replicates
[4] Average of two replicates

eMSCA view

The results based on the IC method demonstrate that some mineralisation occurred. The level of mineralisation at day 28 (15%) is in line with the results of the 1988 ready biodegradation study. Further biodegradation occurred between day 28 and study termination at day 61, up to a maximum of 26%. IC analysis reflects mineralisation of both parent AS100 and degradant DIXD.

HPLC analysis of the test item as DIXT and degradant DIXD demonstrates that some hydrolysis of AS100 occurred in the study. However, as there is no HPLC analysis between day 5 and study termination at day 61 the hydrolysis rate cannot be determined.

The use of PDMSO was anticipated by the Registrant to inhibit the rate of hydrolysis. However, the extent of inhibition achieved is unclear, and the inclusion of the silicone oil only confounds interpretation of the available study data.

In particular the following points are unclear:

- Whether the observed biodegradation reflects mineralisation of parent test item (as DIXT), mineralisation of the hydrolysis product DIXD or a combination of both.
- Whether the concentration of DIXD at day 61 was a maximum.
- The relevance of hydrolysis to the mineralisation of the parent test item AS100.
- The degree of inhibition to the hydrolysis rate of DIXT achieved by the silicone oil.
- Whether degradation of AS100 or DIXD might be greater without silicone oil.

It is not known whether the presence of undissolved test substance caused lower biodegradation. Equally, it is not known whether the use of PDMSO limited biodegradation of the test item.

Overall, the study does not indicate significant biodegradation of AS100. In addition, it is not possible to judge whether the degradant DIXD is readily degradable or not.

Aerobic mineralisation in surface water (Anonymous, 2019)

To address the requirement of the substance evaluation decision dated 16 June 2017, the Registrant has submitted an OECD TG 309 study (aerobic mineralisation in surface water). This was conducted according to GLP using radiolabeled [^{14}C]Robac AS100 (specific activity 385 µCi/mg). The study used aerobic surface water/sediment collected from Lake Tuckahoe, Maryland, USA. The characteristics of the water and sediment are provided in Table 14 . Water and sediment were filtered (0.2 mm and 2 mm sieve respectively) after collection. Test systems were prepared with approximately 30 mg of the sediment and 2 litres of the water, which was mixed thoroughly. Aliquots of 100 mL were transferred to exposure vessels for each replicate.

All test vessels were prepared with 100 mL of the sediment-amended water. Robac AS100 was applied at nominal concentrations of 8 or 80 µg/L (final application rates of 7.9 or 79.4 µg/L) to the low and high dose vessels, respectively. The test material stock solution was prepared in a 1:1 mix of methanol/dichloromethane. Further vessels were prepared for untreated controls, sterile[5] controls (^{14}C-Robac AS100 at a concentration of 79.4 µg/L) and reference control (^{14}C radiolabelled benzoic acid at a concentration of 81.5 µg/L) were also included.

[5] Water/sediment was autoclaved at 250 °C for 30 minutes.

Based on a 9-day preliminary test, the definitive test period was set at 28 days. Vessels were sacrificed for analysis on days 0, 1, 5, 7, 14 and 28 for Robac AS100 (active and sterile systems), and days 7 and 14 for the reference substance. Duplicate vessels were sacrificed for each sampling interval. Radioactive contents in each test vessel and associated volatile traps were analysed by liquid scintillation counting (LSC). Chemical speciation (of Robac AS100[6], DIXD and the reference substance benzoic acid) was performed using HPLC coupled with β–ram detector.

The test was performed in a system allowing humidified air to pass through the sample headspace. A foam plug was used to trap volatile organic components, and aqueous sodium hydroxide was used to trap carbon dioxide (selected samples were treated with barium chloride to confirm the presence of carbon dioxide). The sterile controls did not have associated volatile traps. Test vessels were incubated in the dark under aerobic conditions at 12 ± 2° C.

Table 14: Overview of characteristics of the OECD 309 study

SUMMARY OF WATER AND SEDIMENT CHARACTERISTICS USED IN THE OECD 309 STUDY	
Characteristic	**Value at time of collection**
Water dissolved oxygen (mg/L)	7.5
Water total suspended solids (ppm)	14
Water dissolved organic carbon (ppm)	10.5
Water pH	7.12
Sediment type	Sandy loam
Sediment organic carbon (%)	3.2

Dissolved oxygen during the test ranged between an average of 7.18 to 7.36 ppm across the low and high dose samples. pH measurements ranged from an average of 7.25 to 7.62, and the temperature was maintained between 11 and 12 °C. Based on $^{14}CO_2$ measurements, the reference control substance achieved 57% mineralisation by day 7 and 70% by day 14 confirming the viability of test system.

For the Robac AS100 systems, the mass balance based on applied radioactivity (AR) was 83.1 to 107.1% for the high dose samples and 81.2 to 103.6% for the low dose samples. Losses were considered to be due to volatilisation of the test substance and/or transformation products. While no data were available relating to the potential for the test substance to partition to air, volatilisation appears logical based on extraction and analysis of the volatile traps. Losses from the sterile system were much higher, with recoveries dropping from 92.0% AR early in the study to a final average of 32.8% AR at the end the study. This was considered to be due to the analysis associated with volatilised components. Details of the mass balance for both systems are provided in Table 15.

Table 15: Mass balance

[6] With distinct retention times for the pentasulfide, tetrasulfide and trisulfide.

MASS BALANCE FOR LOW AND HIGH DOSE SYSTEMS AT 28 DAYS IN THE OECD 309 STUDY		
Source	**Low dose* as a % of applied dose**	**High dose* as a % of applied dose**
Water layer	37.2	34.1
Sample bottle rinse	7.3	11.0
Grad. cylinder rinse	0.3	0.3
Foam plug (Trap)	5.9	12.8
NaOH Traps	32.5	25.6
Total Recovery %AR	83.1	83.7

* Average of two replicates

The test report presented a "product balance" for the high dose system, but not the low one.

Robac AS100 concentrations decreased over the study period to an average of 7.9% AR by day 28. DIXD was observed as the major degradant peaking on day 1 in the high dose system at 22.5% AR and subsequently declining to an average of 3% AR by day 28. An unidentified degradant was also observed over the study with a maximum of 25.7% AR by day 28. Radioactive carbon dioxide measurements increased over the study period with a maximum of 25.6 % AR on day 28. It is unclear if this corresponds to mineralisation of Robac AS100 or degradants such as DIXD or a combination. HPLC analysis of the high dose test system is presented below in

Table 16.

Table 16: Product balance

PRODUCT BALANCE OF HIGH DOSE TREATMENT AS % APPLIED RADIOACTIVITY FOR OECD 309 STUDY (average of 2 replicates)						
	Day of sample					
	0	**1**	**5**	**7**	**14**	**28**

Robac AS100	83.5	56.7	26.4	26.4	8.9	7.9
DIXD	10.2	22.5	8.8	4.7	5.5	3.0
Unknown ~2.85 min	3.5	4.8	13.0	11.0	17.3	25.7
Others	10.0	4.2	16.9	19.2	18.4	8.5
Cylinder rinse[7]	NA	NA	NA	NA	0.2	0.3
Foam plug trap	NA	2.3	11.2	10.9	13.0	12.8
CO_2	NA	0.6	7.6	11.6	19.8	25.6

The report documented that the kinetic modelling was performed using CAKE v 3.3. First-order multi-compartment (FOMC) modelling was chosen as the best fit. This results in a transformation half-life for AS 100 (DT_{50}) of 3 days and transformation DT_{90} of 24 days in the high dose treatment (12 °C). Results for the other models were all very similar. The transformation half-lives of the degradants were not calculated.

The CRO considered that there was no difference in carbon dioxide production between the high and low dose treatments and therefore mineralisation of Robac AS100 is not concentration dependent.

eMSCA comments

The eMSCA believes that over all the study was performed to acceptable standards for the purpose of persistence assessment of AS 100. There were a number of points that should have been addressed that include the following:

The study report does not document the reasoning behind terminating the study at 28 d instead of allowing the full 60 d exposure period. The performing laboratory and the registrants have subsequently indicated to the eMSCA that a decision was made to terminate the study once >90% degradation of parent AS100 was achieved – this occurred at the 28 d time point. Their justification was the parent molecule, and its known degradant (DIXD) were not present in appreciable amounts to degrade further. In addition, they indicated a time pressure to obtain results and submit an updated dossier by the beginning of 2019. The eMSCA accepts that these results are accurate but they do not account for the presence of other degradants of interest.

Profiling data indicated that in the High Dose test system (80 µg/L) the [^{14}C]AS 100 was transforming rapidly, with < 10% AR contributing to total radioactivity by 28 d, and $^{14}CO_2$ increasing. The kinetics are described well and the eMSCA agree that the half-life of transformation $t_{1/2}$ for parent [^{14}C]AS 100 is < 40 d. However, the OECD 309 study profiling and kinetics that were presented by the registrant do not take into account the transformation products of [^{14}C]AS 100. This is important as there was an unidentified transformation product that was increasing in percentage at this point (‘unknown ~ 2.58 min’). This transformation product is present in radio-profiles generated at each sampling interval at ≥10% AR from 5 d onward.

[7] The eMSCA has assumed that this should be treated as a volatilised component

The eMSCA asked the registrant and the performing laboratory the reason for not identifying this transformation product (which is a requirement of both the OECD 309 test guideline and the REACH guidance documents: transformation product ≥10% AR or ≥0.1% AR should be identified where feasibly possible). In response the performing laboratory stated that they had identified a correlation of the unknown peak with that of acetone which was noted in the study report. However, after carefully reviewing the data again, based on the position of the label the performing laboratory came to the conclusion that they did not believe that the unknown at ~ 2.85 min was acetone or isopropanol. The eMSCA agrees as both acetone or isopropanol would have eluted earlier in the chromatographic profile e.g. at the solvent front.

The performing laboratory added that the results of the study showed a progressive degradation of AS100 by cleavage of sulfur from penta, tetra, tri and DIXD to the formation of CO_2. Incidentally, the first significant production of CO_2 was seen at day 5 and the formation of the unknown at ~2.85 min was > 10% AR at day 5, which shows transition and cleaving of sulfur compounds before reaching the final degradation product, CO_2. The performing laboratory believes the unknown is likely to be a monosulfide component based on its relative retention time, and this is similar in behaviour to the build-up seen for DIXD.

Results in the study showed that CO_2 is the terminal product of AS100 and therefore the registrant argued that it is expected that the unknown (potentially the monosulfide) also follows the same pattern to ultimate degradation to CO_2. The registrant proposed that it is feasible that carbonyl sulfide could be generated during the abiotic/biotic decomposition, which would explain the loss of the total mass balance (of the radio-label components) across the 28 days as it is a gaseous species that will build-up in the aqueous chambers but will also volatilise and not be captured by the traps (it has a boiling point of - 50.2 °C). As a whole AS100 is not completely compatible with mass spectrometry as it fragments during the ionisation stage, so they have been unable to characterise the unknown peak further. They reiterate that it does play a role in the degradation route of AS100 conversion to CO_2 and may volatilise so may not be trapped. This would explain the increasing losses in total mass balance across the 28-day sampling period.

The eMSCA noted that at the end of the 28 d incubation period this transformation product accounted for ~25% of the applied radioactivity (AR; High Dose vessels), having increased in percentage AR from the 0 d interval, if extrapolated this would continue to increase with time. As it could be attested from the other data that $^{14}CO_2$ and volatile contributions to the mass balances are increasing through the exposure period it is not unreasonable to assume that 'Unknown ~ 2.85 min' was an intermediate in the degradation route of [^{14}C]AS 100 and would therefore have started to degrade and decrease in contribution to the %AR at later sampling intervals. With the premature termination of the study the eMSCA could not determine if, or when, this would have been observed. The eMSCA re-performed the kinetics as per the FOCUS 2006:2014 guidance documents using CAKE v 3.3 software. The results are presented in the table below.

Table 17: Kinetic calculations

KINETIC CALCULATIONS USING FOCUS TO ASSESS THE DEGRADATION OF ROBAC AS100			
Compartment	DT50 (days)	DT90 (days)	DT90 / 3.32 (days)

AS 100 (FOMC)	2.06	26.2	7.89
DIXD (SFO)	1.46	4.85	N/A
Unknown ~2.52 min (SFO)	>10,000	>10,000	N/A

The transformation half-lives were calculated by the eMSCA to be 2.06 d and 1.46 d for AS 100 and DIXD, respectively. The half-life of the Unknown ~2.52 min has been calculated to be > 10,000 d (i.e. very high). This transformation half-life for Unknown ~2.52 min exceeds the thresholds for persistent and very persistent (P/vP), > 40 d and 60 d, according to REACH Annex XIII. Therefore the eMSCA concludes that the unknown transformation product in the simulation test performed with Robac AS100 is P/vP.

Up to now it was not possible to determine experimentally the chemical identity of this transformation product. The registrant claimed in a first instance that this transformation product is acetone, isopropylalcohol or carbon disulphide. In view of the observed retention time of the unknown transformation product the eMSCA is of the opinion that this claim is not very plausible. On the contrary, as the S-S bond is the least stable bond in the transformation product DIXD, it is appropriate to assume that the DIXD splits at this S-S bond and the most likely formed compound is the corresponding dithioacid ($(CH_3)_2$-CH-O-C(=S)-SH). It is believed that this assumption is much more in line with the observed retention time, but no definite conclusion can be drawn on the identity of this transformation product.

The eMSCA applied both CATALOGIC model 301C v.11.15 and EAWAG model to help predict the identity of the transformation product.

CATALOGIC model 301C v.11.15 however does not cover the chemistry relevant for predicting transformation products for these type of substances. No reliable prediction can be made for the transformation products.

As indicated in the Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.11, PBT/vPvB assessment, v3.0, page 63, the EAWAG-BBD Pathway Prediction System is a useful source of information that can help identifying potential metabolites. For the Robac AS100 constituents EAWAG-PPS cannot reliably predict the degradation pattern as the S-S-S fragment is not recognized. On the contrary for DIXD, i.e. the disulfide that is proven to be formed and degraded in the simulation study, the program predicts that the corresponding dithioacid ($(CH_3)_2$-CH-O-C(=S)-SH) is likely to be formed in aerobic circumstances. Further degradation would result in ionized compounds and very small compounds like acetone.

Summary and discussion of persistence

No data are available for photodegradation or fate in soil.

In a hydrolysis study Robac AS100 was more hydrolytically unstable at higher pH than lower pH. The reaction was considered to be pseudo-first order with a half-life of 459 hours (~15 days) at pH 7 and 8.75 hours at pH 9 at 12°C.

Robac AS100 was not readily biodegradable in an OECD 301 ready biodegradation test (15% degradation by day 28) and in an extended OECD 301 ready biodegradation study. During the extended ready biodegradation study limited mineralisation was observed - maximum 15% by day 28 and 26% by day 61. This indicates some ultimate degradation occurred.

In an aerobic surface water simulation study conducted at 12 °C, Robac AS100 underwent significant transformations and mineralisation. The eMSCA kinetic calculations indicate that the transformation DT_{50} and DT_{90} of Robac AS100 are 2.1 and 26.0 days, respectively; and the transformation DT_{50} and DT_{90} of DIXT are 1.5 and 4.9 days, respectively. The identity of the metabolite observed at ~2.85 min remains currently unknown. However, based on the observation that the S-S bond is the least stable covalent bond in DIXD, it is plausible to assume that this metabolite is the corresponding dithioacid ($(CH_3)_2$-CH-O-C(=S)-SH). This assumption is confirmed by the biocatalysis-biodegradation database model developed by Eawag. In turn this metabolite could degrade further to the thioaldehyde ($(CH_3)_2$-CH-O-C(=S)H) and other smaller compounds. Carbon dioxide measurements increased over the study period with a maximum of 25.6 % AR on day 28 while the radiolabel is situated in the most stable part of Robac AS100, i.e. the thiocarbonyl moiety.

7.7.2. Environmental distribution

Adsorption

The log K_{oc} of the tri-, tetra- and penta-S constituents of Robac AS100 were determined in a GLP study conducted according to EU Method C.19 (HPLC) (Anonymous, 2003b). The tetra and penta-S constituents eluted after the last reference substance and are presented as greater than values. The log K_{oc} for the tri-, tetra- and penta-S constituents were 5.49, >5.63 and >5.63 respectively.

The study also identified two chromatogram peaks before elution of Robac AS100 constituents. The study report concluded these were related to the DIXD degradant by injecting the substance as a reference although it is unclear why 2 peaks were observed. The corresponding log K_{oc} was not determined but the retention times lies between 2 of the reference standards with log K_{oc} values of 4.2 and 5.63.

Distribution modelling

No data.

7.7.3. Bioaccumulation

Screening data:

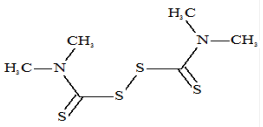
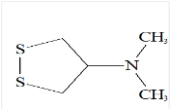
Following GLP and EU Method A.8 (HPLC), similar to OECD Test Guideline 117, the log K_{ow} of Robac AS100 (unknown component composition) was determined to be ≥5.9 at 21 °C (Anonymous, 1988a). The study report notes that traces of the test item were observed in the blank aqueous phase chromatograms. These peaks were of similar size to those observed in the test run aqueous phase chromatograms. Therefore, concentrations of the test item in aqueous phase extracts were quoted as ≤ values meaning they could be lower resulting in an increased log K_{ow} value.

Anonymous (2011b) considers the substance is within the model domain based on log K_{ow}. The REACH guidance (ECHA, 2017a) notes that the EPIWIN model may be unreliable for substances with log K_{ow} values ~6 due to a decreased relationship between BCF and log K_{ow}. Given the measured log K_{ow} for Robac AS100 is considered ≥5.9, there is likely to be uncertainty in BCF QSARs and increasingly so if higher log K_{ow} values are considered which may be appropriate given the 'greater than' experimental value.

Anonymous (2011b) considers the substance is within the structural domain of the model. The Regression equation includes a correction factor of -1.34 for the disulfide fragment in the structure. This value is influential in the BCF equation – for example removing the correction would result in a log BCF of 3.56 (BCF = 3,629 L/kg). The correction for the

disulfide is a recent inclusion in EPI Suite BCFBAF v3.01. The eMSCA has reviewed the training set which consists of two substances (refer to Table 18).

Table 18: EPI Suite training set

EPI SUITE BCFBAF V3.01 TRAINING SET SUBSTANCES WITH S-S COMPONENT						
Substance	**CAS**	**Structure**	**log K_{ow}**	**Measured BCF L/kg**	**Predicted BCF L/kg**	**Remarks**
Thioperoxydicarbonic diamide ([(H2N)C(S)]2S2), tetramethyl-	137-26-8	 MW: 240.42	1.73 (measured)	3.4	6.434	Pesticide called Thiram
4-(N,N-dimethlamino)-1,2-dithiolane	1631589	 MW:149.27	1.38 (predicted)	1.72	3.807	

These chemicals are smaller molecules than Robac AS100 and contain a single S-S component, rather than the three to five membered sulfur chain present in Robac AS100. It could be considered that the single S-S component might allow greater metabolism compared to Robac AS100 with longer sulfur chains. They also have significantly lower log K_{ow} values than the measured value of ≥5.9 available for Robac AS100. Instead the training set values are more in line with the predicted log K_{ow} value of 2.89 for Robac AS100 based on the tri, tetra and penta constituents.

Overall in the opinion of the eMSCA, this is a very limited training set for the correction factor and there is significant uncertainty in applying it. This means there is insufficient confidence in the predicted BCF value for Robac AS100 from this QSAR.

Anonymous (2011b) collates BCF data for proposed structural analogues with values ranging from 2.95 to 248.5. However, the quoted BCF values appear to be QSARs rather than measured data. While alternative QSAR methods may provide BCF values for substances with some structural similarities, they do not validate the EPI Suite BCFBAF v3.01 BCF values.

It can be considered that linear regression QSARs are not recommended for substances with log K_{ow} values >6 (ECHA, 2017a; Pavan, Worth and Natzeva, 2006) due to increased model uncertainty due to training set substances with log K_{ow} values above around 5 to 6 (due to difficulties distinguishing between truly dissolved concentrations and influences from substance concentrations absorbed to or associated with dissolved organic carbon). For substances with log K_{ow} values above 6, non-linear equations may be considered more appropriate.

Given that the experimental log K_{ow} value is a 'greater than or equal to' value and on the border of 6, the eMSCA considers a parabolic equation may be appropriate (ECHA, 2017a; Pavan, Worth and Natzeva, 2006; European Commission, 2003). On this basis, Equation 1 has been used to estimate a log BCF of 4.484 and BCF of 30,479 L/kg using a log K_{ow} of 5.9. It is unclear if this is a realistic value as hydrophobic substances can have lower BCFs than predicted by such methods.

It should be noted that an increase in log K_{ow} results in an increase in BCF to around log K_{ow} 6.9. It is not known if the Robac AS100 log K_{ow} is within the range 5.9-6.9 or above. However, the equation implies a BCF greater than 5,000 L/kg for log K_{ow} values in this range and it can't be excluded that Robac AS100 might fall within the range.

Equation 1 – Parabolic equation for substances with log K_{ow} higher than 6 and molecular weight less than 700 (ECHA, 2017a; Pavan, Worth and Natzeva, 2006; European Commission, 2003)

$$\text{Log BCF} = 0.20(\log K_{ow})^2 + 2.74\log K_{ow} - 4.72$$

The disulfide degradant DIXD has a measured log K_{ow} of 5.72 (Anonymous, 2008). It is also considered that the EPI Suite BCFBAF v3.01 linear regression equation with the disulfide correction factor may not be appropriate for DIXD given the overall lack of validation analogues in the training set. The eMSCA recognises there is one disulfide substance in the training set (CAS: 137-26-8) but the measured log K_{ow} is significantly lower at 1.73 meaning low confidence in predictions based on the training set.

As the measured log K_{ow} is below 6, the QSAR Equation 1 is not appropriate. For substances with log K_{ow} values below 6 Equation 2 is considered appropriate. This results in a log BCF of 3.72 and BCF of 5,248 L/kg for DIXD.

Equation 2 – Linear equation for substances with log K_{ow} below 5.5-6 and molecular weight less than 700 (ECHA, 2017a; Pavan, Worth and Natzeva, 2006; European Commission, 2003)

$$\text{Log BCF} = (0.85*\log K_{ow}) - 0.70$$

Overall the two methods give conflicting BCF predictions as illustrated in Table 19. The eMSCA notes the EPIWIN model limitations given the measured log K_{ow} and lack of suitable analogues in the training set. While the parabolic equation generates a significantly higher

BCF, it is unclear how valid this is for Robac AS100.

Table 19: Overview of information on bioaccumulation

SUMMARY OF INFORMATION ON BIOACCUMULATION FOR ROBAC AS100 AND DIXT			
Substance	**Method**	**Result**	**Remarks**
Robac AS100	EU Method A.8 similar to OECD 117 (HPLC)	Log K_{ow} ≥5.9 at 21 °C	Unknown component composition
Robac AS100	US EPA EPIWIN BCFBAF v3.01 using log K_{ow} input 5.9	Log BCF 2.219 BCF 165.7	Model not validated S-S correction factor included by EPIWIN
Robac AS100	Equation 1 Parabolic method	Log BCF 4.484 BCF 30,479	
Robac AS100	Equation 2 Linear method	Log BCF 4.315 BCF 20,654	
DIXD	EU Method A.8 similar to OECD 117 (HPLC)	Log K_{ow} 5.72 at 40 °C	
DIXD	US EPA EPIWIN BCFBAF v3.01 using log K_{ow} input 5.72	Log BCF 3.441 BCF 2,761	Model not validated S-S correction factor not included by EPIWIN
DIXD	Equation 2 Linear method	Log BCF 3.72 BCF 5,248	

Measured bioaccumulation data:

No experimental data are available.

Unidentified transformation product from simulation study

The key conclusion that can be drawn from the simulation study is that the parent constituents of Robac AS100 nor the DIXD transformation product meet the P criterion. However the simulation study also indicates the formation after 28 days of another major transformation product which is potentially P/vP. Up to now it was not possible to determine experimentally the chemical identity of this transformation product. The eMSCA considers that the unidentified transformation product must be a degradation product of DIXD. As the S-S bond is the least stable bond in DIXD, it is appropriate to assume that DIXD splits at this S-S bond and the most likely formed transformation product is thus the corresponding dithioacid ($(CH_3)_2$-CH-O-C(=S)-SH). This assumption is confirmed by the Biocatalysis-Biodegradation Database predictive model that is made publicly available by Eawag.

The estimated log K_{ow} value (KOWWIN v1.68) is 1.28. It is recognised that in this QSAR only an estimated coefficient is available for the thiocarbonyl moiety but the resulting value is much lower than the 4.5 threshold value and therefore it is concluded that this transformation product is unlikely to be bioaccumulative.

This conclusion is further confirmed by the observation that the unidentified degradation product elutes substantially earlier than the disulfide in the reversed phase chromatographic analysis. Indeed, with this type of column packings chemicals are retained in proportion to their log K_{ow}; the faster a compound elutes from the column the lower its log K_{ow}. This indicates that the unidentified transformation product is very unlikely to be bioaccumulative.

Summary and discussion of bioaccumulation:

Robac AS100 has a measured log K_{ow} of ≥5.9 which suggests a potential for bioaccumulation of the parent constituents.

The REACH registration update and CSR includes QSAR bioaccumulation predictions using EPI Suite BCFBAF v3.01. The eMSCA does not feel that the model is appropriate for Robac AS100 given:

(1) The high experimental log K_{ow} at the cut-off for linear regression model applicability, and

(2) A lack of validation analogues in the training set to support the (disulfide) correction factor used in the QSAR.

In contrast an estimated BCF using a parabolic equation for substances with a log K_{ow} above 6, suggests significant bioaccumulation.

Equally, the eMSCA feels the EPI Suite BCFBAF v3.01 model may not be appropriate to estimate a BCF for the hydrolysis and primary degradation product DIXD given the lack of validation analogues in the training set to support the disulfide correction factor.

The compound DIXD has an estimated BCF of ~5,000 based on linear regression.

Overall, the eMSCA considers the available predicted bioaccumulation data are uncertain, but based on the log K_{ow} value, bioaccumulation of parent constituents cannot be ruled out.

On the other hand, the eMSCA also considers that the only transformation product that is potentially P (i.e. the corresponding dithioacid) is very unlikely B.

7.7.4. Secondary poisoning

A 90-day oral toxicity study in rodents (Anonymous, 2012a) following OECD Test Guideline 408 is available. The NOAEL was considered to be 50 mg/kg bw/day. The age of the animals at study initiation was 5-8 weeks resulting in a NOEC conversion factor of 10 (based on animals ≤ 6 weeks). The CSR applied an Assessment Factor of 300 as a conservative worst case approach resulting in a secondary poisoning $PNEC_{oral}$ of 1.67 mg/kg.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

Available aquatic toxicity data are presented in Table 20 below. The acute ecotoxicity data were accepted under NONS and have not been re-reviewed for the purposes of this evaluation.

No sediment toxicity data are available.

Two additional ecotoxicity studies are included from the REACH Registration / CSR (prolonged toxicity to fish [OECD 204] and chronic toxicity to *Daphnia* [OECD 211]). These were conducted for the Chinese Chemical Notification Scheme and were not conducted to GLP, as China is not a member of the OECD. Brief details have been presented in this report, although these have not been reviewed in detail for this evaluation.

Table 20: Overview of studies on aquatic toxicity

SUMMARY OF AQUATIC TOXICITY INFORMATION				
Study	**EC_{50}/LC_{50} (mg/L)**	**$EC_{10}/NOEC$ (mg/L)**	**Remarks**	**Reference**
Short-term toxicity to fish (OECD 203): *Oncorhynchus mykiss*	96-h LC_{50}: 0.27 nominal	96-h NOEC: 0.18 nominal	Test solutions prepared with Tween 80. Accepted under NONS.	Anonymous (1988d)
Prolonged toxicity to fish (OECD 204): *Gobiocypris rarus*	/	14-d NOEC: >0.00112 based on no effects using saturated solution and analytical limit of detection	Conducted for Chinese Chemical Notification Scheme. Not GLP. Not validated under REACH. Supporting information.	Anonymous (2012b)
Short-term toxicity to aquatic invertebrates (OECD 202): *Daphnia magna*	48-h EC_{50}: 0.15 nominal	48-h NOEC: 0.056 nominal	Test solutions prepared with Tween 80. Accepted under NONS.	Anonymous (1988b)
Chronic toxicity to *Daphnia magna* (OECD 211)	21-d EC_{50} >0.00112 based on no effects using saturated solution and analytical limit of detection	21-d NOEC >0.00112 based on no effects using saturated solution and analytical limit of detection	Conducted for Chinese Chemical Notification Scheme. Not GLP. Not validated under REACH. Supporting information.	Anonymous (2012b)
Toxicity to aquatic algae and cyanobacteria (OECD 201): *Desmodesmus subspicatus* (formerly *Scenedesmus subspicatus*)	72-h E_rC_{50}: > 0.00084 Geometric mean measured	72-h NOE_rC: 0.00084 Geometric mean measured No observed effects	Accepted under NONS. Test solutions prepared with solvent and stirred for 24	Anonymous (2004a)

			hours to allow hydrolysis.	

Fish

Acute toxicity to fish (Anonymous, 1988d)

The study was submitted and accepted under NONS.

The 96 hour study used 'di-iso propyl xanthogen polysulfide' and followed OECD Test Guideline 203 with Rainbow trout (*Oncorhynchus mykiss* – previous name *Salmo gairdneri*). The study was conducted in the dark to GLP using a semi-static test system using the following nominal concentration range prepared with 20% Tween 80-tetrahydrofuran at 0.1 mL:L: solvent control, 0.10, 0.18, 0.32, 0.56 and 1.0 mg/L. Analytical verification was not undertaken and the 96 hour LC_{50} of 0.27 mg/L is based on nominal concentrations.

eMSCA comments

It is noted that treatments were considered to be dispersions (still containing undissolved material) and due to the lack of analytical verification, the LC_{50} may not be fully reliable.

Prolonged toxicity to fish (Anonymous, 2012b)

The study was conducted in China for the Chinese Chemical Notification Scheme and not to GLP.

The semi-static (renewal 3 times per week) study was conducted using a saturated solution (nominally 100 mg/L) of 'Robac AS100' prepared by stirring for 24 hours with subsequent filtration (0.45 µm), performed as a limit test.

The study used the freshwater Chinese Rare Minnow (*Gobiocypris rarus*) and followed OECD test Guideline 204. The fish species is endemic to China – the eMSCA notes differing fish species can result in different toxicity sensitivities and it is unclear how representative the study species is of fish species listed in the OECD test guideline. While appropriate temperature and test conditions are not available for the species, it is noted that no mortalities occurred in study controls. Observations of mortality, growth and weight were included. No mortalities or abnormalities were observed in control or treatment fish.

Analysis by HPLC with a limit of detection of 1.12 ng/mL did not detect the test item in any new or expired solutions. Data was analysed using one-way ANOVA and t-test - no statistical difference between control and saturated solution treatments was observed. On this basis, the Registrant considered the 14-day NOEC > 1.12 ng/mL equating to 0.00112 mg/L.

The eMSCA notes the level of saturation achieved in the study is considerably below the measured water solubility value of 0.752 mg/L. It is not known whether the water solubility is over-estimated or the ecotoxicity solutions did not reach true saturation.

The eMSCA notes the OECD 204 test method is considered a prolonged toxicity to fish test and as such is not considered as a chronic endpoint. In addition, in April 2014, the test guideline was removed by OECD. This means interpretation of endpoint data is not possible.

Aquatic invertebrates

Acute toxicity to invertebrates (Anonymous, 1988e)

The study was submitted and accepted under NONS.

The 48 hour study used 'di-iso propyl xanthogen polysulfide' (90% purity) and followed OECD Test Guideline 202 with *Daphnia magna*. The study was conducted in the dark to GLP using a static test system using the following nominal concentration range prepared with 20% Tween 80-tetrahydrofuran at 0.1 mL:L: solvent control, 0.010, 0.018, 0.032, 0.056, 0.10, 0.32, 0.56 and 1.0 mg/L. Analytical verification was not undertaken and the 48 hour LC_{50} of 0.15 mg/L is based on nominal concentrations with 95% confidence limits of 0.12 – 0.19 mg/L.

eMSCA comments

It is noted that treatments were considered to be dispersions and due to the lack of analytical verification, the LC_{50} may not be fully reliable.

Chronic toxicity to Invertebrates (Anonymous, 2012c)

The study was conducted in China for the Chinese Chemical Notification Scheme and not to GLP.

The semi-static (renewal 3 times per week) study was conducted using a saturated solution of 'Robac AS100' (97.88% purity), performed as a limit test. The study report only states that the test item was dissolved in the test medium and indicates a filtrate was used. Given the study was conducted at the same laboratory at the same time as the prolonged toxicity to fish study, it is possible that treatment solutions were prepared in a similar manner, i.e. 100 mg/L nominal concentrations with 24 hours stir and 0.45 µm filtration.

The study used *Daphnia magna* and followed OECD test Guideline 211. Test guideline validation criteria were met. No aborted eggs or dead offspring were observed during the study. Mortality of the parent animals in the control group was 10% and within validation criteria.

Analysis by HPLC with a limit of detection of 1.12 ng/mL did not detect the test item in any new or expired solutions. The study report concluded the 21-d EC_{50} for mortality and reproduction was above the limit of detection of 1.12 ng/mL equating to 0.00112 mg/L. Additional endpoints such as growth information were not included. The study report did not quote a study 21-d NOEC for any endpoint. Considering the raw data, it is unclear if there was a statistical difference for the different endpoints between the study control and saturated solution treatment.

eMSCA comments

Similar to the prolonged fish test, the level of saturation achieved in this study is considerably below the measured water solubility value of 0.752 mg/L. It is not known whether the water solubility is over-estimated or the ecotoxicity solutions did not reach true saturation.

Algae and aquatic plants

Algal growth inhibition (Anonymous, 2004a)

The study was submitted and accepted under NONS.

The 72 hour study used 'di-iso propyl xanthogen polysulfide' and followed OECD Test Guideline 201 with *Desmodesmus subspicatus* (formerly *Scenedesmus subspicatus*). The study was conducted under constant illumination according to GLP using a static test system using a limit test concentration of 0.1 mg/L prepared with the aid of dimethylformamide (DMF). Analytical verification was undertaken using samples untreated and after centrifugation. No effects were observed and the 72 hour E_rC_{50} was considered >0.00084 mg/L based on geometric mean measured concentrations of the test item in centrifuged samples. The corresponding NOE_rC was 0.00084 mg/L.

Sediment organisms

No available data.

Other aquatic organisms

No additional data available.

7.8.2. Terrestrial compartment

An acute toxicity to earthworms (*Eisenia fetida*) study (Anonymous, 2011c) is included in the REACH Registration.

This was conducted for the Chinese Chemical Notification Scheme and was not according to GLP. It has not been reviewed by the eMSCA. The quoted 14-d LC_{50} (mortality) was >1,000 mg/kg dw based on nominal concentrations. A NOEC does not appear to have been derived.

7.8.3. Microbiological activity in sewage treatment systems

An Activated Sludge Respiration Inhibition Test (ASRIT) is available (Anonymous, 2004b) with a 3 hour IC_{50} >1000 mg/L (nominal) and 3 hour NOEC of 1000 mg/L.

7.8.4. PNEC derivation and other hazard conclusions

Table 21: PNEC derivation

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	PNEC aquatic (freshwater): 0.00015 mg/L	Assessment factor: 1000 using the acute toxicity to invertebrates 48 hour EC_{50} of 0.15 mg/L
Marine water	PNEC aquatic (marine waters): 0.000015 mg/L	Assessment factor: 10000 using the acute toxicity to invertebrates 48 hour EC_{50} of 0.15 mg/L
Sediments (freshwater)	PNEC sediment (sediment freshwater): 1.4 mg/kg wet weight (6.5 mg/kg dry weight)	Assessment factor: derived by equilibrium partitioning method using EUSES

Sediments (marine water)	PNEC sediment (sediment marine water): 0.14 mg/kg wet weight (0.65 mg/kg dry weight)	Assessment factor: derived by equilibrium partitioning method using EUSES
Sewage treatment plant	PPNEC (STP): 100 mg/L	Assessment factor: 10 using the 3 hour IC_{50} of >1000 mg/L
Soil	PNEC (soil): 1.5 mg/kg wet weight (1.3 mg/kg dry weight)	Assessment factor: derived by equilibrium partitioning method using EUSES
Secondary poisoning	PNEC oral (secondary poisoning): 1.67 mg/kg food	Assessment factor: 300

It is noted that the Registrant's environmental PNECs are higher than those calculated by the eMSCA. It is recommended that the Registrant updates its PNECs and uses these values in its CSR, and in the environmental exposure assessment.

7.8.5. Conclusions for classification and labelling

The available data support the harmonised hazard classification.

7.9. Human Health hazard assessment

Although this evaluation was targeted on the environment it was noted that new mammalian toxicity studies had become available since the last assessment under NONS. These were:

- Acute inhalation study in rats (OECD 403) - The LC_{50} in females was 4.56 mg/L which meets the criteria for classification Acute Tox. 4 (H332). Applying this classification was recommended to the Registrant.
- 90-day study (OECD 408) – No adverse effects meeting the classification criteria. NOAEL 50 = mg/kg bw/d.
- Reproduction/developmental toxicity screening test (OECD 421) oral, rat - No adverse effects meeting the classification criteria. NOAEL = 50 mg/kg bw/d.
- Prenatal developmental study (OECD 414) oral, rat - No adverse effects meeting the classification criteria. NOAEL = 23 mg/kg bw/d.

The eMSCA considers that the new studies did not flag up any additional concerns and concluded that the DNELs can be calculated from a starting point of 50 mg/kg bw/d from the 90-day study. This gives the long-term DNELs by the inhalation and dermal routes for workers as 1.76 mg/m^3 for inhalation and 0.5 mg/kg bw/d for dermal exposure.

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

The available data supports the harmonised classification for human health however, the eMSCA recommends that additional classification, Acute Tox. 4 (H332), should be applied.

7.11. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.12. PBT and vPvB assessment

Annex XIII of the REACH Regulation states that PBT/vPvB assessment shall take account of the PBT/vPvB properties of relevant constituents of a substance and relevant transformation and/or degradation products.

Persistence:

Robac AS100 was not readily biodegradable in an OECD 301 test on the basis of between 10 and 15% mineralisation by day 28 based on oxygen depletion.

Hydrolysis of Robac AS100 was observed in an OECD 111 study with a half-life of 8.75 hours at pH 9, 12 °C and 459 hours at pH 7, 12 °C. The hydrolysis products were DIXD and sulfur. The principle degradant was identified as DIXD with sulfur as an additional hydrolysis product. DIXD was observed to increase through the test indicating the rate of hydrolysis of DIXD is slower that the rate of formation.

An extended ready biodegradation study using Robac AS100 in a silicone preparation to minimise hydrolysis of parent substance is available. This showed limited mineralisation (26%) over 61 days. Furthermore, only small amounts of DIXD were detected.

In a radiolabeled aerobic mineralisation in surface water study conducted at 12 °C, Robac AS100 underwent significant primary degradation and mineralisation. The primary degradation DT_{50} was 3 days and DT_{90} was 24 days. Significant mineralisation was also observed and carbon dioxide measurements increased over the study period with a maximum of 25.6 % AR on day 28. Also, the primary degradation product DIXD is broken down rather quickly with a calculated DT_{50} of 1.46 days. In the simulation test one unidentified transformation appeared in a substantial amount and it was impossible to establish its DT_{50} value. Therefore, this unidentified transformation product is probably P and vP. On the contrary, the parent constituents of Robac AS100 or DIXD do not meet the P criterion.

Bioaccumulation:

The substance screens as B based on measured log K_{ow} values above 4.5 for the parent constituents of Robac AS100 and the primary degradant DIXD.

The Registrant has submitted QSAR predictions indicating the substance has low bioaccumulation potential (BCF <500). However, the eMSCA has been unable to validate the QSAR. By contrast, BCF prediction by alternative methods indicates bioaccumulation may be above the REACH Annex XIII BCF thresholds of 2,000 and 5,000 L/kg for B and vB. This contradiction means a reliable QSAR prediction is not available for the parent constituents of Robac AS100 at present.

It is important to note that the eMSCA concludes that the currently unidentified transformation product that is potentially P and vP is unlikely to meet the B criterion.

Toxicity:

Toxicity was observed in the three acute ecotoxicity studies (lowest result: EC_{50} = 0.15 mg/L). Due to the current chronic toxicity data gaps for the parent and degradant, it cannot be concluded if the environmental T crit erion is met or not. However, because neither the parent constituents, nor the unidentified degradation product meets both the P and the B criterion, this is a low priority to address for the purposes of the PBT assessment.

The substance is not classified for relevant human health toxicity for repeated dose, carcinogenicity, mutagenicity or reproductive toxicity.

Overall conclusion:

The eMSCA concludes that Robac AS100 is not a PBT/vPvB substance.

7.13. Exposure assessment

The environmental exposure has not been reviewed as the PBT/vPvB concern was not confirmed.

The human health exposure assessment has not been evaluated but the eMSCA provided initial quality observations to the registrants by e-mail (Unpub. 2019b).

7.14. Risk characterisation

Not reviewed as the concern evaluated in this Substance Evaluation was PBT/vPvB.

7.15. References

Environment Agency UK (2013) Review of the BCFBAF model within EPIWEB v4. Environment Agency UK. Unpublished report.

European Chemical Agency (ECHA) (2017a) Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7c: Endpoint specific guidance. Version 3.0 – June 2017.

European Chemical Agency (ECHA) (2017b) Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment. Version 3.0 – June 2017.

European Chemical Agency (ECHA) (2019) https://echa.europa.eu/registration-dossier/-/registered-dossier/5085. Last updated 14-July-2019 and accessed 25-September-2019.

European Commission (EC) (2003). Technical Guidance Document in Support of Commission Directive 93/67/EEC on risk assessment for new notified substances and commission regulation (EC) No. 1488/94 on risk assessment for existing substances.

FOCUS (2014) Generic guidance for estimating persistence and degradation kinetics from environmenta fate studies on pesticides in EU registration. The report on which this document is based is that of the FOCUS Degradation Kinetics workgroup, which is an official guidance document in the context of 91/414/EEC and Regulation (EC) No 1107/2009 [full citation is FOCUS (2006) "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration" Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0, 434 pp]. This document does not replace the official FOCUS report.

Pavan, M., Netzeva, T.I. and Worth, A.P. (2006). EUR Technical Report 22327 EN. Review of QSAR Models for Bioconcentration. Ispra, Italy.

7.16. Abbreviations

B	Bioaccumulative
BCF	Bioconcentration factor
CLP	Classification, labelling and packaging (of substances and mixtures)
CoRAP	Community Rolling Action Plan
CSR	Chemical Safety Report
d	Day
DMEL	Derived Minimal Effect Level
DNEL	Derived No Effect Level
DSD	Dangerous Substances Directive
ECETOC TRA	European Centre for Ecotoxicology and Toxicology of Chemicals Targeted Risk Assessment
ECHA	European Chemicals Agency
EPA	Environmental Protection Agency
ES	Exposure Scenario
ERC	Environmental release category
EU	European Union
FSDT	Fish Sexual Development Test
GC	Gas chromatography
GC/FID	Gas chromatography – Flame Ionisation Detection
GC/MS	Gas chromatography – mass spectrometry
GLP	Good laboratory practice
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database
IUPAC	International Union of Pure and Applied Chemistry
K_{oa}	Octanol-air partition coefficient
K_{oc}	Organic carbon-water partition coefficient
K_{ow}	Octanol-water partition coefficient
LEV	Local Exhaust Ventillation
LOD	Limit of detection
LOQ	Limit of quantitation
MS	Mass spectrometry
MSCA	Member State Competent Authority
m/z	Mass to charge ratio
NOAEL	No observed adverse effect level
NOEC	No-observed effect concentration
NOEL	No observed effect level
OC	Operational condition

OECD	Organisation for Economic Co-operation and Development
p	Statistical probability
P	Persistent
PBT	Persistent, Bioaccumulative and Toxic
PC	Product category
pKa	Acid dissociation constant
PNEC	Predicted no effect concentration
PPE	Personal Protective Equipment
PROC	Process Category
QSAR	Quantitative structure-activity relationship
r^2	Correlation coefficient
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals (EU Regulation No. 1907/2006)
RCR	Risk characterisation ratio
RMM	Risk Management Measures
RPE	Respiratory protective equipment
T	Toxic (hazard classification)
TG	Test Guideline
UK	United Kingdom
UV	Ultraviolet
vB	Very bioaccumulative
vP	Very persistent
vPvB	Very persistent and very bioaccumulative