Justification for the selection of a substance for CoRAP inclusion

Substance Name (Public Name):	O,O,O-triphenyl phosphorothioate
Chemical Group:	
EC Number:	209-909-9
CAS Number:	597-82-0
Submitted by:	Bureau REACH on behalf of the Ministry of Infrastructure and the Environment as the Competent Authority of the Netherlands
Date:	17/03/2015

Note

This document has been prepared by the evaluating Member State given in the CoRAP update.

Contents

1 IDENTITY OF THE SUBSTANCE

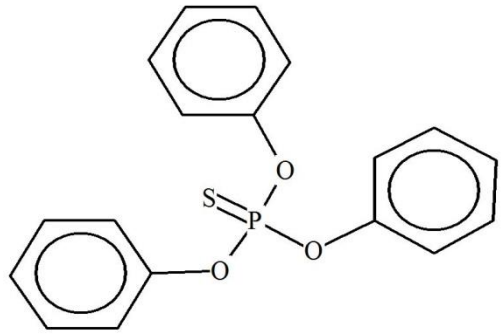
1.1 Other identifiers of the substance

Table 1: Substance identity

EC name:	O,O,O-triphenyl phosphorothioate
IUPAC name:	O,O,O-triphenyl thiophosphate
Index number in Annex VI of the CLP Regulation	
Molecular formula:	$C_{18}H_{15}O_3PS$
Molecular weight or molecular weight range:	342.3487
Synonyms/Trade names:	*Phosphorothioic acid, O,O,O-triphenyl ester; Phenyl phosphorothioate, ((PhO)3PS); Triphenyl thiophosphate; tris(phenoxy)-sulfanylidenephosphorane*

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

Structural formula:



1.2 Similar substances/grouping possibilities

The current substance has (a strong) interference or similarity with other substances which are already listed on the CoRAP or which are already in the process of substance evaluation:

- Tris(methylphenyl)phosphate (EC 215-548-8, CoRAP 2014, NL)
- Triphenyl phosphite (EC 202-908-4, CoRAP 2013, UK)
- Since it is main constituent of a mixture of: triphenylthiophosphate and tertiary butylated phenyl derivatives (EC 421-820-9, CoRAP 2016, UK).

2 CLASSIFICATION AND LABELLING

2.1 Harmonised Classification in Annex VI of the CLP

Not classified.

2.2 Self classification

- In the registration:

  Aquatic Chronic 4, H413: May cause long lasting harmful effects to aquatic life.

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:

  Repr. 2, H361: Suspected of damaging fertility or the unborn child.

  Aquatic Chronic 3, H412: Harmful to aquatic life with long lasting effects.

2.3 Proposal for Harmonised Classification in Annex VI of the CLP

Not applicable.

3 INFORMATION ON AGGREGATED TONNAGE AND USES

From ECHA dissemination site		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☐ 100 – 1000 tpa
☒ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	☐ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential

☒ Industrial use	☒ Professional use	☒ Consumer use	☐ Closed System

During manufacture of the substance opportunity for exposure arises as closed and non-closed processes are used. Substance is transferred to vessels in dedicated and non-dedicated facilities. The substance is used as laboratory reagent, and added to lubricant additives, lubricants and greases. The lubricants and greases are used in vehicles, machinery and open systems by consumers, professionals and at industrial sites. For the industrial and professional uses the open systems are further specified as high temperature/ high energy open systems. Taking all together, wide dispersive use and emissions are expected.

4 OTHER COMPLETED/ONGOING REGULATORY PROCESSES THAT MAY AFFECT SUITABILITY FOR SUBSTANCE EVALUATION

☐ Compliance check, Final decision	☐ Dangerous substances Directive 67/548/EEC
☐ Testing proposal	☐ Existing Substances Regulation 793/93/EEC
☐ Annex VI (CLP)	☐ Plant Protection Products Regulation 91/414/EEC
☐ Annex XV (SVHC)	☐ Biocidal Products Directive 98/8/EEC ; Biocidal Product Regulation (Regulation (EU) 528/2012)
☐ Annex XIV (Authorisation)	☐ Other (provide further details below)
☐ Annex XVII (Restriction)	
No data.	

5 JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

5.1 Legal basis for the proposal

☒ Article 44(2) (refined prioritisation criteria for substance evaluation)

☐ Article 45(5) (Member State priority)

5.2 Selection criteria met (why the substance qualifies for being in CoRAP)

☐ Fulfils criteria as CMR/ Suspected CMR

☐ Fulfils criteria as Sensitiser/ Suspected sensitiser

☐ Fulfils criteria as potential endocrine disrupter

☒ Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB

☒ Fulfils criteria high (aggregated) tonnage (*tpa > 1000*)

☐ Fulfils exposure criteria

☐ Fulfils MS's (national) priorities

5.3 Initial grounds for concern to be clarified under Substance Evaluation

Hazard based concerns		
CMR ☐C ☐M ☐R	Suspected CMR[1] ☐C ☐M ☐R	☐ Potential endocrine disruptor
☐ Sensitiser	☐ Suspected Sensitiser[1]	
☐ PBT/vPvB	☒ Suspected PBT/vPvB[1]	☐ Other (please specify below)
Exposure/risk based concerns		
☐ Wide dispersive use	☐ Consumer use	☐ Exposure of sensitive populations
☐ Exposure of environment	☐ Exposure of workers	☐ Cumulative exposure
☐ High RCR	☐ High (aggregated) tonnage	☐ Other (please specify below)

The substance meets the P screening criteria. Hydrolysis of the substance occurs slowly at environmentally relevant conditions with DT50 values at 12 °C amounting to 284, 270, and 57 days, at pH 4, 7 and 9, respectively. The substance is not readily biodegradable with degradation after 29 days amounting to 17.8-19.3% based on CO_2 measurements, and 39.2-48.5% based on residual measurements (% AR). The substance is also not inherently biodegradable, as after 28 days degradation amounted to 59.5-66.8% based on residual measurements (LSC analysis of AR). To conclude on P/vP, one or more simulation studies are needed. The registrant concluded based on read-across to a BCF study with a multi-constituent substance that the substance meets the B criterion. The evaluating MSCA considers this study insufficient to conclude that the substance will not meet the vB criterion. A BCF study with the registered substance is thus needed to conclude on B/vB. There is insufficient toxicity data with the substance to conclude on the T criterion, i.e. long-term toxicity to aquatic organisms is not available, and mammalian toxicity data is based on read-across.

Persistence:
Substance is not considered rapidly hydrolysable at environmentally relevant conditions. GLP-compliant hydrolysis study according to OECD TG 111 was available. Recalculation to 12 °C, which is the default value used in current risk assessment reflecting the average environmental conditions in the EU, yielded DT50 values of 284, 270, and 57 days, at pH 4, 7 and 9, respectively. Thus even at pH 9 where hydrolysis occurs most rapidly, the P criterion (DT50 >40 days in fresh water) is exceeded, while the vP criterion (DT50 >60 days in fresh water) is almost met.

Substance is not considered readily biodegradable. Two CO_2 evolution tests (OECD TG 301B) were available. The first study showed no biodegradation (0-2% after 29 days). However, this study is not considered reliable as the tested concentrations (10 and 20 mg/L) were much higher than the water solubility of O,O,O-triphenyl phosphorothioate (0.020 mg/L at 20°C, pH 7). The second CO_2 evolution test was GLP compliant and was conducted with 0.26 µg/L ^{14}C-labbeled O,O,O-triphenyl phosphorothioate. After 29 days, degradation amounted to 17.8-19.3% based on CO_2 measurements, and 39.2-48.5 % based on residual measurements (% AR). Since degradation was below 60%, the substance is considered not to be ready biodegradable.

Substance is not considered inherently biodegradable. GLP compliant Zahn-Wellens test (OECD TG 302B) was conducted with 0.26 µg/L ^{14}C-labbeled O,O,O-triphenyl phosphorothioate. After 28 days, degradation amounted to 59.5-66.8% based on residual measurements (LSC analysis of AR). Degradation based on O_2 demand was not reported. Registrant noted that the test item concentration was too low for DOC

[1] CMR/Sensitiser: known carcinogenic and/or mutagenic and/or reprotoxic properties/known sensitising properties (according to CLP harmonized or registrant self-classification or CLP Inventory)
Suspected CMR/Suspected sensitiser: suspected carcinogenic and/or mutagenic and/or reprotoxic properties/suspected sensitising properties (not classified according to CLP harmonized or registrant self-classification)
Suspected PBT: Potentially Persistent, Bioaccumulative and Toxic

measurements. Considering the solubility, a higher concentration (up to 20 µg/L) could have been tested. Nevertheless, this study is considered reliable, and as the measured degradation was below 70%, the substance is considered not to be inherent biodegradable.

Simulation studies in water/sediment and soil were waived.

Thus, O,O,O-triphenyl phosphorothioate is considered to meet the P screenings criteria. To conclude on P/vP, one or more simulation studies should be requested during substance evaluation.

Bioaccumulation:
A log k_{OW} of 5 (23 °C; pH 6.4), which is above the B screen criterion of 4.5, was estimated using the HPLC method (OECD TG 117). It should be noted that the reference substances were not specified and it could not be determined if the log k_{OW} was obtained by extrapolation. Two QSAR estimates were included, i.e. 4.9 (ACD/labs v11.02) and 6.5 (KOWWIN v4.0). The evaluating MSCA additionally estimated a log k_{OW} of 5.98 (Marvin v6.2.2.). Thus, considering that two out of three QSARs estimate a considerably higher log k_{OW} and that HPLC method is only suitable for screening, the log k_{OW} should be determined with the slow-stirring method (OECD TG 123) that allows accurate determination up to a log k_{OW} of 8.2. This should be requested during CCH.

Nevertheless, as the log k_{OW} certainly exceeds 3.5 a BCF study with fish is mandatory (9.3.2.). The registrant did not perform a BCF study with the registered substance. Instead read-across was proposed with the multi-constituent substance named 'a mixture of triphenylthiophosphate and tertiary butylated phenyl derivates' (CAS 192268-65-8). BCF values for O,O,O-triphenyl phosphorothioate, which is a major constituent (29.2% w/w), ranged between 641 and 2508. The registrant concluded that O,O,O-triphenyl phosphorothioate meets the B criterion, but not the vB criterion. The evaluating MSCA considers the read-across approach in principle acceptable, but notes that the BCF study has several shortcomings. The study was GLP, but not according to OECD TG 305, i.e. common carp (length start 10 cm; weight start 26.4 g; weight at end 30 g) was exposed in a flow-through system for 56 days followed by a depuration time of 7 days in fresh water. Test substance was not radio-labelled. The two tested concentrations, i.e. 0.5 and 0.05 mg /L (w/v), were above the water solubility of O,O,O-triphenyl phosphorothioate which is 0.020 mg/L at 20 °C at pH 7. The study reports that sampling was conducted on day 7, 14, 21, 28, 42 and 56 of exposure and day 7 of depuration, and that following dichloromethane extraction concentrations of each individual constituent were determined by GC. However, measurement data in fish or water were not included in the report, and BCF values could not be verified. In addition, there is no mentioning of lipid content and it remains unclear if the BCF values were corrected to 5% lipid content. Conclusion, based on this study it cannot be concluded that O,O,O-triphenyl phosphorothioate does not meet the vB criterion. Therefore, during the substance evaluation a new BCF study should be requested that is to be conducted according to OECD TG 305 with radio-labelled O,O,O-triphenyl phosphorothioate.

Toxicity:
Aquatic toxicity tests are complicated by the low water solubility of O,O,O-triphenyl phosphorothioate. Three aquatic toxicity tests were reported, i.e. short-term toxicity to daphnia (OECD TG 202), short-term toxicity to zebra fish (OECD TG 203) tests, and a toxicity to algae test (OECD TG 201). All tests were performed as limit tests with a saturated solution. Solution was prepared by stirring 100 mg test substance per L water for 3 to 4 days (without the use of a solvent). Subsequently it was filtered and used as test solution. The actual concentrations were not determined (only noted that below LoQ (<0.1 mg test substance/L). The effect concentrations were reported as >100 mg/L. These effect concentrations are not reliable, but they do indicate that acute toxicity to aquatic organisms is probably limited. For algae, a NOEC of >100 mg/L was also reported. This NOEC is considered unreliable. Long-term toxicity to fish and aquatic invertebrates was not available. Therefore, it cannot be excluded that they will meet the $T_{environment}$ criterion even though it seems unlikely. Substance does not meet the $T_{mammalian}$ criterion, as it is not classified as CMR or STOT RE. However, the toxicological studies that are relevant for classification of the substance as CMR or STOT RE (Ames assay, Chromosome aberration assay, Mammalian gene mutation HPRT assay, Reproduction/Developmental toxicity screening test, Repeated dose toxicity study) were conducted with the multi-constituents substance that contains O,O,O-triphenyl phosphorothioate (CAS 192268-65-8). Thus, it cannot be excluded that O,O,O-triphenyl phosphorothioate meets the T criterion.

Human Health toxicity:
The read-across substance which has been used for gentoxicity, reproduction toxicity and repeated dose toxicity (as mentioned above) is a multi-constituent, which contains for 31% O,O,O-triphenyl phosphorothioate. The remaining part of the substance is a mix of mono-, di-, tri- and tetra-butylated triphenylthiophosphates. All gentox tests are negative. In addition, an Ames test of less quality has been performed with O,O,O-triphenyl phosphorothioate, which is also negative. There are no data on carcinogenicity, but these are also not required given the absence of effects in the genotoxicity studies.

With respect to repeated dose toxicity and reproduction toxicity 3 studies are available:

1) A 28-day (OECD 407) with above described read-across substance, Klimisch score 2
2) A OECD 421, (Reproduction / Developmental Toxicity Screening Test) with O,O,O-triphenyl phosphorothioate, (No data on test substance identity and purity, Klimisch score 4, TSCA 2010)
3) A OECD 422, (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test) with the read-across substance, Klimisch score 2

In the OECD 421 (Klimisch score 4) repro effects (decreased viability in offspring) have been observed, which have not been observed in the OECD 422. For this reason the registrant proposes to perform a one-generation toxicity study (OECD TG 443) with O,O,O-triphenyl phosphorothioate. The read-across seems appropriate, since 31% of the actual substance is included next to 69% of structurally close-related substances. Based on these data there seems no basis for concern with respect to reproduction toxicity of O,O,O-triphenyl phosphorothioate. The repeated dose toxicity studies do not demonstrate effects that require classification.

Conclusion: no indications for concern with respect to mutagenicity, carcinogenicity, reproduction toxicity or STOT.

Conclusion:
Substance meets P screen and definitive B criterion. Insufficient data to conclude on T criterion; **Potential PBT/vPvB**. Proceed with CoRAP.

5.4 Preliminary indication of information that may need to be requested to clarify the concern

☒ Information on toxicological properties	☒ Information on physico-chemical properties
☒ Information on fate and behaviour	☐ Information on exposure
☒ Information on ecotoxicological properties	☐ Information on uses
☐ Information ED potential	☐ Other (provide further details below)

5.5 Potential follow-up and link to risk management

☐ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)