Justification Document for the Selection of a CoRAP Substance

EC/List number	CAS RN	Public Substance name	Chemical structure	Registration type (t/y) [1]
300-340-2	93925-38-3	2-Propenoic acid, methyl ester, reaction products with mixed O,O-bis(branched and linear pentyl and iso-Bu) phosphorodithioates	-	Full ≥ 10 to < 100

Authority: Swedish Chemicals Agency

Date: 21 March 2023

Revision history

Version	*Date*

Cover Note

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

[1] Note that the total aggregated tonnage band may be available on ECHA's webpage at https://echa.europa.eu/information-on-chemicals/registered-substances

1. Background

1.1 Analogue substances

2-Propenoic acid, methyl ester, reaction products with mixed O,O-bis(branched and linear pentyl and iso-Bu) phosphorodithioates (EC 300-340-2), hereinafter "the Substance", is a member of the group "Thio alkyl acids and esters of dialkyldithiophosphates" assessed by ECHA in 2022.

Link to the assessment of regulatory needs (ARN) report: Assessment of regulatory needs list - ECHA (europa.eu)

ECHA grouped together structurally similar substances based on the presence of the alkylated dithiophosphate moiety. This group is structurally related (because of the dithiophosphate moiety) to the group dialkyl (and diaryl) dithiophosphates (DDP) for which potential PBT properties have been identified for 3 members and data generation is either proposed or already ongoing, and to the group zinc dialkyl (and diaryl) dithiophosphates (ZDDP) for which an assessment of regulatory needs is planned in the future.

The group "Thio alkyl acids and esters of dialkyldithiophosphates" consists of 9 substances, 6 are identified as mono-constituent (though one of them, having chiral centers should be considered to be more complex, i.e., multi-constituents) and 3 as UVCB.

Based on the ARN report, there is a concern for ED properties for the Substance and also for the analogue substance listed in the table below.

EC/List number	CAS RN	Public Substance name	Chemical structure	Registration type (t/y)
Not available	-	2-Propenoic acid, ethyl ester, reaction products with mixed substituted alkyl esters of phosphorodithioic acid and propylene oxide	-	Full ≥ 100 to < 1 000

1.2 Overview of ongoing / completed / other processes & other EU legislation

EC / List number	Evaluation			CLH	Restriction	Authorisation
	CCH	TPE	Previously on CoRAP	Annex VI (CLP)	Annex XVII*	Candidate List/ Annex XIV
300-340-2	-	-	-	-	-	-

**Some of the broad restriction entries in the Annex XVII of REACH are not represented in the overview, e.g. when the scope of the restriction is defined by its classification or the substance identification is broad (e.g. entries 3, 28-30 and 40)*

EC / List number	Other EU legislation	Previous legislation	Stockholm convention	Other
	PPP/ BPR	NONS/ RAR	POP	(e.g. UNEP)
300-340-2	-	-	-	-

2. Classification

Not classified.

3. Tonnage and uses

3.1 Aggregated Tonnage

EC/ List No	Aggregated tonnage (as per ECHA dissemination website)* §
300-340-2	≥ 10 to < 100 t/y

** The total tonnage band has been calculated by excluding the intermediate uses,- See also the Manual for Dissemination and Confidentiality under REACH (section 2.6.11): https://echa.europa.eu/documents/10162/22308542/manual_dissemination_en.pdf/7e0b87c2-2681-4380-8389-cd655569d9f0*

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3.2 Overview of the Uses

The Substance is used in the formulation of lubricants or other technical fluids (e.g. hydraulic fluid, metalworking fluid) used by industrial and professional workers as well as consumers. Based on the information in the registrations, all group members (Thio alkyl acids and esters of dialkyldithiophosphates) registered according to Article 10 have a homogenous use profile.

Overall, there is a high potential for release to the environment and exposure for professional workers and consumers. Furthermore, exposure in the industrial setting is also considered likely due to high energy open processes and use of air dispersive techniques (e.g., industrial spraying).

Main types of applications	EC 300-340-2 Key information
Industrial use	Washing and cleaning products Lubricants, greases Metal working fluids
Professional use	Washing and cleaning products Lubricants, greases Metal working fluids Indoor and outdoor use as processing aid
Consumer Use	Lubricants, release products indoor and outdoor use as processing aid
Article service life	-
Intermediate use (if TII)	-
Formulation	Laboratory chemical

4. Justification for inclusion on the CoRAP

4.1 Legal basis

☒ Article 44(2)[2]

☐ Article 45(5)[3]

4.2 Identification of initial grounds of concern

Hazard-based concerns	
Suspected CMR	☐ Carcinogenic ☐ Mutagenic ☐ Reproductive toxicant
Potential ED	☒ Human Health ☒ Environment
Suspected Sensitiser	☐ Respiratory ☐ Skin
Specific target organ toxicity – repeated (STOT RE)	☐ (as defined in section 4.3 below)
Suspected PBT/ vPvB Suspected PMT/ vPvM	☐ Persistent ☐ Bioaccumulative ☐ Mobile ☐ Toxic (as defined in section 4.3 below) ☐ very Persistent ☐ very Bioaccumulative ☐ very Mobile
Other human health hazard(s)	☐ (as defined in section 4.3 below)
Other environmental hazard(s)	☐ (as defined in section 4.3 below)
Exposure / risk-based concerns	
Wide dispersive use	☒
Consumer use	☒
Exposure of workers	☒
Exposure of sensitive populations	☒
Exposure of environment	☒
Cumulative exposure	☐
High RCR	☐
High (aggregated) tonnages	☐
Others (to be specified)	☐

[2] "The Agency shall use the criteria in paragraph 1 […]. Substances shall be included if there are grounds for considering (either on the basis of a dossier evaluation carried out by the Agency or on the basis of any other appropriate source, including information in the registration dossier) that a given substance constitutes a risk to human health or the environment."

[3] "A Member State may notify the Agency at any time of a substance not on the Community rolling action plan, whenever it is in possession of information which suggests that the substance is a priority for evaluation. […]".

4.3 Justification of the concern(s) – to be clarified under Substance evaluation

Existing data supporting the hazard-based concern

Available information in the registration

Repeated dose toxicity studies

A 28-day toxicity study (OECD TG 407) with the Substance is available (2013). Rats were dosed by gavage at 30, 300 and 750 mg/kg bw/day. At 750 mg/kg bw/day body weight gain was lower during the last two weeks of treatment and the first week of the recovery period. Erythrocyte count, haemoglobin, haematocrit and mean cell haemoglobin concentration were lower at 750 mg/kg bw/day. At 300 and 750 mg/kg bw/day, dose-related and statistically significant increases in absolute and relative liver and thyroid weights were apparent for both sexes. At 750 mg/kg bw/day, centrilobular hypertrophy for the liver and follicular cell hypertrophy for the thyroid was reported.

Another 28-day repeated dose toxicity study in rats exposed via gavage is available (1988). Doses were 50, 158 and 500 mg/kg bw/day. Increased kidney and liver weights was reported in this study. It is not reported if thyroid weights were analysed in this study.

Also, a reproductive/developmental toxicity screening study (OECD TG 421) with the Substance is available (2016). Rats were treated at 200, 400 and 800 mg/kg bw/day by oral gavage. At 800 mg/kg bw/day, there was an increase in the appearance of vacuolated/pale cells in the pituitary. Analysis of the thyroid weight or histopathology were not reported (study summary available on ECHA's dissemination site).

The Registrant considers that these vacuolated cells probably reflect hypertrophy of thyroid-stimulating hormone-producing cells (thyrotrophs), a common finding following administration of liver enzyme inducers where the underlying mechanism is considered to be increased hepatic clearance of thyroid hormones followed by a compensatory increase in the pituitary secretion of TSH. According to the Registrant, this correlates with changes in the liver and thyroid gland noted in the 28-day study and it is the most likely explanation for the change.

In the SE MSCA view, based on the observed changes in thyroid weight and histopathology there is a concern for ED properties of the Substance. However, available data are not sufficient to conclude on this concern.

The Substance is considered as a potential endocrine disruptor for human health due to effects on the thyroid and the pituitary. Based on ECHA's assessment of the available information, there is a concern for ED properties also for the similar substance "2-Propenoic acid, ethyl ester, reaction products with mixed substituted alkyl esters of phosphorodithioic acid and propylene oxide" (no EC number available).

No data are available indicating environmental ED properties. However, the potential ED concern for human health, if confirmed, may be equivalently applicable for other species in the environment.

Other relevant information to justify the inclusion in CoRAP

The SE MSCA notes that there is an "additional concern" for bioaccumulation for the substance.

According to the data in the registration, the substance has 14 constituents. Several of

these constituents have a high log Kow (>4,9).

Information to be potentially requested

Further information is needed to clarify the concern for ED properties, i.e. potential toxicity of the Substance to the thyroid pathway.

Available validated in-vitro and/or in-vivo tests for the thyroid pathway could be requested to assess potential endocrine activity of the Substance. Moreover, lower tier or short-term tests could inform on choice for which higher tier studies would be needed.

Potentially, a LAGDA (OECD TG 241) could be requested under SEV to address the effects of the Substance on the thyroid pathway. If toxicity to the thyroid is confirmed data may clarify the ED concern for both HH and ENV.

BCF studies may be needed to address potential bioaccumulation concern for the Substance.

If read-across to the data for the similar substance "2-Propenoic acid, ethyl ester, reaction products with mixed substituted alkyl esters of phosphorodithioic acid and propylene oxide" is proposed, sufficient information to justify the read-across will be needed.

***Possible follow-up** (demonstrating the improvement of risk management measures)*

EC/ List number	Harmonised C&L	Restriction	Authorisation	Other
300-340-2	☐	☒	☐	☒

Other: SVHC identification