SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Phenol, paraalkylation products with C10-15 branched olefins (C12 rich) derived from propene oligomerization, carbonates, calcium salts, overbased, sulfurized, including distillates (petroleum), hydrotreated, solvent-refined, solvent-dewaxed, or catalytic dewaxed, light or heavy paraffinic C15-C50

List No 701-251-5

CAS No 68784-26-9

Evaluating Member State(s): The Netherlands

Dated: 28 February 2019

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Evaluating Member State Competent Authority

Bureau REACH on behalf of the Ministry of Infrastructure and Water Management and the National Institute for Public Health and the Environment
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Year of evaluation in CoRAP: 2013

Before concluding the substance evaluation a Decision to request further information was issued on: 24 November 2015.

Following a compliance check targeted to the substance identity and carried out by ECHA, the identifiers of the substance have been changed, in agreement with the registrants, as presented below.

Previous Substance name: Phenol, dodecyl-, sulfurized, carbonates, calcium salts, overbased
Previous EC Number submitted: 272-234-3
Previous CAS Number submitted: 68784-26-9

Current Substance name: Phenol, paraalkylation products with C10-15 branched olefins (C12 rich) derived from propene oligomerization, carbonates, calcium salts, overbased, sulfurized, including distillates (petroleum), hydrotreated, solvent-refined, solvent-dewaxed, or catalytic dewaxed, light or heavy paraffinic C15-C50
Current List Number: 701-251-5
Current CAS Number: 68784-26-9

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Phenol, paraalkylation products with C10-15 branched olefins (C12 rich) derived from propene oligomerization, carbonates, calcium salts, overbased, sulfurized, including distillates (petroleum), hydrotreated, solvent-refined, solvent-dewaxed, or catalytic dewaxed, light or heavy paraffinic C15-C50, previously registered as Phenol, dodecyl-, sulfurized, carbonates, calcium salts, overbased, and hereafter referred to as PDSC-Ca, overbased was originally selected for substance evaluation in order to clarify concerns about:

- Human health/CMR
- Exposure/wide dispersive use
- Consumer use
- Aggregated tonnage.

During the evaluation also another concern was identified. The additional concern was:

- Worker exposure (dermal and inhalation route).

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Several processes on related substances are ongoing or have been completed during the substance evaluation process.

- Phenol Dodecyl branched (EC 310-154-3), also named tetrapropenylphenol (TPP), is one of the constituents of PDSC-Ca, overbased. During the evaluation stage, ECHA's Risk Assessment Committee (RAC) adopted the opinion that TPP should be classified as Repr. 1B, Skin Corr. 1C, Aquatic Acute 1 and Aquatic Chronic 1 (December 2013).

- Phenol Dodecyl branched (EC 310-154-3) is being evaluated under Substance Evaluation by Germany. The evaluation started in 2018. The initial ground for concern is potential endocrine disruption for the environment.

- Phenol, dodecyl-, sulfurized, calcium salts (EC 272-486-4) was evaluated under Substance Evaluation by France, in 2016. The initial grounds for concern were environment/suspected PBT, suspected CMR, exposure/wide dispersive use, consumer use and aggregated tonnage. The evaluation has been concluded in November 2017. France indicated in the conclusion document that due to remaining unclarities related to the hazard profile, the evaluating Member State considers that continuing the assessment of the alkylphenolates may be appropriate, possibly within a category approach including the substances which are currently under discussion for EU-wide risk management measures.

- A Risk Management Option Analysis (RMOA) is currently under development by Sweden for Phenol, dodecyl-, sulfurized, carbonates, calcium salts (EC 272-233-8), together with the two substances evaluated under Substance Evaluation (List number 701-251-5, previously registred as EC 272-234-3 and EC 272-486-4). More information is available on on the Public Activities Coordination Tool (PACT)[2].

[2] Available at: https://echa.europa.eu/pact

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 Table 1 below. The evaluation is based on the Chemical Safety Report (CSR) jointly submitted by the Lead Registrant and the members.

As the management options analysis is not yet finalised, the evaluating Member State is not in a position to select one of the follow-up regulatory actions.

Table 1

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

4. FOLLOW-UP AT EU LEVEL

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

4.1.1. Harmonised Classification and Labelling

PDSC-Ca, overbased has shown to induce reproduction toxicity at a level meeting the criteria for Repr. 1B. These reproductive toxic effects can be attributed to the constituent TPP, which has a harmonised classification for Repr. 1B. According to the CLP regulation, PDSC-Ca, overbased shall be classified as a reproductive toxicant based on the presence of TPP (present at or above 0.3%). Therefore, a separate entry for a harmonised classification of PDSC-Ca, overbased for Repr. 1B is deemed not necessary because it is not expected to contribute further to safe use as it will not trigger additional Risk Management Measures (RMMs).

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

Based on the concentration of TPP in PDSC-Ca, overbased, the substance meets the criteria for classification as toxic for reproduction category 1 as described in Art 57c of REACH. The uses are within the scope for authorization. On the basis of this, further evaluation of RMMs under REACH seems an appropriate follow-up. At present, Germany has started the evaluation of TPP based on a concern for potential endocrine disruption. Furthermore, Sweden is developing a Risk Management Options Analysis (RMOA) for the group of phenol alkylates in which PDSC-Ca, overbased has been included. The evaluating Member State will share the outcome of this Substance Evaluation with Sweden to support the RMOA. As a consequence, it is concluded that follow-up may be

warranted, but further analysis is needed first. No initiative from the Netherlands is currently foreseen.

4.1.3. Restriction

At this moment, the exposure information for this substance does not seem to indicate an unacceptable risk for the EU population at large for the evaluated endpoints. Further evaluation of appropriate RMMs for the group of phenols, including PDSC-Ca, overbased, shall be considered and will be taken into account in the RMOA by Sweden.

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

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

Not applicable.

5.2. Other actions

Not applicable.

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

As indicated in section 4, follow-up may be warranted, but no separate initiative from the Netherlands is currently foreseen.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Phenol, paraalkylation products with C10-15 branched olefins (C12 rich) derived from propene oligomerization, carbonates, calcium salts, overbased, sulfurized, including distillates (petroleum), hydrotreated, solvent-refined, solvent-dewaxed, or catalytic dewaxed, light or heavy paraffinic C15-C50, previously registered as Phenol, dodecyl-, sulfurized, carbonates, calcium salts, overbased, and hereafter referred to as PDSC-Ca, overbased, was originally selected for substance evaluation in order to clarify concerns about:

- Human health/CMR;
- Exposure/Wide dispersive use;
- Consumer use;
- Aggregated tonnage.

During the evaluation also another concern was identified. The additional concern was:

- Worker exposure (dermal and inhalation route).

Regarding Exposure scenario (ES) 1 (Manufacturing of lubricant additives, lubricant and greases), ES2 (Industrial formulation of lubricant additive, lubricant and greases) and ES4 (Professional use of lubricants and greases in vehicles or machinery), there was a concern for health risks in workers caused by the estimated dermal exposure. The dermal exposure estimations were not considered acceptable, and could be underestimated, hence risks from dermal exposure may not be sufficiently controlled.

Regarding ES1 (Manufacturing of lubricant additives, lubricant and greases) and ES2 (Industrial formulation of lubricant additive, lubricant and greases) there was a concern for health risks in workers caused by the estimated inhalation exposure. The exposure by inhalation leads to a health risk (Risk Characterisation Ratios (RCRs) >1) when following ECHA Guidance in the risk assessment. Additionally, aggregated exposure has not been determined and considered.

Table 2

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Human health/CMR	No concerns on carcinogenicity and mutagenicity, no further action. Sufficient information available for reproduction toxicity, no new information required.
Dermal exposure workers	Concern not substantiated. No further action
Inhalation exposure workers	Concern not substantiated. No further action
Consumer exposure	Concern not substantiated. No further action

7.2. Procedure

Pursuant to Article 45(4) of the REACH Regulation, PDSC-Ca, overbased was included in the Community rolling action plan (CoRAP) for evaluation in 2013. The Competent Authority of the Netherlands was appointed to carry out the evaluation.

The evaluating Member State considered that further information was required to clarify the human health/CMR, exposure/wide dispersive use, consumer use, and aggregated tonnage. Therefore, it prepared a draft decision pursuant to Article 46(1) of the REACH Regulation to request further information. It submitted the draft decision to ECHA on 13 March 2014. The decision was agreed by the Member State Committee and the final decision was issued to the registrants on 13 October 2015. See Decision on PDSC-Ca, overbased dated 24 November 2015 (ECHA, 2015).

The lead Registrant updated the registration dossier and included an updated Chemical Safety Report, dated 22 February 2017. The report was evaluated by the evaluating Member State and a conclusion document was written based on the information provided in this Chemical Safety Report.

7.3. Identity of the substance

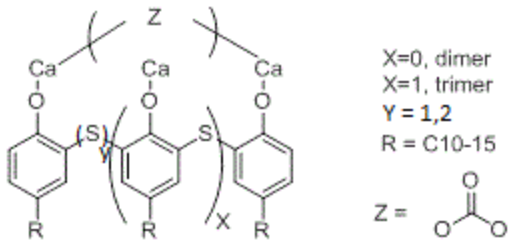
Table 3

SUBSTANCE IDENTITY	
Public name:	Phenol, paraalkylation products with C10-15 branched olefins (C12 rich) derived from propene oligomerization, carbonates, calcium salts, overbased, sulfurized, including distillates (petroleum), hydrotreated, solvent-refined, solvent-dewaxed, or catalytic dewaxed, light or heavy paraffinic C15-C50
List number:	701-251-5
CAS number:	68784-26-9 (Other CAS numbers: 122384-86-5, 68784-25-8, and 122384-87-6)[1]
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	Formula for a representative structure is $C_{36}H_{58}Ca_2O_4S_x$ where x=1,2. Actual molecular formula is not possible to generate. Substance is a UVCB.
Molecular weight range:	-
Synonyms:	PDSC-Ca, overbased Calcium alkylphenolate OLOA 219 OLOA 219C

[1] from SIDS document (OECD, 2008)

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

Structural formula:



Multiconstituent/UVCB substance/others

The substance is a UVCB substance. There are multiple registrants, which may have described different constituents. The constituents are listed in Table 5-10, based on public information obtained from the ECHA dissemination website. The typical concentrations are not publicly available and therefore not included in the tables below.

Table 4. Composition 1 and 5 - PDSC-Ca, overbased

Constituent			
Constituents	**Typical concentration [a]**	**Concentration range [a]**	**Remarks**
Phenol, dodecyl-, sulfurized, carbonates, calcium salts, overbased (List 701-251-5; CAS 122384-87-6)	ca. 57 % (w/w)	CBI	For composition 5, the typical concentration range and CAS number were not indicated in the public field.
Phenol, dodecyl-, branched (TPP) (EC 310-154-3)	CBI	CBI	
Distillates (petroleum), hydrotreated heavy paraffinic (EC 265-157-1)	CBI	CBI	Phenol, alkyl branched (species comprising decyl, undecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, substituents)

[a] CBI: Confidential Business Information. This information was available to the eMSCA and taken into account in the evaluation.

Table 5. Composition 2 - PDSC-Ca, overbased

Constituent			
Constituents	**Typical concentration [a]**	**Concentration range [a]**	**Remarks**
Phenol, dodecyl-, sulfurized, carbonates, calcium salts, overbased (CAS 122384-87-6)	CBI	CBI	

[a] CBI: Confidential Business Information. This information was available to the eMSCA and taken into account in the evaluation.

Table 6. Composition 3 - Phenol, paraalkylation products with C10-15 branched olefins (C12 rich) derived from propene oligomerization, carbonates, calcium salts, overbased, sulfurized, including distillates (petroleum), hydrotreated heavy paraffinic C10-C50.

Constituent			
Constituents	**Typical concentration [a]**	**Concentration range [a]**	**Remarks**
Phenol, dodecyl-, sulfurized, carbonates, calcium salts, overbased (List 701-251-5; CAS 68784-26-9)	CBI	CBI	
Phenol, dodecyl-, branched (TPP) (EC 310-154-3)	CBI	CBI	

Linear Alkane Constituent of Highly Refined Mineral Oil	CBI	CBI	
Branched Alkane Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C17-C35), 1 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C18-C35), 2 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C18-C34), 3 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C18-C33), 4 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C19-C31), 5 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C21-C27), 6 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	

[a] CBI: Confidential Business Information. This information was available to the eMSCA and taken into account in the evaluation.

Table 7. Composition 4 - PDSC-Ca, overbased.

Constituent **Constituents**	**Typical concentration** [a]	**Concentration range** [a]	**Remarks**
Phenol, dodecyl-, sulfurized, carbonates, calcium salts, overbased (List 701-251-5; CAS 121158-58-5)	CBI	CBI	
Phenol, dodecyl-, branched (TPP) (EC 310-154-3)	CBI	CBI	
Linear Alkane Constituent of Highly Refined Mineral Oil	CBI	CBI	

Branched Alkane Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C17-C35), 1 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C18-C35), 2 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C18-C34), 3 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C18-C33), 4 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C19-C31), 5 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	
Cycloalkanes (C21-C27), 6 Unsaturation - Constituent of Highly Refined Mineral Oil	CBI	CBI	

[a] CBI: Confidential Business Information. This information was available to the eMSCA and taken into account in the evaluation.

Table 8. Composition 6 - Phenol, paraalkylation products with C12-rich branched olefins derived from propene oligomerisation, calcium salts, sulfurized, overbased, including distillates (petroleum), heavy paraffinic C10-C50.

Constituent **Constituents**	**Typical concentration [a]**	**Concentration range [a]**	**Remarks**
Sulfurized C12 rich branched paraalkylphenol oligomers, calcium salts	CBI	CBI	
Sulfurized C12 rich branched paraalkylphenol oligomers, calcium salts, thioglycol derivatives	CBI	CBI	
Phenol, dodecyl-, branched (TPP) (EC 310-154-3)	CBI	CBI	
Ethane-1,2-diol (EC 203-473-3)	CBI	CBI	Ethylene glycol

Ethane-1,2-diol, calcium salt	CBI	CBI	
Ethanedioic acid, calcium salt	CBI	CBI	
Calcium carbonate (EC 207-439-9)	CBI	CBI	
Water	CBI	CBI	
Branched alkanes, C11-C48	CBI	CBI	
Cyclo alkanes, C10-C50	CBI	CBI	
Mono aromatics, C10-C50	CBI	CBI	
Di aromatics, C11-C50	CBI	CBI	
Tri aromatics, C12-C43	CBI	CBI	
Linear alkanes	CBI	CBI	
Linear alkenes	CBI	CBI	
Branched alkenes	CBI	CBI	
Cyclo alkenes	CBI	CBI	

[a] CBI: Confidential Business Information. This information was available to the eMSCA and taken into account in the evaluation.

Table 9. Composition 8 - PDSC-Ca, overbased.

Constituent **Constituents**	**Typical concentration** [a]	**Concentration range** [a]	**Remarks**
Phenol, dodecyl-, sulfurized, carbonates, calcium salts, overbased (List 701-251-5; CAS 68784-26-9)	CBI	CBI	
Lubricating oils (EC 278-012-2)	CBI	CBI	

[a] CBI: Confidential Business Information. This information was available to the eMSCA and taken into account in the evaluation.

7.4. Physico-chemical properties

Table 10

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**

Physical state at 20°C and 101.3 kPa	PDSC-Ca, overbased is described as a dark brown viscous liquid.
Melting/freezing point	The test was conducted in accordance with the procedure described in EU Regulation (EC) 440/2008, Annex Part A test A1. The freezing temperature was determined to be between -16.7 and -12.8 °C.
Boiling point	The test is conducted in accordance with the procedure described in EU Regulation (EC) 440/2008, Annex Part A test A2. The boiling point was determined to be >250 °C.
Density	The test is conducted in accordance with the procedure described in EU Regulation (EC) 440/2008, Annex Part A test A3. The density was determined to be 1411 kg.m-3 at 21 °C, the relative density was reported as 1.141.
Vapour pressure	The vapour pressure of PDSC-Ca, overbased was evaluated using a modified method most appropriate for the large molecular weight, highly viscous, substance that has a very low vapor pressure that cannot be measured by traditional means. The vapor pressure in this study was 0.0009 Pa at 20 °C.
Water solubility	The water solubility of PDSC-Ca, overbased was determined to be approximately 0.082 mg/L. According to the EU Directive 67/548/EEC, a poorly soluble substance can be defined as a substance with a solubility of less than 1 mg/L.
Partition coefficient n-octanol/water (Log Kow)	The octanol/water partition coefficient (log Kow) of has been evaluated using the HPLC method (OECD 117). Log Kow (weighted average) of 9.5 has been calculated using polycyclic aromatic hydrocarbons as retention time calibrants.
Water solubility	The water solubility was determined to be approximately 0.082 mg/L. According to the EU Directive 67/548/EEC, a poorly soluble substance can be defined as a substance with a solubility of less than 1 mg/L.
Flash point	The test is conducted in accordance with the procedure described in EU Regulation (EC) 440/2008, Annex Part A test A9. The flash point was determined to be 172 °C.
Auto flammability	The Auto ignition temperature was determined to be 359 °C at 745 mm Hg according to the ASTM E659 method. The test was performed in accordance with the procedure and within the linear range of the calibration. The result is therefore valid.
Viscosity	Test was conducted according to the CIPAC method MT 22 1994, reprinted 2007, this is considered to be comparable to OECD 114. The viscosity of the test material was determined to be 206820 cSt.

7.5. Manufacture and uses

7.5.1. Quantities

10,000-100,000 tonnes per annum.

Table 11

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☐ 100 – 1000 t	☐ 1000- 10,000 t	☒ 10,000-50,000 t
☒ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

Described uses in the registration(s) as presented in Table 12.

Table 12

USES	Use(s)
Manufacture	Manufacture or use as substance itself
Formulation	Industrial formulation of lubricant additives, lubricants and greases.
Uses at industrial sites	Industrial use of lubricants and greases in vehicles or machinery. Includes filling and draining of containers and enclosed machinery (including engines).
Uses by professional workers	General professional use of lubricants and greases in vehicles or machinery (including engines). Includes filling and draining of containers and enclosed machinery.
Consumer Uses	General consumer use of lubricants and greases in vehicles or machinery. Includes filling and draining of containers and enclosed machinery (including engines).
Article service life	-

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

No separate entry for harmonized classification for PDSC-Ca, overbased exists.

Harmonized classification for phenol dodecyl branched (EC 310-154-3), one of the constituents of PDSC-Ca, overbased: Repr. 1B, Skin Corr. 1C, Eye Dam. 1, Aquatic Acute 1 and Aquatic Chronic 1.

7.6.2. Self-classification

Self-classification by the registrants in the joint registration dossier:

Repr. 1B. H360: May damage fertility or the unborn child

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

Other mentioned classifications according to the notifications in Classification and Labelling Inventory on ECHA website:

Repr. 2. H361

Aquatic Chronic 3. H412

Skin irrit. 2. H315

7.7. Environmental fate properties

Not evaluated.

7.8. Environmental hazard assessment

Not evaluated.

7.9. Human Health hazard assessment

Summaries on data of the studied endpoints (mutagenicity, carcinogenicity and reproductive toxicity) were obtained from a Screening Information Dataset (SIDS) document (OECD, 2008). In this document, a whole category of substances was assessed, namely the "Combined Alkyl Phenol Sulfide and Alkyl Phenate Sulfide" category. According to the SIDS, *"the members of this category are mixtures of oligomers of alkyl phenol or alkyl phenate molecules that are linked by one to three sulfur atoms. The alkyl phenoxy group that is common to all the members of the category can contain saturated branched chain C10-C15 (predominantly tetrapropenyl) or saturated linear C18-C30 (alpha-olefin) alkyl groups (R and R') attached primarily at the para ring position. Alkyl phenate sulfides are made when the alkyl phenol group is reacted with calcium hydroxide or oxide to form the corresponding calcium salt. Alkyl phenol sulfides are not neutralized with calcium hydroxide during their manufacture."*

It is noted that the substances' names and CAS numbers given for studies of the same date in the public IUCLID database are sometimes different from those given in this OECD SIDS tables. Multiple names and CAS numbers can be valid for the same substance.

The data of the other members of the category than PDSC-Ca, overbased were mainly important for the evaluation of mutagenicity, as read-across was performed there.

Due to the presence of TPP in PDSC-Ca, overbased, which is classified as Repro 1B, the evaluation of the reproductive toxicity included an analysis of whether any effects seen for PDSC-Ca, overbased were only caused by TPP or possibly also by other constituents.

7.9.1. Toxicokinetics

Not evaluated.

7.9.2. Acute toxicity and Corrosion/Irritation

Not evaluated.

7.9.3. Sensitisation

Not evaluated.

7.9.4. Repeated dose toxicity

Not evaluated.

7.9.5. Mutagenicity

7.9.5.1. Non-human information

7.9.5.1.1. In vitro data

7.9.5.1.1.1. Studies in Bacteria

From the SIDS document

The mutagenic potential of four different members of the "Combined Alkyl Phenol Sulfide and Alkyl Phenate Sulfide" category has been determined in Bacterial Reverse Mutation Tests conducted using methods that are similar to OECD Test Guideline 471. The results are summarized in Table 13 below. In all key studies, these substances did not produce an increase in mutation frequency that exceeded the criteria for a mutagenic response in *Salmonella typhimurium* or *E. coli* with and without metabolic activation.

Table 13. Bacterial Reverse Mutation Assay Data for several alkyl phenol sulfide substances (from OECD SIDS, 2008 and references therein)

Substance	Test System	Test Result	Klimisch Code	Comment/Reference
Nonyl phenol sulfide CAS No. 68515-93-5	NA	No data could be located	NA	Bridge from CAS No. 68815-67-8
C10-C15 alkyl phenol sulfide CAS No. 68815-67-8	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1538	No positive increases in mutation frequency were observed at dose levels of 0.01 to 50.0 µl/plate in all strains with and without an S-9 metabolic activation system.	1	Key Study Entrup & Lavelle, 1982
C10-C15 alkyl phenate sulfide CAS No. 122384-85-4 (and 68855-45-8)	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537, and *E coli* WP2 uvrA	No increases in mutation frequency were observed at dose levels of 5 to 1000 µg/plate in all strains with and without an S-9 metabolic activation system that exceeded the criteria for determination of no mutagenic activity: mean revertant colonies per plate < 2-fold higher than concurrent controls for strains TA 98 and TA 100 and WP2 uvrA and < 3-fold higher for strains TA 1535, TA 1537.	1	Key Study Lawlor, 1997
C10-C15 alkyl phenate sulfide carbonates CAS No. 122384-86-5 (and 68784-25-8) and C10-C15 alkyl phenate sulfide carbonates, overbased	*Salmonella typhimurium* TA98, TA100, TA102 and *E coli* WP2 uvrA	No increases in mutation frequency were observed at dose levels of 0.033 to 3.33 mg/plate in all strains with and without an S-9 metabolic activation system that exceeded the criteria for determination of	1	Key Study Machado *et al*., 1985

CAS No. 122384-87-6 (and 68784-26-9)		no mutagenic activity: mean revertant colonies per plate < 2-fold higher than concurrent controls for strains TA 98, TA 100 and TA 102 or < 2.5-fold higher for strain WP2 uvrA.		
Mixed C10-C15 and C18-C30 alkyl phenate sulfide overbased CAS No. 122384-84-3 (and 73758-62-0)	*Salmonella typhimurium* TA98, TA100, TA1535, TA1537	No increases in mutation frequency were observed at dose levels of 0.1 to 10.0 mg/plate in all strains with and without an S-9 metabolic activation system that exceeded the criteria for determination of no mutagenic activity: mean revertant colonies per plate < 2-fold higher than concurrent controls for strains TA 98, TA 100 and < 2.5-fold higher for strains TA 1535, TA 1537.	1	Key Study Machado *et al*., 1986

7.9.5.1.1.2. Studies in mammalian cells

From the SIDS document

Two "*Combined Alkyl Phenol Sulfide and Alkyl Phenate Sulfide*" category members were tested for mutations in two different mammalian cell test systems *in vitro*. The results are summarized in Table 14 below. In both tests, neither substance produced a statistically significant increase in mutation frequency with or without an S-9 metabolic activation system in either Chinese hamster ovary cells or mouse lymphoma cells.

Table 14. Summary of Genetic Toxicity Data in Mammalian Test Systems for alkyl phenol sulfide substances (from OECD SIDS, 2008 and references therein)

Substance	Test System	Test Result	Klimisch Code	Comment/Reference
Nonyl phenol sulfide CAS No. 68515-93-5	NA	No data could be located	NA	Bridge from CAS No. 68815-67-8

C10-C15 alkyl phenol sulfide CAS No. 68815-67-8	*In vitro* point mutation HGPRT test in CHO cells	No statistically significant increases in mutation frequency were observed at dose levels of 2.0 to 7.5 mg/mL with an S-9 metabolic activation system or at dose levels of 1.5 to 5.0 mg/mL without S-9.	2	Gorodecki *et al.*, 1983
C10-C15 alkyl phenate sulfide CAS No. 122384-85-4 (and 68855-45-8)	Mammalian Erythrocyte Micronucleus Test with Crl:CD-1® (ICR) BR Mice	No increased proportion of micronucleated PCEs was observed at dose levels from 1250 to 5000 mg/kg.	1	Ivett, 1997
C10-C15 alkyl phenate sulfide carbonates CAS No. 122384-86-5 (and 68784-25-8) and C10-C15 alkyl phenate sulfide carbonates, overbased CAS No. 122384-87-6 (and 68784-26-9)	Mouse Lymphoma Cells L5178Y-3.7.2C	Not mutagenic at dose levels of 75 to 275 μg/mL with an S-9 metabolic activation system or dose levels of 60 to 110 μg/mL without S-9.	1	Winiger *et al.,* 1985
Mixed C10-C15 and C18-C30 alkyl phenate sulfide overbased CAS No. 122384-84-3 (and 73758-62-0)	NA	No data could be located	NA	Bridge from CAS No. 122384-85-4

Evaluation of the data

In the registration dossier, Ames test data are provided for strains TA98, TA100, TA102 and E coli WP2 uvrA only (Machado et al., 1985), thus lacking the required TA1535 and TA1537 strains (according to OECD 471). For these strains, read-across is performed from Mixed C10-C15 and C18-C30 alkyl phenate sulfide overbased (CAS No. 122384-84-3) and C10-C15 alkyl phenate sulfide (CAS No. 122384-85-4, 68855-45-8, and 220794-90-1), which gave negative results for these strains as well as the other strains. These source substances differ with the target substance in either a different alkyl chain length or in an absence of carbonate. These differences do not cause alerts for genotoxicity in the target substance. Rather, the presence of carbonates in the target substance seems to protect for quinone formation after hydrolysis of the substance, according to modelling performed by the registrants. The evaluating Member State considers the read-across to be plausible and does not see a concern based on this data.

There are no in vitro data on clastogenicity or aneugenicity, (see section 5.7.1.2.), however, based on the information from in vivo micronucleus data from structurally similar substances, the evaluating Member State does not see a concern for clastogenicity and aneugenicity.

7.9.5.1.2. In vivo data

From SIDS document

C10-C15 alkyl phenate sulfide (CAS No. 122384-85-4) was evaluated in an *In Vivo* Mouse Bone Marrow Assay similar to OECD Test Guideline 474 (see table 11). The test material was administered in peanut oil to mice at dose levels of 0, 1250, 2500, and 5000 mg/kg. Five mice/sex from each group were sacrificed at 24, 48, and 72 hours after treatment. The bone marrow cells were extracted from hind limb bones and processed for cytogenetic analysis. Slides from each animal were examined for chromosomal aberrations for the 24, 48, and 72-hour groups. One thousand polychromatic erythrocytes (PCEs) per animal were scored for micronuclei. The relative frequency of PCEs versus normochromatic erythrocytes (NCEs) was determined by scoring at least the first 1000 erythrocytes.

There were no significant differences of group mean PCE/NCE ratios between treatment and control groups at any dose for all harvest times and for males and females. No increased proportion of micronucleated PCEs was observed in any test group. Both males and females of the positive control group had significantly elevated (>50-fold) proportion of micronucleated PCEs while PCE/NCE ratios were not affected confirming the sensitivity of the assay. Under the conditions of this study, the members of this category are not clastogenic.

Evaluation of the data

The in vivo micronucleus data are derived by read-across from a test with PDSC, Ca (not the carbonate, overbased form). The addition of a carbonate, overbased, group is not expected to affect the mutagenic potential of the target substance, rather, modelling performed by the registrants shows that the presence of carbonates, especially in overbasing levels, seems to protect against quinone formation after hydrolysis. Therefore the evaluating Member State concludes that the available information does not raise a concern for mutagenicity.

7.9.5.2. Human information

From SIDS document

No experimental or anecdotal information on mutagenic or clastogenic effects for the members of the "Combined Alkyl Phenol Sulfide and Alkyl Phenate Sulfide" category in humans has been located.

7.9.5.3. Summary and discussion of mutagenicity

All mutagenicity endpoints have been covered and according to the evaluating Member State the data do not indicate genotoxic potential.

7.9.6. Carcinogenicity

7.9.6.1. Non-human information

From SIDS document

No experimental or anecdotal information on the carcinogenic potential of the members of the "Combined Alkyl Phenol Sulfide and Alkyl Phenate Sulfide" category in animals has been located. However, some conclusions on the carcinogenic potential of these substances can be derived from other data. The lack of mutagenic and clastogenic potential suggests that these substances do not cause cancer by a genetic mechanism. Considering the potential for carcinogenicity by a non-genotoxic mechanism, no evidence of sustained cell proliferation or hyperplasia was observed in repeated-dose toxicity studies.

7.9.6.2. Human information

From SIDS document

No experimental or anecdotal information on the carcinogenic effects of the members of the "Combined Alkyl Phenol Sulfide and Alkyl Phenate Sulfide" category in humans has been located.

7.9.6.3. Summary and discussion of carcinogenicity

The available data from studies in animals with the SIDS category members do not raise a concern that these substances are carcinogenic by a genotoxic or non-genotoxic mechanism.

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

The constituent TPP has a harmonized classification as Repro 1B, H360f (May damage fertility; CLP Regulation) based on the RAC opinion in December 2013. Among the supportive data were the following results:

- Uterotropic assay: dose-dependent increases in wet and blotted mean uterine weights;
- Female pubertal assays: estrogenic effects (e.g. earlier vaginal pattency, earlier first estrus, persistent estrus);
- Androgen Receptor Competitive Binding Assay: binding to androgen receptor;
- Estrogen Receptor Competitive Binding Assay: binding to estrogen receptor.

These test results indicate that constituent TPP could potentially act as an endocrine disruptor. This is important background information in the assessment of the data on reproductive toxicity of PDCS-Ca, overbased as well as for the assessment of the endocrine disrupting (ED) properties of the substance.

7.9.7.1. Effects on fertility

7.9.7.1.1. Non-human information

From SIDS document

In the first of two key studies for this substance (Lamb 1993), male and female rats were repeatedly dosed orally by gavage with phenol, dodecyl-, sulfurized, carbonates, calcium salts (CAS No. 122384-87-6) [i.e. PDSC-Ca, overbased] for 28 days prior to mating with dose levels of 0, 50, 200 and 1000 mg/kg bw/day. Dosing continued through 10 weeks for males and through the mating, gestation and lactation periods until the study was terminated on PND (post-natal day) 4 for females. The results of this reproductive toxicity screening study showed that the test substance caused a significant decrease in mean body weight at the highest dose level in males, but there were no effects on mean body weight gain in females during the premating phase or in the lactation phase. There was a significant decrease in body weight gain in the high dose females during gestation. Neither mean testes weights nor mean ovary weights were affected, but there were significant increases in mean pituitary and adrenal gland weights in high-dose males. There were no effects on the fertility index at any dose level. A decrease in the mean number of corpora lutea was also observed in the high-dose group, and although it was not statistically significantly different from the concurrent controls, it was lower than the historical control range (14.4-19.2/dam) at this laboratory. And there was a significant decrease in mean live litter size, a significant decrease in the mean number of former implantation sites, and a significant increase in pre-implantation loss in the high-dose group. This study is considered to be reliable without restrictions (Klimisch Code = 1). The key findings are summarized in Table 15 below.

Table 15. Summary of Key Findings – Oral (Gavage) Reproductive / Developmental Screening Study with CAS No. 122384-87-6 in Rats (Lamb 1993)(from OECD SIDS, 2008)

Parameter	**Dose Level (mg/kg bw/day)**			
	0	**50**	**200**	**1000**
Fertility Index (#pregnant/#mated)	100 (12/12)	91.7 (11/12)	91.7 (11/12)	91.7 (11/12)
Mean live litter size (#pups/#litters)	12.8 (154/12)	12.9 (142/11)	11.5 (127/11)	7.7** (85/11)
Mean Corpora Lutea (#)	16.0	14.9	15.6	13.8
Mean Former Implantation Sites (#)	14.7	13.8	13.5	9.7*
Mean Pre-implantation Loss (absolute #)	1.3	1.1	2.1	4.1*
Mean Body Weight Gain				
Males, Wks 0-10	235	233	241	185**
Females, Wks 0-4	52	57	53	47

Females, Gestation Days 0-20	142	129	124	107**
Females, Lactation Days 1-4	15	12	14	13
Mean Organ Weights				
Testes (g)	3.30	3.41	3.33	3.33
Ovaries (g)	0.1221	0.1220	0.1259	0.1127
Pituitary (g), Males	0.0132	0.0135	0.0146	0.0156**
Pituitary (g) Females	0.0175	0.0168	0.0160	0.0160
Adrenal Glands (g), Males	0.0538	0.0498	0.0530	0.0746*
Adrenal Glands (g), Females	0.0640	0.0676	0.0740	0.0741

*$p \leq 0.05$; **$p \leq 0.01$

In the second of two key studies for this substance (Nemec 1995), male and female rats were repeatedly dosed orally by gavage with CAS No. 122384-87-6 [i.e. PDSC-Ca, overbased] with dose levels of 0, 50, 300 and 1000 mg/kg/day over the span of two generations. After a decrease in fertility and mean live litter size was observed in the F0 high-dose group, a satellite study was conducted with F1 animals in which high-dose males were cross-bred with control females, and control males were bred with high-dose females. This study is considered to be reliable without restrictions (Klimisch Code = 1). The key findings of the main study are summarized in Table 16 below. The key findings of the satellite study are summarized in Table 17 below.

Mean body weights were significantly less than control in the F0 male high-dose group from Weeks 3 to 20 and in the F0 male mid-dose group from Weeks 14 to 20. There were no effects on mean body weight in F0 males in the low-dose group at any time. There were no effects on mean body weight in F0 females at any dose level at any time except in the high-dose group during gestation. In the F1 males, mean body weights were significantly less that control in the high-dose group from Weeks 20 to 38 and in the mid-dose group from Weeks 23 to 38. There were no effects on mean body weight in F1 males in the low-dose group at any time. In F1 females, mean body weights were significantly less than control in the high-dose group in the pre-mating period from Weeks 20 to 29 and during gestation on days 0, 4, and 20, but there were no effects on mean body weights during lactation. There were no effects on mean body weight in F1 females at the mid-dose level at any time except Week 27 or at the low-dose level at any time.

Table 16. Summary of Key Findings – 2-Generation Oral (Gavage) Reproductive Toxicity Study with CAS No. 122384-87-6 in Rats – Main Study (Nemec 1995)(from OECD SIDS, 2008)

Parameter	**Dose Level (mg/kg bw/day)**			
	0	**50**	**300**	**1000**
F0 Fertility Index (#pregnant/#mated)	96.7 (29/30)	93.3 (28/30)	93.3 (28/30)	73.3* (22/30)
F1 Fertility Index (#pregnant/#mated)	93.3 (28/30)	93.3 (28/30)	100 (30/30)	76.7 (23/30)
F0 Mean live litter size (#pups/#litters)	12.6 (365/29)	13.3 (373/28)	12.4 (346/28)	8.8** (168/19)

F1 Mean live litter size (#pups/#litters)	13.0 (338/26)	13.0 (363/28)	12.3 (368/30)	6.8** (116/17)
Mean Organ Weights				
F0 Testes (g)	3.64	3.59	3.67	3.55
F1 Testes (g)	3.82	3.66	3.79	3.52*
F0 Epididymides (g)	1.47	1.47	1.43	1.35**
F1 Epididymides (g)	1.50	1.46	1.43	1.25**
F0 Pituitary (g), males	0.0157	0.0151	0.0180**	0.0192**
F1 Pituitary (g), males	0.0153	0.0143	0.0165	0.0193**
F0 Ovaries (g)	0.1508	0.1529	0.1427	0.1221**
F1 Ovaries (g)	0.1532	0.1573	0.1487	0.1365
F0 Pituitary (g), females	0.0184	0.0170	0.0175	0.0200
F1 Pituitary (g), females	0.0158	0.0155	0.0166	0.0190**

*p $\leq$ 0.05; **p $\leq$ 0.01

The fertility index was reduced in both the F0 and F1 mating to both concurrent and mean historical control values, and the difference from the concurrent control was statistically significant in the F0 mating. In addition, mean live litter size in the high-dose group was significantly less than the concurrent control at each mating.

Mean epididymides weights in the high-dose group were significantly less than control values in both the F0 and F1 males. Mean testes weights in the high-dose group were also less than control values, and the difference between the F1 high-dose males and F1 control values was statistically significant. Mean pituitary weights in the F0 and F1 high-dose males were significantly greater than their respective control groups. Mean pituitary weights in the F0 mid-dose males were also significantly greater than control males.

Qualitative evaluations of spermatogenesis were performed on all males that failed to sire a litter in all F0 and F1 dose groups. These evaluations did not reveal any treatment-related changes in gross sperm morphology, apparent relative numbers or motility in the epididymides.

Mean ovary weights in both the F0 and F1 high-dose females were less than controls, and the difference was statistically significant in the F0 females. Mean pituitary weights in both the F0 and F1 high-dose females were greater than controls, and the differences were statistically significant in the F1 females. Mean liver weights were also significantly increased in the F0 and F1 high-dose females compared to their respective controls.

In the satellite reproductive toxicity study with CAS No. 122384-87-6, there were no effects on fertility index or mean live litter size when F1 high-dose males were cross-bred with F1 control females. However, when F1 control males were cross-bred with F1 high-dose females, the fertility index and mean live litter size were both significantly reduced. Thus the adverse effects on fertility with this test substance are occurring in the females in this study.

Table 17. Summary of Key Findings – 2-Generation Oral (Gavage) Reproductive Toxicity Study with CAS No. 122384-87-6 in Rats – Satellite Study (Nemec 1995) (from OECD SIDS, 2008)

Treatment (mg/kg bw/day)	**Fertility Index**	**Mean Live Litter Size**
Males (1000) x Females (1000)	76.7 (23/30)	6.8** (116/17)
Males (0) x Females (1000)	55.2** (16/29)	5.8** (70/12)
Males (1000) x Females (0)	96.7 (29/30)	12.6 (366/29)
Males (0) x Females (0)	93.3 (28/30)	13.0 (338/26)

*p $\leq$ 0.05; **p $\leq$ 0.01

Evaluation of the data

The joint submission for PDSC-Ca, overbased provides one dataset of toxicological information. However, different compositions are given by the different registrants. It is not clarified or founded whether the toxicological data are relevant for each of the registered compositions. For example, if the toxicity studies have been performed with a composition with lower TPP concentration than marketed by one registrant, the risk of this marketed product may be underestimated.

Furthermore, it was initially not substantiated by the registrants why only TPP was considered as contributing to the reproduction toxic effects of PDSC-Ca, overbased. In order to get an impression on this contribution of TPP to fertility effects, the evaluating Member State compared the doses and effects found in fertility studies with TPP with the doses and effects found in fertility studies with PDSC-Ca, overbased. Part of this analysis is confidential as it includes the TPP content of the PDSC-Ca, overbased product used to perform the studies. In short, it was observed that there is quite some similarity between the effects at comparable dosages of TPP, either directly or within PDSC-Ca, overbased. However, the increase in the weight of the liver, kidney, and brain, as well as the decreased fertility index and number of litters, and the increase of the incidence of dystocia and of the number of dead pups, all reported for PDSC-Ca, overbased, were not reported for TPP at any dose (see Table 18).

Table 18. Comparison of observed effects at the different doses in the 2-generation reproductive toxicity tests of TPP and PDSC-Ca, overbased

	TPP (Study report, 2012)			PDSC-Ca, overbased (Nemec, 1995)		
	1.5 mg/kg bw/d	15 mg/kg bw/d	75 mg/kg bw/d	50 mg/kg bw/d	300 mg/kg bw/d	1000 mg/kg bw/d
Parental toxicity		Renal mineralization ♂ F_1	Body weight ♀ ♂ F_0 and F_1 ↓ Food consumption ♀ during lactation F_0 and F_1 ↓ [2] Pituitary weight ♂ F_1 ↑		Body weight ♂ F_0 and F_1 ↓ Rel. pituitary	Body weight F_0 and F_1 ↓ ♂ ♀ , not stat. sign. Food consumption ♀ during lactation F_0 and F_1 ↓

					weight ♂ F_0 and F_1 ↑ Rel. liver weight ♀ F_1 ↑ Rel. kidney weight ♂ F_0 and F_1 ↑ Rel. brain weight F_1 ↑ Rel. testes weight ♂ F_0 and F_1 ↑	Rel. pituitary weight F_0 and F_1 ↑ Rel. liver weight F_0 and F_1 ↑ Rel. kidney weight ♂ F_0 ↑ Rel. brain weight ♂ F_0 ↑ Abs. testes weight F_1 ↓ , rel. weight F_0 and F_1 ↑ Ovary weight F_0 ↓
			Abs. testes weight F_0 and F_1 ↓ Ovary weight F_0 and F_1 ↓ Weight seminal vesicles, left and right epididymis, and prostate F_0 and F_1 ↓ Length oestrus cycle F_0 and F_1 ↑ Corpora lutea ♀ F_0 and F_1 ↓ Renal mineralization ♂ F_0 and F_1 Sperm concentration F_0 ↓			
Reprod. toxicity			# Live pups F_1 ↓ Live litter size F_1 ↓			Fertility index F_0 ↓ # Litters F_0 and F_1 ↓ Live litter size F_1 and F_2 ↓ Dystocia F_1 ↑

			# Implant. Sites F_0 ↓ (F_1 not examined)			
Neonatal toxicity			Postnatal survival F_2 and F_{2a} ↓ Pup weights F_2 ↓ Pup growth F_1 and F_2 ↓ Abs. and rel. pituitary weight ♂ F_1 ↑ Ovary weight ♀ F_1 ↓ Time to sex. matur. F_1 ♀ ↓ , ♂ ↑ Length oestrus cycle F_1 ↑ Corpora lutea ♀ F_1 ↓		# Dead pups F_1 ↑ [1] Body weight ♂ F_1 ↓	# Dead pups F_1 and F_2 ↑ Pup body weight F_1 on PD 14, 21 and 28 ↓ Pituitary weight F_1 ↑ Liver weight ♀ F_1 ↑ Ovary weight ♀ F_1 ↓ Testes weight ♂ F_1 ↓

[1] Not reproduced in F_2 → equivocal

[2] Ascribed to smaller litter size (less food necessary), higher body weights than in controls were seen in later part of lactation period, supporting this theory
Red= effect from PDSC-Ca, overbased that is not reported for TPP
Green = effect from PDSC-Ca, overbased that is also reported for TPP

The observed organ effects were compared to the effects seen in repeated dose toxicity studies, to determine the consistency of these findings. The effects on liver, kidney and brain as seen in the 2-generation study with PDSC-Ca, overbased are not (consistently) observed in any study with TPP and could thus be caused by other constituents of PDSC-CA, overbased. It was concluded that the reproductive effects of PDSC-Ca, overbased seem to be largely attributable to the component TPP, but that some effects reported for PDSC-Ca, overbased are not seen at the related dose (but still somewhat lower dose) of TPP. Additionally, not all details of the TPP studies were available, due to the lack of the full study reports. Therefore, uncertainty remained whether TPP truly is the sole responsible component for the fertility effects of PDSC-Ca, overbased.

During the substance evaluation process, the registrants have firstly provided supporting information that it is indeed only TPP that causes the reproductive toxicity, by adding a study to the dossier of PDSC-Ca, overbased from which the TPP was stripped (study report, 2012). Comparing these results to those of the unstripped PDSC-Ca, overbased, none of the effects in parents found with unstripped PDSC-Ca, overbased are found (only

a new effect in prostate). This indicated TPP indeed seems responsible for the effects seen with PDSC-Ca, overbased, at least for the effects in parents. It is not clear whether this is also the case for effects on offspring, as these data were not provided. Due to this remaining uncertainty the evaluating Member State prefer to base the risk assessment on the data of the PDSC-Ca, overbased UVCB, and not on TPP. However, the final request for measuring the exposure to workers made it necessary to apply TPP-data as exposure data, thus necessitating to base the risk assessment on TPP nonetheless, and not on PDSC-CA, overbased. This way, the issue of different TPP-levels in different PDSC-Ca, overbased products was also solved. The risk assessment steps are further described in section 7.9.11, 7.12 and 7.13.

7.9.7.1.2. Human information

There were no human data on fertility effects.

7.9.7.2. Developmental toxicity

7.9.7.2.1. Non-human information

From SIDS document

In the key study (Nemec 1994), pregnant rats were treated with CAS No. 122384-87-6 [i.e. PDSC-Ca, overbased] at dose levels of 0, 50, 300 and 1000 mg/kg bw/day on Gestation Days 6-15. This study is considered to be reliable without restrictions (Klimisch Code = 1). The key findings of the study are summarized in Table 19 below.

All animals survived to study termination on Gestation Day 20. There was a decrease in mean body weight gain in the high-dose dams on Gestation Days 6-10, 6-11, 6-12, 6-13, 6-14, 6-15, and 6-16, which could be due to reduced implantation. Mean food consumption was not affected at any dose level at any time during the study.

Intrauterine growth and survival were not affected at any dose level. The malformations observed in this study were considered to be spontaneous in origin. A significantly increased incidence in the number of litters with fetuses that had bent ribs, a fetal developmental variant, was observed in the high-dose group.

Table 19. Summary of Key Findings – Oral (Gavage) Developmental Toxicity Study with CAS No. 122384-87-6 in Rats (Nemec 1994)(From OECD SIDS, 2008)

Parameter	**Dose Level (mg/kg bw/day)**			
	0	**50**	**300**	**1000**
Mean Body Weight Gain (g), Days 6-16	72	74	70	61*
Bent Ribs (incidence in fetuses)	1/432	1/370	3/403	14/333
Bent Ribs (incidence in litters)	1/25	1/22	2/24	8/21*

*p $\leq$ 0.05; **p $\leq$ 0.01

Evaluation of the data

The increased incidence of bent ribs, seen with PDSC-Ca, overbased at 1000 mg/kg bw/d in the study of Nemec (1994), overbased should be seen as a reversible skeletal variant, most probably caused by the observed maternal toxicity at this dose. PDSC-Ca, overbased therefore does not show developmental toxicity up to the top dose of 1000 mg/kg bw/d.

7.9.7.2.2. Human information

No human data on developmental toxicity have been reported.

7.9.7.2.3. Summary and discussion of reproductive toxicity

In summary, PDSC-Ca, overbased does not cause developmental toxicity in the available studies, but fertility effects are observed for this UVCB. The new study with PDSC-Ca, overbased stripped of TPP (study report, 2012) shows the constituent TPP is responsible for the effects in parents, and data from TPP studies show it contributes to the effects in offspring. It is noted that it remains uncertain whether TPP is the only constituent contributing to these effects in offspring, as the results in offspring were not provided in the 2012 study report of the stripped PDSC-Ca, overbased and not available to the evaluating Member State. Nevertheless, as it is clearly the main responsible/contributing constituent, the concentration of TPP in PDSC-Ca, overbased is regarded as determinant for the level of reproductive toxicity of this UVCB.

7.9.8. Hazard assessment of physico-chemical properties

Not evaluated.

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

Initially, the risk assessment was based on PDSC-Ca, overbased, and Derived No Effect Levels (DNELs) for this UVCB were derived by the registrants. The evaluating Member State commented on the derivation of these DNELs, e.g. on the assumed oral absorption in the extrapolation from an oral key study and on the uncertainty factor for intraspecies variability of workers (5, not 3). With DNELs derived by the evaluating Member State, the evaluating Member State found RCRs >1 for some worker exposure scenarios. This led to the request for improved exposure data based on measurements. Because the exposure to PDSC-Ca, overbased itself could not be measured, exposure to the main toxic constituent, TPP, was measured. Subsequently, the risk assessment had to be based on TPP. Thus, only DNELs for TPP and the underlying studies for TPP are finally relevant, which are described here, as only the PDSC-Ca, overbased studies have been described in the former sections.

The key study for TPP, i.e. the one with the lowest point of departure, is a two-generation reproductive toxicity study with doses of 0, 1.5, 15 & 75 mg/kg bw/day (nominal in the diet), according to OECD Guideline 416 (Two-Generation Reproduction Toxicity Study; study report of 2012*).*

In this study, parental toxicity was evidenced by lower mean body weights, body weight gains, and food consumption in the F0 and F1 males and females in the 75 mg/kg bw/day group. In addition, several organ weight changes (lower weights of the cauda epididymides, epididymides, prostate, and seminal vesicles/coagulating glands, and higher pituitary weight for F0 and F1 males; lower left and right testes weight for F1 males; lower ovary weights for F0 and F1 females; and higher adrenal glands weight for F1 females) were noted for parental animals at 75 mg/kg bw/day. Furthermore, histopathologic changes of renal mineralization in F0 males at 75 mg/kg bw/day and F1

males at 15 and 75 mg/kg bw/day, as well as decreased corpora lutea in F0 and F1 females at 75 mg/kg bw/day were noted. Therefore, the no-observed-adverse-effect level (NOAEL) for F0 and F1 parental toxicity was considered to be 15 and 1.5 mg/kg bw/day, respectively.

Decreased implantation sites (F0 females), increased estrous cycle lengths (F0 and F1 females), and a reduction in mean epididymal sperm concentration (F0 males) were noted at 75 mg/kg bw/day. Therefore, the NOAEL for male and female reproductive toxicity was considered to be 15 mg/kg bw/day.

Based on reductions in F2 and F2a postnatal survival, lower F1, F2, and F2a offspring body weights and body weight gains (that resulted in a delay in the mean age of balanopreputial separation, lower spleen and thymus weights, and post-weaning mortality) and the accelerated onset of vaginal patency in F1 females at 75 mg/kg bw/day, the NOAEL for neonatal toxicity was considered to 15 mg/kg bw/day.

The evaluating Member State commented on the initial DNELs derived by the registrants for TPP based on this study, e.g. on the selected point of departure and (again) on the assumed oral absorption in the extrapolation from an oral key study. This has led to adaptations by the registrants. Table 20 presents the final DNELs as derived by the Registrants.

Table 20. DNELs as derived by the Registrants.

CRITICAL DNELS/DMELS					
Endpoint of concern	**Type of effect**	**Critical study(ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL/ DMEL**	**Justification/ Remarks**
Reproduction toxicity/ repeated dose toxicity *by TPP*	Renal mineralization	Study report, 2012 (oral)	BMD: 3.93 mg/kg bw/day	DNEL (worker, dermal, long-term systemic effects): 0.66 mg/kg bw/day	An assessment factor of 100 is based on the following: 4 for allometric scaling; 2.5 for remaining differences; 5 for intraspecies differences (workers); 2 for duration extrapolation; 1 for quality of the data
Reproduction toxicity/ repeated dose toxicity *by TPP*	Renal mineralization	Study report, 2012 (oral)	BMD: 3.93 mg/kg bw/day	DNEL (worker, inhalation, long-term systemic effects): 0.14 mg/m^3	Correction factor for oral to inhalation: ((1/sRVrat(0.38))x(ABSoral-rat(50)/ABSinh-human(100))x(sRVhuman(6.7)/wRV(10))) An assessment factor of 25 is based on the following: 2.5 for remaining differences; 5 for intraspecies differences (workers); 2 for duration extrapolation; 1 for quality of the data
Reproduction toxicity/ repeated dose toxicity *by TPP*	Renal mineralization	Study report, 2012 (oral)	BMD: 3.93 mg/kg bw/day	DNEL (general population, dermal, long-term systemic effects): 0.33 mg/kg bw/day	An assessment factor of 200 is based on the following: 4 for allometric scaling; 2.5 for remaining differences; 10 for intraspecies differences (consumers); 2 for duration extrapolation; 1 for quality of the data
Reproduction toxicity/ repeated dose toxicity *by TPP*	Renal mineralization	Study report, 2012 (oral)	BMD: 3.93 mg/kg bw/day	DNEL (general population, inhalation, long-term systemic effects): 0.034 mg/m^3	Correction factor for oral to inhalation: ((1/sRVrat(1.15))x(ABSoral-rat(50)/ABSinh-human(100)) An assessment factor of 50 is based on the following: 2.5 for remaining differences; 10 for intraspecies differences (consumers); 2 for duration

					extrapolation; 1 for quality of the data

Though suitable changes to the derivation of the DNEL have been made by the registrants during the substance evaluation process, the evaluating Member State still does not agree with one last point in the derivation of these DNELs for TPP. For the point of departure from the 2-generation reproduction toxicity study of 2012, the registrants have derived a lowest benchmark dose (BMDL) of 3.93 mg/kg bw/d, instead of the formerly applied NOAEL of 1.5 mg/kg bw/d. This BMDL was based on the weighted average of all models in PROAST, and a bench mark response (BMR) set at 10% (quantal data). The registrants are acknowledged for their application of state of the art dose response modelling techniques. However, there are a few improvements to be made to their BMDL derivation.

The registrants state that they applied the model averaging method as proposed by Piegorsch (2014a and 2014b). Piegorsch first weighs the BMDs of each accepted model to arrive at an averaged BMD (eq 3.1 in Piegorsch 2014b). Secondly, a correction is made for the standard error to arrive at the (averaged) BMDL (eq 3.4). The method applied to analyse the TPP data is NOT according to Piegorsch. The registrants applied the first step (weighing) on the BMDLs instead of the BMDs. The second step is not performed at all. Therefore, the derived weighted average BMDL is NOT correct.

As an alternative to the Piegorsch method, the weighted average BMDL (and Benchmark dose upper bound, BMDU) may be calculated by the method proposed by Wheeler and Bailer (e.g. 2007). This method is implemented in the newest PROAST version (which can be requested at proast@rivm.nl). The evaluating Member State has quickly performed this analysis using PROAST and obtained a BMDL of 2.8 and BMDU of 14 mg/kg bw/day.

Furthermore, the analysis contains some deviations from current European guidelines (EFSA 2017), which are useful for the registrants to consider in future exercises:

1) The Log-logistic, Log-probit and Weibull models were restricted to have a slope of 1. This constraint is not appropriate, and should be turned off. "The constraint that the steepness parameter should be larger than one is inappropriate and should not be applied, as it may lead to artificially high BMDLs." (EFSA 2017, paragraph 2.5.3).

2) EFSA guidelines state that some more details about the results should be presented:
A table presenting the models used (preferably in the order of Table 3 in EFSA document), including the null and full model and their Akaike Information Criterion (AIC)s, with the BMD confidence intervals. BMDL **and BMDU** values should be reported with two significant figures. (EFSA 2017, paragraph 2.5.9). The benchmark dose lower bound (BMDL) is needed as a potential Reference Point (RP), and the upper bound (BMDU) is needed for establishing the BMDU/BMDL per ratio reflecting the uncertainty in the BMD estimate. (EFSA 2017, paragraph 2.5.7).
A plot of the fitted average model. If model averaging was not used, a plot of all the models fitted to the data for the critical endpoint(s). In case of nested families, a plot of the selected model for each family. (EFSA 2017, paragraph 2.5.9).

Thus, the evaluating Member State considers that a BMDL of 2.8 mg/kg bw/d should be applied in the derivation of DNELs for TPP, which is a factor 1.4 lower than the BMDL derived by the registrants (3.93 mg/kg bw/d). This would lead to TPP DNELs for inhalation and dermal route that are factor 1.4 lower.

According to registrants: DNEL (dermal worker TPP) = 3.93 mg/kg bw/d (as BDML) *0.5 (oral abs) /0.03 (dermal abs) /(10 interspecies*5 intraspecies * 2 duration * 1 quality data) **= 0.66 mg/kg bw/d.**

According to evaluating Member State: DNEL (dermal worker TPP) = 2.8 mg/kg bw/d (as BDML) *0.5 (oral abs) /0.03 (dermal abs) /(10 interspecies*5 intraspecies * 2 duration * 1 quality data**) = 0.47 mg/kg bw/d**.

According to registrants: DNEL (inhalation worker TPP) = 3.93 mg/kg bw/d (as BDML) *(1/0.38 (sRV rat)*0.5 (abs oral)/1 (abs inh)*6.7 (sRV human)/10 (wRV)) /(2.5 interspecies*5 intraspecies * 2 duration * 1 quality data) = **0.14 mg/m³.**

According to evaluating Member State: DNEL (inhalation worker TPP) = 2.8 mg/kg bw/d (as BDML) *(1/0.38 (sRV rat)*0.5 (abs oral)/1 (abs inh)*6.7 (sRV human)/10 (wRV)) /(2.5 interspecies*5 intraspecies * 2 duration * 1 quality data) = **0.099 mg/m³**.

Likewise, the DNELs for the general population are a factor 1.4 lower (table 21).

It is to be noted that these DNELs are for the general toxicity and reproduction effects, the potential impact of an ED assessment has not been included in the current assessment.

Table 21. Comparison of DNELs as derived by the registrants, and as derived by the evaluating Member State.

DNEL TPP	DNEL reg 2017	DNEL evaluating Member State 2018
Dermal, worker	0.66 mg/kg bw/day	0.47 mg/kg bw/day
Inhalation, worker	0.14 mg/m^3	0.099 mg/m^3
Dermal, general population	0.33 mg/kg bw/day	0.24 mg/kg bw/day
Inhalation, general population	0.034 mg/m^3	0.024 mg/ m^3

However, as the lower DNEL of the evaluating Member State still does not lead to RCRs > 1 (see 7.13), no further action is taken on this aspect. It is to be noted that this assessment does not include the potential impact of an ED assessment of the substance.

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

The human health hazard assessment did not raise a concern for mutagenicity or carcinogenicity and found that the reproductive toxicity of PDSC-Ca, overbased seem to be largely attributable to the constituent TPP. The classification of PDSC-Ca, overbased on reproductive toxicity may thus be based on the level of this constituent. The risk assessment is also best based on TPP, as this can be more easily measured for exposure determination. Some of the final DNELs derived by the registrants for TPP are a little higher than what the evaluating Member State would derive, but do not lead to RCRs > 1. Therefore, no further action is taken by the evaluating Member State.

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated and therefore not included in the intrinsic hazard assessment and DNEL assessment.

7.11. PBT and VPVB assessment

Not evaluated.

7.12. Exposure assessment

7.12.1. Human health

7.12.1.1. Worker

Regarding ES1 (Manufacturing of lubricant additives, lubricant and greases), ES2 (Industrial formulation of lubricant additive, lubricant and greases) and ES4 (Professional use of lubricants and greases in vehicles or machinery), there was a concern for health risks in workers caused by the estimated dermal exposure. The dermal exposure estimations were not considered acceptable, and could be underestimated, hence risks from dermal exposure may not be sufficiently controlled.

This concern resulted in the following requests in the SEV decision for dermal exposure information following a tiered approach:

a) **Dermal exposure modelling using the RISKofDERM Model, including aggregrate exposure calculations in case time reduction factors are applied.** In case the RISKofDERM Model indicates that the exposure estimation is outside the validity range of the model, or in case RCRs>1 are obtained for aggregated (8h) exposures, it is requested to perform (next tier):
b) **Dermal exposure measurements of workers in ES-1 Manufacture of lubricant additives, lubricants and greases (ATIEL-ATC Group A Prime), ES 2 Industrial formulation of lubricant additive, lubricant and greases (ATIEL/ATC Use Group A) and ES 4 Professional use of lubricants and greases in vehicles or machinery.** Dermal exposure shall be measured according to the absorbent glove method by OECD (OECD, 1997), by analyzing TPP contamination of cotton gloves that are worn under the chemically protective gloves used. Reasonable worst case situations shall be tested regarding both the TPP concentration in PDCS-CA, overbased used for a typical exposure scenario, and the work performed during an 8 hour shift, to account for aggregated dermal exposure. Considering TPP is a UVCB, the analysis of TPP should be performed through the analysis of its main constituents, forming 95% of the UVCB composition.

Dermal exposure

ES1: Manufacture of lubricant additives and lubricants.

During a sampling campaign ES1 was divided into five contributing exposure scenarios (CES):

- CES 1.1: Synthesis

- CES 1.2: Further processing
- CES 1.3: Packaging
- CES 1.4: Laboratory analysis
- CES 1.5: Cleaning and maintenance

Regarding CES 1.1, CES 1.2 and CES 1.4, dermal exposure measurements were performed according to the absorbent glove method, by analyzing TPP contamination of cotton gloves that are worn under the chemically protective gloves used (Buick, 2016). Reasonable worst case situations were selected over an 8-hour shift, to account for aggregated dermal exposure during the 8-hour shift.

Regarding CES 1.3 read across was applied by using dermal exposure measurements of exposure scenario CES 2.1. According to the evaluating Member State, the reasoning is well documented.

CES 1.5 comprises less routinely performed cleaning and maintenance tasks. Dermal exposure was estimated by read across of literature data (Christopher et al., 2011) and was comparable to the tasks in this exposure scenario. The evaluating Member State agrees with this approach.

Conclusion ES1: The evaluating Member State considers dermal exposure measurements and estimates are well performed. There are no further concerns.

ES 2: Industrial formulation of lubricant additives and lubricants.

ES2 is divided into ES2A (Industrial formulation of lubricant additives) and ES2B (Industrial formulation of lubricants). Processing operations, plant and equipment, operators' work practices and patterns, activities and tasks, conditions of use and operating conditions, RMM and Personal Protective Equipment (PPE) were identical for both exposure scenarios. The concentration TPP in phenate-based process streams used in ES2A was 7-25 times higher compared to ES2B. Measurements were performed in ES2A and the 90th percentile of the distribution was used. For ES2B, read across off the measurement data of ES2A was done. The 75th percentile of the distribution was used to account for the lower TPP concentration in ES2B. By doing this, the concentrations in ES2B are about half of ES2A, which is defendable since TPP concentrations in ES2B are 7-25 times lower.

Exposure scenario 2A: Industrial formulation of lubricant additives

During a sampling campaign ES 2A was divided into six contributing exposure scenarios:

- CES 2A.1: raw material reception and handling
- CES 2A.2: formulation
- CES 2A.3: packaging as drumming
- CES 2A.4: packaging as loading
- CES 2A.5: laboratory analyses
- CES 2A.6: cleaning and maintenance

Regarding CES 2A.1, CES 2A.2, CES 2A.3, CES 2A.4 and CES 2A.5, dermal exposure was measured under the chemically protected gloves according to the absorbent glove method, and TPP contamination was measured (see ES1). Reasonable worst case situations were selected over an 8-hour shift, to account for aggregated dermal exposure during the 8-hour shift.

CES 2A.6 comprises less routinely performed cleaning and maintenance tasks. Dermal exposure was estimated by read across of literature data (Christopher et al., 2011) and was comparable to the tasks in this exposure scenario.

Conclusion ES2A and ES2B: According to the evaluating Member State dermal exposure measurements and estimates of exposure scenario 2A are well performed. The only difference between exposure scenario 2A and 2B is the TPP concentration, which is 7-25 times lower in exposure scenario 2B. Regarding the exposure for ES 2B, the evaluating Member State agrees to take the 75th percentile of the distribution of the measurements of ES2A.

ES 4:Professional use of lubricants in vehicles or machinery.

There is only one contributing scenario comprising vehicle, vessel and light machinery servicing. A simulation study was performed with an experienced mechanic. Lubricant oil and filter of a passenger car was changed during a full-shift (14-16 cars). Lubricant oil with the highest TPP concentration was used. Dermal exposure was measured according to the absorbent glove method during 6 working days, and TPP contamination was measured (see ES1). The 90th percentile of the distribution was used.

Conclusion ES4: The evaluating Member State agrees to take the 90th percentile of the dermal exposure measurements that were performed.

Inhalation exposure

Regarding ES1 (Manufacturing of lubricant additives, lubricant and greases) and ES2 (Industrial formulation of lubricant additive, lubricant and greases) there was a concern for health risks in workers caused by the estimated inhalation exposure. The exposure by inhalation leads to a health risk (RCRs >1) when following ECHA Guidance on risk assessment and aggregated exposure has not been determined and considered.

This concern resulted in the following request for inhalation exposure information following a tiered approach:

Inhalation exposure measurements for similar exposure groups of workers in ES 1 Manufacture of lubricant additives, lubricants and greases (ATIEL-ATC Group A Prime) and in ES 2 Industrial formulation of lubricant additive, lubricant and greases (ATIEL/ATC Use Group A). Inhalation measurements shall be measured according to the internationally accepted guidelines, such as EN 689 and EN 482, or according to the guidance 'Testing Compliance with Occupational Exposure Limits for Airborne Substances' (https://www.arbeidshygiene.nl/-uploads/files/insite/2011-12-bohs-nvva-sampling-strategy-guidance.pdf), or similar, analysing TPP. Reasonable worst case situations shall be tested regarding both the TPP concentration in PDCS-CA, overbased used for a typical exposure scenario, and the work performed during an 8 hour shift, to account for aggregated inhalation exposure. Considering TPP is a UVCB, the analysis of TPP should be performed through the analysis of its main constituents, forming 95% of the UVCB composition.
This information is requested unless the Registrant(s) proves with adequate and documented justification that for technical or scientific reasons this information cannot be provided.

ES1: Manufacture of lubricant additives and lubricants.

During a sampling campaign ES1 was divided into 5 contributing exposure scenarios:

- CES1.1: Synthesis
- CES1.2: Further processing
- CES 1.3: Packaging
- CES 1.4: Laboratory analysis
- CES 1.5: Cleaning and maintenance

Regarding CES 1.1, CES 1.2 and CES 1.4 inhalation exposure was measured by personal air sampling (PAS) using OSHA Versatile Sampler tubes during the working day (Time Weighted Average TWA 8 h).

Regarding CES 1.3 read across was applied by using inhalation exposure measurements of exposure scenario CES 2.1. The reasoning is well documented according to the evaluating Member State.

Regarding CES 1.5 inhalation exposures were estimated by using the Advances Reach Tool (ART) using the 90th percentile. Exposure duration was based on Christopher et al. (2011). These exposure estimations were well performed according to the evaluating Member State.

Conclusion ES1: The evaluating Member State considers inhalation exposure estimates are well performed.

ES 2: Industrial formulation of lubricant additives and lubricants.

ES2 is divided into ES2A (Industrial formulation of lubricant additives) and ES2B (Industrial formulation of lubricants). For more explanation between the two scenarios see "Dermal exposure" of ES 2.

During a sampling campaign ES 2A was divided into 6 contributing exposure scenarios:

- CES 2A.1: raw material reception and handling
- CES 2A.2: formulation
- CES 2A.3: packaging as drumming
- CES 2A.4: packaging as loading
- CES 2A.5: laboratory analyses
- CES 2A.6: cleaning and maintenance

Regarding CES 2A.1, CES 2A.2, CES 2A.3, CES 2A.4 and CES 2A.5 inhalation exposure was measured by personal air sampling (PAS) using OSHA Versatile Sampler tubes during the working day (TWA 8 h).

CES 2A.6 comprises less routinely performed cleaning and maintenance tasks. Inhalation exposure was modelled with ART and exposure duration was based on Christopher et al

(2011). These exposure estimations were well performed according to the evaluating Member State.

Conclusion ES2A and ES2B: According to the evaluating Member State inhalation exposure measurements and estimates of exposure scenario 2A are well performed. The only difference between exposure scenario 2A and 2B is the TPP concentration, which is 7-25 times lower in exposure scenario 2B. Regarding the exposure for ES 2B, the evaluating Member State agrees to take the 75th percentile of the distribution of the measurements of ES2A.

ES 4: Professional use of lubricants in vehicles or machinery

There is only one contributing scenario comprising vehicle, vessel and light machinery servicing. For more explanation see "Dermal exposure" of ES4. Inhalation exposure was estimated using ART, exposure duration 8 hours. The evaluating Member State could not recalculate the inhalation exposure of ES4 based on the input variables used in the Institute of Occupational Medicine (IOM) report (IOM, 2013). However, the inhalation exposure is estimated to be very low according to the evaluating Member State.

Conclusion ES4: According to the evaluating Member State, the inhalation exposure is higher than the exposure estimated by the registrants, but still very low compared to the DNEL.

Combined exposure

The sum of dermal and inhalation exposures of each contributing scenario has to be considered for the risk assessment. This criterion is met since similar exposure groups were formed for every CES, dermal and inhalation exposure measurements and estimations were performed during the 8-hour working day, and the sum of inhalation and dermal exposures were taken into account.

7.12.1.2. Consumer

The exposure scenario for consumer use is as follow:

ES1: General consumer use of lubricants and greases in vehicles or machinery. Includes filling and draining of containers and enclosed machinery (including engines).

Initially the registrants used the higher tier model ConsExpo to calculate consumer exposure. Regarding the model, scenario and justification on used defaults, the evaluating Member State expressed a concern whether the provided exposure assessment for consumers covers all uses of the registered substance. Exposure levels may be underestimated and risks may therefore not be adequately controlled. The registrants were asked to provide additional information on uses and justification of model defaults and to update the dossier. Based on updates of the dossier during the substance evaluation process, the concern on consumer exposure was withdrawn within the scope of the current evaluation and no request was included in the Decision. Based on the current data in the dossier, an evaluation of the data is still described below.

In the dossier of February 2017 the consumer exposure was assessed with two different models: the CONCAWE SCED and the consumer ECETOC TRA V3.1 tool. The registrants provided additional information on density, frequency of use, dermal contact area and decreased the amount of substance in the product. The registrants refer to the ECHA guidance, paragraph "R.15.3.2. Dermal exposure" (ECHA 2016). The guidance presents the calculation and the allowed defaults. The registrants assessed the dermal exposure

according to the "layer thickness (0.01 cm) x surface area (hands)" approach which is in line with the guidance and the CONCAWE SCED. Additionally the registrants added a factor for transfer frequency and a frequency interval to calculate the chronic exposure. These two additional factors are invalid and not supported by the evaluating Member State.

About the dermal transfer frequency the CONCAWE SCED (CONCAWE_SCED_24_1_a_v1) states: "Dermal transfer factor (DTF) represents the % of total amount handled that is transferred to the skin. If this factor is being applied in a tool with an algorithm that uses skin surface area and the thickness of the layer to calculate dermal loading, such as ECETOC TRA v3, the DTF would need to be adjusted so that the final dermal loading remains the same as when the DTF is applied to the total amount." The evaluating Member State concludes that based on the amount used in the ES1 scenario, the use of DTF was done incorrectly.

For conclusions related to consumer exposure via general consumer use, see section 7.13.

ES2: Use in open system. Application of lubricant to work pieces or equipment by dipping or brushing (without exposure to heat), e.g. mould releases, corrosion protection, slideways.

In the initial dossier, the registrants provided no details on uses of lubricant/grease to work pieces or equipment by dipping or brushing, but assumed the ES1 scenario to cover the consumer use in open systems. The evaluating Member State expressed a concern on the consumer exposure assessment for this use.

Based on further informal communication, the dossier was updated and the use in open system was no longer included in the CSR.

Conclusion ES2: The evaluating Member State concludes that the consumer exposure is sufficiently controlled.

7.12.2. Environment

Not evaluated.

7.12.3. Combined exposure assessment

Not evaluated.

7.13. Risk characterisation

7.13.1. Workers

According to the evaluating Member State, combined inhalation and dermal RCRs for the endpoints within the scope of this evaluation are well below 1. This counts for ES1 (manufacture of lubricant additives and lubricants), ES2 (industrial formulation of lubricant additive and lubricants) and ES4 (professional use of lubricants in vehicles or machinery).

7.13.2. Consumers

Based on calculation by the evaluating Member State according the relevant guidance documents, using the defaults from the registration dossier, the evaluating Member State

calculated an RCR slightly larger than 1 (below 2). Following the ECHA R.15 guidance, the frequency of use as described in the dossier qualifies as infrequent. Considering this infrequent use, this RCR does not pose a concern.

Conclusion ES1: The evaluating Member State concludes that the consumer exposure is sufficiently controlled for the endpoints within the scope of the substance evaluation.

The evaluating Member State concludes that the consumer exposure is sufficiently controlled for the endpoints within the scope of the current evaluation. It is to be noted that further work is conducted by other Member States on the potential ED properties.

7.14. References

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7.15. Abbreviations

BMD	Benchmark dose
BMDL	Benchmark dose lower bound
BMDU	Benchmark dose upper bound
BMR	Benchmark response
CMR	Carcinogenic, Mutagenic, Reprotoxic
CSR	Chemical Safety Report
DTF	Dermal transfer factor
ES	Exposure scenario
NCE	Normochromatic erythrocytes
OECD	Organisation for Economic Co-operation and Development
PACT	Public Activities Coordination Tool
PCE	Polychromatic erythrocytes
PDSC-Ca	Phenol, dodecyl-, sulfurized, carbonates, calcium salts
RCR	Risk Characterization Ratio
RMMs	Risk Management Measures
RMOA	Risk Management Options Analysis
SIDS	Screening Information Dataset
TPP	Tetrapropenylphenol