MINISTERSTVO HOSPODÁRSTVA SLOVENSKEJ REPUBLIKY

Justification Document for the Selection of a CoRAP Substance

Substance Name (public name):	**2,6,10-trimethyldodecane (Farnesane)**
EC Number:	**622-542-2**
CAS Number:	**3891-98-3**
MSCA Austria	Umweltbundesamt GmbH (Spittelauerlände 5, 1090 Vienna) on behalf of the Austrian Competent Authority (Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management, Stubenring 1, 1010 Vienna, Austria)
and	
MSCA Slovakia	Ministry of Economy of Slovakia (Mierová 19, 827 15 Bratislava)
Date:	**22/03/2016**

Note

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

Table of Content

1 IDENTITY OF THE SUBSTANCE

1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	2,6,10-Trimethyldodecane (Farnesane)
IUPAC name (public):	2,6,10-trimethyldodecane
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	
Molecular weight or molecular weight range:	
Synonyms:	*Farnesane*

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

Structural formula:

Other relevant information about substance composition
The typical conc. of Fasarane is indicated, but for PBT assessment all constituents present at conc. ≥ 0.1% have to be indicated. Detailed information is missing.

Table: Constituent

EC number:	622-542-2
EC name (public):	-
CAS number:	3891-98-3
CAS name (public):	-
IUPAC name (public):	2,6,10-trimethyldodecane
Index number in Annex VI of the CLP Regulation:	
Molecular formula:	
Molecular weight or molecular weight range:	
Synonyms:	Farnesane 2,6,10-TRIMETHYLDODECANE

Structural formula:

1.2 Similar substances/grouping possibilities

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2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table: Completed or ongoing processes

RMOA	☐ Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	☐ Compliance check, Final decision
		☒ Testing proposals - Sub-chronic toxicity (90 days) oral - Reproductive toxicity (2-generation reproductive toxicity) - Reproductive toxicity (pre-natal developmental toxicity)
		☐ CoRAP and Substance Evaluation
	Authorisa-tion	☐ Candidate List
		☐ Annex XIV
	Restri-ction	☐ Annex XVII
Harmonised C&L	☐ Annex VI (CLP) (see section 3.1)	
Processes under other EU legislation	☐ Plant Protection Products Regulation Regulation (EC) No 1107/2009	
	☐ Biocidal Product Regulation Regulation (EU) 528/2012 and amendments	
Previous legislation	☐ Dangerous substances Directive Directive 67/548/EEC (NONS)	
	☐ Existing Substances Regulation Regulation 793/93/EEC (RAR/RRS)	
khol m conv entio n (POP	☐ Assessment	

	☐ In relevant Annex
Other processes / EU legislation	☐ Other (provide further details below)

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

There is no harmonised classification of Farnesane available in Annex VI of CLP.

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

Table: Harmonised classification

Index No	International Chemical Identification	EC No	CAS No	Classification		Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)		
-	-	-	-	-	-	-	-

3.1.2 Self classification

- In the registration:

Aspiration Hazard: Asp. 1 Tox. 1, H304: May be fatal if swallowed and enters airways.

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

  Skin Irrit. 2 H315: Causes Skin Irritation

  Eye Irrit. 2 H319: Causes serious eye irritation

  STOT SE 3 H335: May cause respiratory irritation

  Aquatic Chronic 4, H413

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

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4 INFORMATION ON (AGGREGATED) TONNAGE AND USES

4.1 Tonnage and registration status

Table: Tonnage and registration status

From ECHA dissemination site		
☒ Full registration(s) (Art. 10)	☐ Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per dissemination site)		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☒ 100 – 1000 tpa
☐ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	☐ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential
Joint submission		

4.2 Overview of uses

2,6,10-trimethyldodecane is used for the manufacture of fuels, hydraulic oils, lubricants, special fluids, other oils and cosmetics. Referring to the formulation and use of these products, industrial, professional and consumer uses exist. Total tonnage band: 100 – 1000 tonnes per year.

The uses of Farnesane are described by the following use descriptors in the registration dossier:
1.Formulation of cosmetics, special fluids and other oils:
ERC 2, PROC 1, PROC 2, PROC 3, PROC 4, PROC 5, PROC 8a, PROC 8b, PROC 9, PROC 15.
2.Uses at industrial sites as a fuel, lubricant and hydraulic oil:
ERC 4, ERC 7, PROC 5, PROC 8b, PROC 9, PROC 16, PROC 17, PROC 20, SU 0, Su 8, SU 10, SU 17.
3.Uses by professional workers as a fuel and lubricant:
ERC 8c, ERC 9a, ERC 9b, PROC 8a, PROC 17, SU 0, SU 8.
4.Consumer uses within cosmetic products:
ERC 8a, PC 39.

Table: Uses

Part 1:

☒ Manufacture	☒ Formulation	☒ Industrial use	☒ Professional use	☒ Consumer use	☐ Article service life	☐ Closed system

5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

5.1. Legal basis for the proposal

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

☐ Article 45(5) (Member State priority)

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

☐ Fulfils criteria as CMR/ Suspected CMR

☒ Fulfils criteria as Sensitiser/ Suspected sensitiser

☐ Fulfils criteria as potential endocrine disrupter

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

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

☒ Fulfils exposure criteria

☐ Fulfils MS's (national) priorities

5.3 Initial grounds for concern to be clarified under Substance Evaluation

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

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

Human Health Hazard

For the substance no CLH classification for skin sensitisation, no self-classification for skin sensitisation, conflicting study results for skin sensitisation or ambiguous results for skin sensitisation.

Based on the results of acute toxicity studies the substance is nontoxic for tested animals by oral and dermal routes.

Toxicokinetic data for Farnesane is very limited, except *in vitro* absorption study from the small intestine. There are available data on other alkanes of similar carbon chain length. Based on that data is apparent that the small intestine is the major site of absorption but that extensive faecal excretion (66%) of unchanged hydrocarbon occurs. It can be assumed that Farnesane has similar toxicokinetic properties.

Acute skin irritation/corrosion of the substance was investigated by *in vivo* study (key study), *in vitro* test and by three clinical studies on human subjects in large concentration ranges of Farnesane (10-100%). Results of submitted studies indicated not irritant/corrosive potential of the substance.

Acute eye irritation was examined by *in vivo* and *in vitro* tests. *In vivo* key study recorded no irritation of animal eyes after ocular administration of Farnesane. *In vitro* test showed minimal irritation of the test substance to eyes.

Sensitisation

Five *in vivo* tests on skin sensitisation have been submitted by the registrants.

Key LLNA study from 2014 (EU method B.42, TG 429) showed inability of 10%, 20% and 40% of Farnesane to induce proliferation of mouse lymph node cells which indicates no sensitising potential.

The negative outcome of the key study is additionally supported by studies on human volunteers (Repeat insult patch tests performed according to Good Clinical Practices) examined NEOSSANCE TMD (Farnesane) isolated from plants in concentration range 20% to 100%. Tests based on induction-challenge procedure recorded negative responses.

In contrast, another LLNA study (2010) indicates sensitising properties. The study was assigned by registrant as not reliable (3) and disregarded, because analysis of the lymph node proliferation was performed using BrdU flow cytometry and not using any of validated B.42, B.50 or B.51 EU methods.

However, test was performed under GLP conditions and seems to be reliable and well documented. Thus, the reliability categorisation carried out by the registrants needs to be examined. Detection of lymph node cells proliferation is based on the same principle (BrdU-specific antibody binding) as LLNA:BrdU-ELISA (EU method B.51, TG 442B) with the exception of the last step (direct fluorescent versus indirect colorimetric detection of immunocomplex). Detection of immunocomplexes using flow cytometry is validated and internationally accepted method, equal and even more sensitive to ELISA.

Applying criteria of LLNA:BrdU-ELISA method (positivity at SI>1,6) Farnesane at concentration of 50% shows clear sensitising properties. Positivity appeared at the highest tested dose (100%) cannot be taken into account due to severe dermal irritation observed in animals of the treated group.

There is a suspicion for skin/respiratory sensitising ability of Farnesane at concentrations above 40%. Respiratory sensitisers can also be captured by LLNA and there is a growing body of evidence that effective sensitisation of the respiratory tract by chemicals defined as respiratory allergens can and does occur in response to dermal contact (reviewed by Kimber et al., 2002).

Based on the ambiguous outcomes of the studies, a concern regarding the potential of Farnesane having sensitising properties has been identified. This concern needs further clarification and will be addressed during substance evaluation.

Mutagenicity

Three *in vitro* screening studies on mutagenicity have been performed: Bacterial reverse mutation assay (TG 471), *In vitro* mammalian chromosome aberration test (TG 473) on human peripheral lymphocytes and *In vitro* mammalian cell gene mutation test (TG 476) on mouse lymphoma cells.

Bacterial and mammalian mutation assays were concluded to be negative.

Clastogenicity of Farnesane at concentration 100 µg/mL in the presence of exogenous metabolic activation was found in mammalian chromosome aberration test. Dose-response relation was not observed and precipitation at the end of treatment was noted.

However, reliability of chromosome aberration test is questionable based on reported discrepancy in high water solubility of the test substance (50 mg/mL) and selection of water as vehicle; Farnesane is highly insoluble substance (reported ws in µg/L). Therefore the reliability of the study needs further evaluation.

QSAR prediction tools (TOXTREE, CAESAR and SarPy models for mutagenicity) were used to screen for structural alerts. In contrast to the above mentioned test results, Farnesane appears as compound without mutagenic potential; reliability of predictions is high.

Results of the screening tests together with QSAR prediction are ambiguous and thus, for clarification of mutagenic potential of the substance further evaluation is needed.

Carcinogenicity

There are no standard information requirements according to REACH; experimental data on carcinogenicity of the substance are not available. QSAR predictions (VEGA, carcinogenicity models CAESAR, TOXTREE) are not applicable due to equivocal readout and low reliability.

For integrated assessment for carcinogenicity sub-chronic toxicity data and clarification on mutagenic potential of the substance are necessary.

Summary of Human Health hazard:

There are two testing proposals in process: 90-day sub-chronic toxicity study and Pre-natal developmental toxicity study; the deadline for submitting the study results is October 2016.
To clarify the sensitising potential of the substance further evaluation is needed. Furthermore, there is a concern regarding mutagenicity and possible further testing would be needed to clarify the concern.
However, for overall conclusion on human health hazard the results of two proposed tests need to be available.

ENVIRONMENT

The registrant(s) stated that the substance is not a PBT/vPvB substance.

Environmental hazard

1.) estimated data (ECOSAR, v.1.00)

The toxicity of the substance, which is a neutral organic substance was calculated using the following smiles code CCC(C)CCCC(C)CCCC(C)C, the substance had a very low water solubility 0.004 mg/L = 4 µg/L (WskowWin estimated) and a log Kow of 7.5 (KowWin estimate). The chronic toxicity of Farnesane is high towards fish and daphnids (0.000366 and 0.000853 mg/L).

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Neutral Organics	: Fish	96-hr	LC50	0.002
Neutral Organics	: Fish	14-day	LC50	0.003
Neutral Organics	: Daphnid	48-hr	LC50	0.003
Neutral Organics	: Green Algae	96-hr	EC50	0.016 *
Neutral Organics	: Fish	30-day	ChV	0.000366
Neutral Organics	: Daphnid		ChV	0.000853
Neutral Organics	: Green Algae		ChV	0.015 *
Neutral Organics	: Fish (SW)	96-hr	LC50	0.002
Neutral Organics	: Mysid Shrimp	96-hr	LC50	4.84e-005
Neutral Organics	: Fish (SW)		ChV	0.008 *
Neutral Organics	: Mysid Shrimp (SW)		ChV	8.22e-007
Neutral Organics	: Earthworm	14-day	LC50	99.622 *

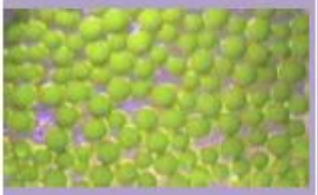
Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect.

2.) experimental data

The registrant stated that Farnesane is insoluble in water and showed no toxicity in chronic fish and daphnia studies at the water solubility limit of 0.25 µg/L. Short-term toxicity towards fish is not available. The short-term effects on daphnia cannot be evaluated by the screening member staes, because results are based on nominal concentrations and the used concentrations are unknown. The toxicity towards algae was investigated and no effects were observed at concentrations higher than 9 µg/L based on cell number. The estimated water solubility is 4 µg/L, so all NOEC values obtained (daphnids, algae, fish) were higher than the predicted water solubility; if the test were performed at concentration higher than the water solubility, all toxicity values seem questionable. No data are available for the terrestrial and sediment toxicity. The toxicity to soil organisms was waived. But taking into account the use of the substance, sediment and soil organisms are affected; here, an additional concern is identified.

At a Workshop on the Ecotoxicity Testing of "Difficult to Test" Substances in the Aquatic Environment: Evaluation and Testing of Poorly Water Soluble Substances Farnesane was included as case study (US EPA, 2014).
Following results were presented by Wildlife the laboratory who conducted the ecotoxicity tests (see Table below) on the WS. Herein, the tested concentrations of Farnesane were summarized, which are higher than the predicted water solubilty and in addition in contrast to the data presented by the registrant(s) a LOEC (based on length and reduction of neonates production) of 77 µg/L was derived from a chronic Daphnia study. EPA reviewed the study reports and determined that the results indicated no effects at saturation (NES); this interpretation is questionable. PNEC for freshwater was not derived by the registrant(s).

Summary of results

Test Organism	Measured test concentrations (µg a.i./L)	Recoveries	NOEC (µg/L)	Comments
Algae 	1.6, 2.5, 3.3, 4.4, 6.6, 9.3 (geometric mean measured) Test material not detected at end of study, likely due to adsorption to algae	77-99%	86	Results are based on Day 0 measured concentrations*
Fish 	11, 18, 34, 44, 66 (measured on days 1,6,14,21,28, 32)	66-94%	66	No significant effects at highest concentration tested
Daphnia 	12, 20, 36, 54, 77	77-100%	54	Reduction in length and neonate production at highest concentration tested (LOEC = 77 µg/L)

Environmental Fate Properties
Biodegradation

Summary of the phys – chem properties: ws(m) 0.25 µg/L, ws(e) 1.3 – 4.4 µg/L, log Kow at 30 °C (m) = 7.2, log Kow (e) = 6.5 (kow method) or 4.3 (MCI method).
In the registration dossier there are two different measured values of water solubility for the substance:
1) ws(m) = 0.25 µg/L; source - published meeting poster of SETAC Europe meeting 2007. In a published poster study the water solubility of a number of poorly soluble aliphatic hydrocarbons was investigated using a published 'slow-stir' method, analysis was by SPME coupled with GC-MS. No other details on the study were provided in the registration dossier.
2) ws(m) = 51.5 ug/L determined by WAF method. The study was developed based on the need to more accurately determine the level of solubility of a poorly water soluble substance in preparation for aquatic chronic testing; the study is assigned as scientifically valid.
However, the registrant assigned as key value of water solubility the value of ws(m) = 0.25 µg/L while no details on study were provided; so that according to screening MS the selected key value of ws is questionable and doubtful.
Determination of reliable value of water solubility is crucial as it represents the essential parameter in ecotoxicological testing.

1.) Estimated data

Hydrolysis study was waived by the registrant as the substance is highly insoluble in water. No further information on abiotic degradation is available from the dossier. For this chemical structure rate constants could not be estimated by HYDROWIN (v 2.00).
According to estimation obtained by AopWIN (v1.92) the substance is expected to be degraded by hydroxyl radicals in the atmosphere; a calculated half-life is of 6.856 hrs.

The substance was investigated according to the screening criteria for P (Guidance R11 document: Table R.11-4). Biowin 2 (non-linear model prediction) and Biowin 3 (ultimate biodegradation time) or Biowin 6 (MITI non-linear model prediction) and Biowin 3 (ultimate

biodegradation time) were used to assess the P criterion. Results are summarized in Table below.

Persistency estimation based on Biowin v.4.10 (EPISUITE 4.10)

Persistence	**Criterion**	**Conclusion**	**Probability of Rapid Biodegradation (BIOWIN v4.10):**
Biowin 2 (non-linear model prediction) and Biowin 3 (ultimate biodegradation time) or Biowin 6 (MITI non-linear model prediction) and Biowin 3 (ultimate biodegradation time)	Does not biodegrade fast (probability <0.5), and ultimate biodegradation timeframe prediction: ≥months (value < 2.2) or Does not biodegrade fast (probability <0.5) and ultimate biodegradation timeframe prediction: ≥months (value < 2.2)		Biowin 2: 0.4881 Biowin 3: 2.73 Biowin 6: 0.31

Biowin Models used are only recommended for "negative" screening, concluding on the non biodegradability (P). The overall prediction of the ready biodegradability was "NO".

Half-lives in soil, water and sediment based on Epi Suite

Degradation 50%	**Days**	**References**
Air	0.28	Epi Suite, level III fugacity model
Water	37.5	Epi Suite, level III fugacity model
Soil	75	Epi Suite, level III fugacity model
Sediment	338	Epi Suite, level III fugacity model

Sediment revealed the highest half-live (338 days).

2.) Experimental data

The submitted biodegradation study shows 32.4 % degradation after 28 days concluding, that the substance is not readily biodegradable (Schäfer, 2011). Another OECD 301 B test is available, showing 11.7% degradation after 28 days; the conclusion made by the registrant was that the substance is inherently biodegradable which is wrong as test system is for determining the ready biodegradability. Summarising, both studies show that the substance is not readily biodegradable.
In non-guideline study the primary degradation of individual hydrocarbons was measured in seawater at concentrations at or below their limit of solubility. The biodegradability was investigated for up to 180 days using a novel technique; the primary biodegradation rate constant for Farnesane was 0.1993 and calculated a half-life was 3.5 days in seawater. There is no information on GLP compliance and some experimental details of the study are missing. No higher tier degradation (simulation tests) respective half-life data according to Annex XIII of REACH are available for the substance; these tests have been waived by the registrant(s). Only an estimated log koc value(s) of 4.3 and 6.5 are available. Based on the available dataset on degradation no final conclusion on the P and vP criterion is possible.

Bioaccumulation

There are several indications for the bioaccumulation potential of the substance.

Terrestrial bioaccumulation: No data are available in the dossier.

Aquatic bioaccumulation

There are several indications for the bioaccumulation potential of the substance.

1.) Estimated data

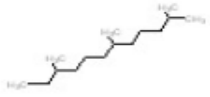
It has a log kow ≥3 (estimated log KOW = 7.5), a molecular weight ≤ 700 g/mol (MW: 212 g/mol) and the substance is adsorptive (log koc (e)= 6.5) and considered as immobile in soil and sediment. Hydrolysis is not expected. The bioaccumulation was estimated with EpiSuite (BCFBAF v3.01) and revealed a BCF of 1944 L/kg wet-wt based on the regression based method.

The PBT profiler (http://www.pbtprofiler.net/) summarizes the estimated data.

Results

Orange or red highlights indicate that the EPA criteria have been exceeded.
Black-and-white version

Persistence			Bioaccumulation	Toxicity
CCC(C)CCCC(C)CCCC(C) Farnesane				
PBT Profiler Estimate = PBT				
Media	Half-Life (days)	Percent in Each Medium	BCF	Fish ChV (mg/l)
Water	38	62%	1,900	0.00037
Soil	75	1%		
Sediment	340	27%		
Air	0.88	9%		



2.) Experimental data

No experimental data are currently available. But based on the available screening data (log kow) and estimated BCF values the substance is considered as potentially B/vB.

Summary PBT and vPvB criteria

Persistence: The substance is not readily biodegradable; the substance is therefore considered as potential P and vP by the screening Member States. No higher tier degradation tests are available. Due to the high log koc the substance is considered as immobile in soil and sediment. The registrant didn´t provide any information on degradation /transformation products.

Bioaccumulation: The substance is considered as potential B and vB by the screening Member states, based on the estimated log kow and BCF values. No experimental BCF data are available.

Toxicity: In general, due to the low water solubility, Farnesane is a difficult substance to be tested for aquatic toxicity. Nevertheless determination of reliable value of water solubility is crucial as it represents the essential parameter in ecotoxicological testing. No short-term studies for fish are available in the registration dossier. Estimated data show that the substance might be highly chronic toxic towards fish (ref. results obtained by the PBT profiler) and daphnids (ECOSAR). The available chronic toxicity values for daphnids and fish have to be carefully evaluated and cannot be assessed based on the rare information presented in the dossier. Nevertheless, toxicity values might be questionable, as the test might have been performed at higher concentrations than the water solubility, therefore the substance is considered as potential T based on the estimated results obtained by ECOSAR. LOEC values have been obtained for Daphnia (US EPA, 2014) at a concentration of 77 µg/L and these effects have not been stated in the dossier There is no human health data available for Farnesane to allow classification for repeat dose toxicity endpoints. There are two testing proposals in process - 90-day sub-chronic oral toxicity study and Pre-natal developmental toxicity study; the deadline for submitting study results is October 2016.

No additional data concerning the P, B and T properties have been found in the NITE database for the substance. No information on potential occurring metabolites are in the registration dossier.

Additional concern identified: missing data on sediment and soil toxicity

According to the Fugacity model III, water and sediment seems to be the target compartment of the substance; however, no toxicity information is given for sediment. The uses of the substance in personal care products (cosmetics) can lead to exposure of wastewatertreatment plants and receiving waters. The testing of microoganisms performed is considered as invalid, as it has been performed far above the water solubility limit. The uses of the substance as fuels and as hydraulic fluids might also lead to soil exposure and in addition, no tests are available.

USES

2,6,10-trimethyldodecane is used for the manufacture of fuels, hydraulic oils, lubricants, special fluids, other oils and cosmetics. Referring to the formulation and use of these products, industrial, professional and consumer uses exist. Total tonnage band: 100 – 1000 tonnes per year.

Human exposure (industrial, professional and consumer use)

The Registrant(s) classified the substance based on potential aspiration hazard as Asp. Tox. 1. Aspiration of hydrocarbon substances like 2,6,10-trimethyldodecane can result in severe acute effects such as chemical pneumonitis, varying degrees of pulmonary injury or death. This property relates to the potential for low viscosity material to spread quickly into the deep lung and cause severe pulmonary tissue damage. No further hazards for human health were identified by the Registrant(s). No DNELs, quantitative hazard reference values were derived. Therefore, the Registrant(s) provided qualitative instructions instead of a quantitative exposure assessment how to ensure appropriate handling of the substance, as no RCRs could have been derived.

Assuming Registrant(s) view of low(no) toxicity except for aspiration hazard, the qualitative approach is considered to be applicable and acceptable for ensuring safe use for industrial and professional users of this substance. Nevertheless, considering the concerns related to more severe effects for human health identified by the eMSCAs, the proposed risk management might be too generic and non-binding. In addition, regarding consumer use, these instructions are not considered to be applicable. Particular statements referring to consumer use are not provided. Considering the only registered consumer use"use in cosmetics", oral uptake of paraffins via lip stick, dermal uptake via skin creams, oils, etc., significant uptake of paraffins via this use is possible referring to open literature. As several or mixtures of paraffins are used for cosmetics, they maybe need to be considered in a cumulative approach. Uptake and accumulation also vary between the different members of this group of substances. Based on the potential concerns for human health, the risk management proposed and consumer uses like cosmetics, unacceptable risk for human health cannot be excluded at this stage.

Environmental exposure assessment and man via the environment

The Registrants did not identify any hazards for the environment: No PNECs were derived. Therefore, no quantitative risk assessment (derivation of RCRs) could have been calculated. Nevertheless, the Registrants performed a quantitative exposure assessment for the environment and for man via the environment. The Registrant(s) did not specify uses and any risk management measures. Tonnages and standard default values were used for prediction. Based on the lack of PNECs and RCRs, the Registrants concluded that the uses are considered to be safe for the environment independent from the derived exposure levels.

Based on the given exposure levels, this conclusion is not shared and not accepted. Referring to the calculations of the Registrant(s), significant parts of 2,6,10-trimethyldodecane imported into the EU enter the environment. Due to the confidentiality of these registration data, any numbers and examples are not provided.

The predicted levels are not considered to be acceptable for the environment and for man via the environment. Regarding exposure of the aquatic compartment, paraffins float on water and are barely miscible with water, therefore, they are a concern for aquatic organisms even if they are considered to have a low toxicity - especially assuming releases in the order of magnitude as calculated by the Registrant(s). Referring to the use of hydrocarbons, regulatory limit values for concentrations in water and drinking values exist. These values are significantly exceeded by the provided calculations.

These calculations do not demonstrate safe use of this substance. Risk management measures and descriptions for correct use are missing and required. In addition, new ecotoxicological data and data related to the PBT/vPvB status need to be taken into account, if requested based on concerns identified during evaluation.

References:

EPIWEB 4.1 (US EPA, 2011). Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.10 or insert version used]. United States Environmental Protection Agency, Washington, DC, USA.

Kimber I and Dearman RJ. 2002. Chemical respiratory allergy: role of IgE antibody and relevance of route of exposure. Toxicology 181-182, 311-315.

PBT profiler (http://www.pbtprofiler.net/): Developed by the Environmental Health Analysis Center under contract to the Office of Chemical Safety and Pollution Prevention , U.S. Environmental Protection Agency Computer Resources Donated by SRC, Inc. Ver 2.000 Last Updated September 4, 2012; information requested at 25.06.2014

US. EPA, 2014: Docket EPA-HQ-OPPT-2014-0516 > Federal Document ID EPA-HQ-OPPT-2014-0516-0002, Case Study 1: Farnesane Final

NITE database, National Institute of Technology and evaluation (http://www.safe.nite.go.jp/english/db.html)

Final Conclusion

The substance is not readily biodegradable, therefore the substance fulfils the screening criteria for P and vP. Simulation tests, terrestrial and sediment toxicity tests are missing. Short-term aquatic toxicity test for fish are not available. In addition, only estimated koc – values are available. The substance fulfils the screening criteria for B and vB criterion, based on the log kow values (estimated and experimentally derived). Due to the low water solubility, chronic ecotoxicity values have to be evaluated in depth. The evaluating member states considers the substance as pot. T, based on the ECOSAR estimates.

Based on available data the substance meets the screening criteria for PBT/vPvB. However, further evaluation is needed to be able to come to final conclusion on PBT/vPvB potential of the substance.
Due to the missing information to complete the PBT assessment for Farnesane, AT and SK consider this substance suitable candidate for inclusion of the substance in CoRAP. An extended compliance check before start of substance evaluation is proposed for targeting the standard data requirements that are missing according to REACH.

Clarification of sensitising properties and mutagenicity concern of the substance needs further evaluation.For overall conclusion on human health hazard the results of two proposed tests need to be available: 90-day sub-chronic toxicity study and Pre-natal developmental toxicity study.

Finally, both the new information for the human health endpoints and the missing information for environment (toxicity, fate and behavior) should be evaluated within the SeV process. The exposure assessment and risk management needs to be adapted accordingly based on the identified and verified hazards for man and environment.

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

☒ Information on toxicological properties	☒ Information on physico-chemical properties
☒ Information on fate and behaviour	☒ Information on exposure
☐ Information on ecotoxicological properties	☒ Information on uses
☐ Information ED potential	☐ Other (provide further details below)
Before substance evaluation starts, standard information requirments according to REACH can be targeted via an extended CCH and should inlcude: Simulation testing; Bioaccumulation in aquatic species, preferable fish; Effects on soil-microorgansims; and Adsorption/Desorption. Besides the PBT concern, further concern has been identified for the sediment and soil compartment, but this concern has to be dealt with under the SeV process. Water solubility and aquatic tests have to be carefully evaluated.	

5.5 Potential follow-up and link to risk management

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