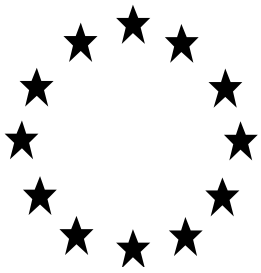
Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



EMPENTHRIN

Product-Type 18 (Insecticide)

March 2019 (revised version)

RMS = *Belgium*

Table of Contents

1 STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 PRINCIPLE OF EVALUATION

This assessment report has been established as a result of the evaluation of the active substance ***EMPENTHRIN*** as product-type 18 (Insecticides, acaricides and products to control other arthropods) carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012, with a view to the possible approval of this substance.

1.2 PURPOSE OF THE ASSESSMENT

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and a decision on the approval of ***EMPENTHRIN*** for product-type **18**, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available from the Agency web-site shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data for that purpose has been granted to that applicant.

1.3 PROCEDURE FOLLOWED

This assessment report has been established as a result of the evaluation of the active substance ***EMPENTHRIN*** as product-type 18 (Insecticides, acaricides and products to control other arthropods) carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012, with a view to the possible approval of this substance.

EMPENTHRIN (CAS no. 54406-48-3) was notified as an existing active substance, by Sumitomo Chemical (UK) plc, hereafter referred to as the applicant, in product-type 18.

Commission Regulation (EC) No 1451/2007 of 4 December 2007 lays down the detailed rules for the evaluation of dossiers and for the decision-making process..

In accordance with the provisions of Article 7(1) of that Regulation, Belgium was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for ***EMPENTHRIN*** as an active substance in Product Type 18 was April 30th 2006, in accordance with Annex V of Regulation (EC) No 1451/2007.

On 26/04/2006, BELGIUM competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 31/01/2007.

On 24/06/2016, the Rapporteur Member State submitted to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report.

Please note that in February 2014 the first draft CAR was submitted. This submission was rejected because the P (persistence) assessment was unclear and no CLH dossier was submitted. Based on this no acceptance, the eCA enhanced the P-assessment and finalized the CLH.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Agency. Revisions agreed upon were presented at the Biocidal Products Committee and its Working Groups meetings and the competent authority report was amended accordingly. **The competent authority report included a recommendation for the non-approval of *EMPENTHRIN*.**

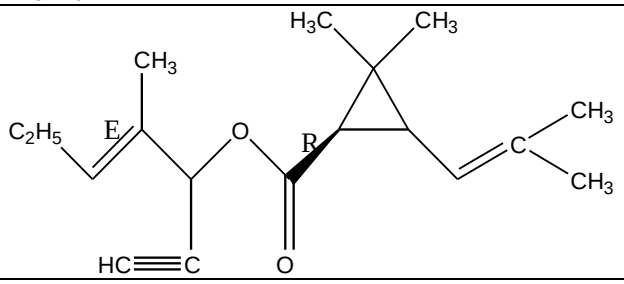
2 OVERALL SUMMARY AND CONCLUSIONS

2.1 PRESENTATION OF THE ACTIVE SUBSTANCE

2.1.1 Identity, Physico-Chemical Properties & Methods of Analysis

2.1.1.1 Identity

The exact identity of the active substance could not be proven due to the lack of a validated analytical method.

CAS-No.	54406-48-3 *
EINECS-No.	/
Other No. (CIPAC, ELINCS)	/
IUPAC Name	1-ethynyl-2-methylpent-2-enyl 2,2-dimethyl-3-(2-methylprop-1-enyl) cyclopropanecarboxylate
Common name, Synonym	-
Molecular formula	$C_{18}H_{26}O_2$
Structural formula	
Molecular weight (g/mol)	274.40 g/mol
Purity of a.s.	> 96%

* According to the discussion during the BPC-WG IV (from Sept. 2017), "only four isomers are present in the substance with a significantly high concentration, hence these four isomers should be considered for the substance naming that would be covered by the CAS entry with the number 918500-11-5".

The WG members agreed that only the four "major" isomers contribute to the naming of the substance. The minimum purity of the substance should be derived from the content of the four "major" isomers. Concentration ranges should be provided for the four "major" that contribute to the naming of the substance. The remaining 12 isomers are impurities, independent whether they contribute to the efficacy of substance and should be indicated with their maximum concentration level in the composition of the substance. However, since no validated analytical methods are available it was not possible to conclude on the exact substance identification.

2.1.1.2 Physico-Chemical Properties

Purified (99.4 %) ***EMPENTHRIN*** is a pale yellow transparent liquid. No strong characteristic odour is noted during handling.

The freezing point is determined to be less than -20 °C. The boiling point is 295.5 °C. Its relative density is 0.931 at 20.8 °C. Its vapour pressure is 0.01 Pa at 20 °C and is 0.0154 Pa at 25 °C. Henry's Law Constant is 3.187 Pa m^3/mol. Its solubility in water is low: 0.861 mg/L at 20 °C, at pH 5.84-6.45. It is highly soluble in n-heptane, dichloromethane, methanol, acetone, toluene, ethyl acetate, n-octanol: > 250 g/L at 20 °C.

The partition coefficient log P_{ow} = 6.30 at 20 °C and log P_{ow} = 4.76 at 25 °C. Its mean kinematic viscosity is 35.11 mm^2 /s at 20 °C and 11.89 mm^2 /s at 40 °C.

UV/VIS, IR, Proton-NMR and MS spectra are consistent with the structure of ***EMPENTHRIN***.

EMPENTHRIN does not dissociate.

EMPENTHRIN is thermally stable : the test substance is stable when stored for 14 days at 53-56 °C.

EMPENTHRIN is not flammable.

Auto ignition temperature is 266 ± 5 °C.

Flash point is 146 ± 2 °C.

The compound is non-oxidizing and non-explosive and is unlikely to react with container material.

2.1.1.3 Methods of Analysis

Adequate methodology exists for the determination of EMPENTHRIN and its isomers in the technical substance, in the product, in air and water. Also an analytical method for the determination of inert ingredients and impurities in technical grade EMPENTHRIN is given (confidential). They are based on analysis, using gas chromatography with hydrogen flame ionisation detector (GC-FI), with mass spectrometer or electron capture detector.

According to the discussion during the BPC-WG IV (from Sept. 2017), the currently provided analytical methods for monitoring in soil, air and water are not validated and therefore not acceptable. No

additional information is available to the applicant, which could be used for the identification of the active substance.

In addition, due to the unacceptability of the analytical method used, the reference specification was not accepted by the working group members.

A majority of the WG members expressed their concerns to include the active substance in the Union list without clear substance identification.

2.1.2 Intended Uses and Efficacy

- What is claimed :

The applicant does claim an insecticidal activity of ***EMPENTHRIN*** (pyrethroid insecticide) against "textile-attacking insects" i.e. case-making clothes/fur moth (*Tinea pellionella*) and webbing clothes moth (*Tineola bisselliella*) at all the development stages of the insects.

The product is represented by mothproofing strips made of EMPENTHRIN -impregnated filter paper strips framed with plastic holder.

This product is intended to be used for indoor use to protect stored clothing and other textiles in domestic permises in wardrobes and drawers by the non-professional (grand public).

- What kind of tests have been performed :

Efficacy tests against *Tineola bisselliella* and *Tinea pellionella* have been provided.

Please note that most of the studies provided by the applicant (6 out of 7 studies) will be only considered as supportive studies since they are old studies conducted more than 20 years ago and, for some of them, dosage rate used in wardrobe is not stated and no control /topical & contact is reported.

- What has been demonstrated at the AS approval stage :

Only one study has been recently conducted and assessed the efficacy of mothproofing strips made of ***EMPENTHRIN***-impregnated filter paper strips against eggs and mid-instar larvae of *Tineola bisselliella*. In this simulated-use study, conducted during a period of 6 months (which corresponds to the period of efficacy claimed by the applicant), eggs and mid-instar larvae of *Tineola bisselliella* were exposed to vapour from 1, 2 or 4 cassettes (each containing 166 mg a.i.) in wardrobe (0.48 m^3 containing 6 shirts) for 7 days, after which hatching, mortality and feeding damage were assessed. Even without statistical analysis, it seems that 4 cassettes (containing 166 mg a.i.) in an 0.48 m^3 wardrobe is needed to achieve more than 90% mortality of egg and mid-instar larvae and to inhibit fabric damage :

166 mg a.i. / cassette

4 cassettes ⇔ 664 mg a.i. / 0.48 m^3 => 1.38 g a.i./m^3

To observe a good efficacy against eggs and mid-instar larvae of *Tineola bisselliella*, an application rate of 1.38 g a.i./m^3 is needed.

The claimed residual effect of 6 months can't be supported.

As the consequence, in order to achieve the effective application rate of 1.38 g a.i./m^3, three mothproofing strips (each containing 0.5g EMPENTHRIN) are necessary to observe a good efficacy (as required in the TN$_s$G requirements) against eggs and mid-instar larvae of *Tineola bisselliella*. This application rate (⇔1.5 g a.i./ m^3) is much higher than the application rate claimed by the Applicant (i.e. 1 unit per 1.5 m^3 ⇔ 0,5 g a.i./1.5 m^3 ⇔ 0,333 g a.i./ m^3).

However, even if only one study was considered as key study, it is sufficient to demonstrate a basic efficacy of *EMPENTHRIN* against the one of the claimed target organisms and sufficient for AS approval.

<u>- What kind of tests have to be provided at the Product Authorisation Stage to allow a claim against "textile attacking insects" in general :</u>

According to the TNsG on product authorisation - product type 18, a product against textile-attacking insects should normally be tested on one of the moth species (*Tineola bisselliella, Tinea pellionella* or *Hofmannophila pseudospretella*) and on one carpet beetle species (*Anthrenus sp* or *Anthrenocerus sp*.) if a general claim against textile attacking insects is intended.

Tests showing sufficient residual efficacy against the target organisms should be also provided.

2.1.3 Classification and Labelling

<u>Proposal for the Classification and Labelling of the Active Substance :</u>

Classification	**as proposed by the BE CA according to Regulation EC 1272/2008 CLP**	
Hazard Class and Category Codes Hazard statement Code(s)	Acute oral tox cat. 4 STOT (SE) 2 Aquatic Acute 1 Aquatic Chronic 1	H302 H371 H400 H410
Labelling		
Pictograms	 GHS09 GHS07 GHS08	
Signal Word	Warning	
Hazard Statement Codes	H302: Harmful if swallowed H371: May cause damage to organs (Nervous system) H410: Very toxic to aquatic life with long lasting effects	

Precautionary statements	P102, P260, P264, P270, P273, P301+P312, P330, P309+P311, P391, P405, P501
Risk Mitigation measure	No access for cats to treated areas.
Specific Concentration Limits, M-factors	Acute 1: M = 100, based on 96h EC50 of 0.0017 mg/L for *Oncorhynchus mykiss* Chronic 1: M = 100, based on M-factor for aquatic acute 1

It should be noted that information on the carcinogenic properties is lacking so the carcinogenic classification could not be determined.

Please note that, during the BPC-WG IV (Sept. 2017), the WG noted that it will not be possible for RAC to conclude on classifying or not classifying for carcinogenicity, and this should be taken into account in deciding on the approval.

Proposal for the Classification and Labelling of the representative product :

Classification (based on calculation method)	**as proposed by the BE CA according to Regulation EC 1272/2008 CLP**
Hazard Class and Category Codes Hazard statement Code(s)	Acute toxicity, oral – cat. 4 H302 STOT (SE) 2 Nervous System H371 Aquatic Acute 1 H400 Aquatic Chronic 1 H410
Labelling	
Pictograms	 GHS09 GHS08
Signal Word	Warning
Hazard Statement Codes	H302: Harmful if swallowed H371: May cause damage to organs (Nervous system) H410: Very toxic to aquatic life with long lasting effects
Precautionary statements	P102, P260, P264, P270, P273, P301+P312, P330, P309+P311, P391, P405, P501
Risk Mitigation measure	No access for cats to treated areas.

2.2 SUMMARY OF THE RISK ASSESSMENT

2.2.1 Human Health Risk Assessment

As a summary :

Please note that, as agreed during the BPC-WG IV meeting and the ad hoc follow-up, the following values are taken into account to perform the HH risk assessment :

$AEL_{long\ term}$	0.0015 mg/kg bw/d
$AEL_{medium\ term}$	0.003 mg/kg/d
$AEL_{short\ term}$	0.014 mg/kg bw/d with NOAEL = 13.7 mg/kg/d
ARfD	0.03 mg/kg bw/d
ADI	0.005 mg/kg bw/d
Dermal absorption value	10%
Oral absorption value	30%
Inhalation absorption	100%

2.2.1.1 Hazard Identification of the Active Substance EMPENTHRIN

An assessment of the mammalian toxicology of EMPENTHRIN"has been conducted and presented within Section 6 of Document IIIA and Section 3 of Document IIA.

EMPENTHRIN is quickly (ca. 1 hr) and well absorbed (75-95%), distributed to the liver and kidney, metabolized by glucuronidation and completely eliminated (ca. 3 days). It is not acutely toxic by dermal and inhalatory route. It is moderately acutely toxic by oral route. It is not irritating to skin or eye. It does not cause sensitisation. Repeat dose studies suggest that toxicity (at 100 mg/kg bw and higher) is due to normal pyrethroid neurotoxicity and hepato and nephrotoxicity.

Concerning the carcinogenicity, there was no 2-years carcinogenicity study conducted, instead the applicant made a waiver.

Even though the waiver cited different arguments, it did not contain enough scientific evidence to proof that ***EMPENTHRIN*** is not carcinogenic, because:

- Results obtained with the (Q)SAR tools are sufficiently convincing to recognize the lack of alerts for genotoxicity but not for the lack of alerts for carcinogenicity.

- The results of the proliferation assay (Doc IIIA 6.7.1.) are not clearly negative. Moreover, an hyplerplasia of the biliary ducts was observed in the 6 months study in rats. The evolution of this kind of effects should be investigated.

- The comparison with 2 of the pyrethroids (Prallethrin and Imiprothrin) is probably too limited. It doesn't take into consideration the metabolism or 3D structure of the EMPENTHRIN molecule.

- We also note that there are different observations in the 6 months study (hyperplasia of bile ducts, droplet in the zona fasciculata of the adrenals, nephropathy without clear demonstration of the accumulation of the α2μ-globulin) justifying the request of a long term study.

Based on neurotoxicity symptoms (tremor and muscular fibrillation) in the acute oral and inhalation toxicity studies, ***EMPENTHRIN*** requires classification for STOT SE.

In the repeated oral and inhalation toxicity studies, no specific organ toxicities were observed within the guidance value ranges. There is no indication of any teratogenicity or reproductive toxicity associated with this compound. Human data are limited but medical surveillance indicates no effects.

2.2.1.2 Effects Assessment, AEL setting

NOAEL, Acute Exposure

At 1000 mg/kg bw (the lowest dose tested) in the acute oral rat study, muscular fibrillation, tremor and soft faeces were seen in 1, 7, and 1 animal respectively. Since acute effects of EMPENTHRIN are entirely symptomatic, it is also appropriate to consider results following the first dose in repeat-dose studies. In a 28-day oral rat study (with symptoms recorded daily) no early symptoms were seen at doses up to and including 30 mg/kg bw; in dogs, no first-day symptoms were seen at doses up to 1000 mg/kg bw. An acute oral NOAEL for EMPENTHRIN is therefore proposed as 30 mg/kg bw.

In the acute inhalation study, muscular fibrillation was seen in one animal after exposure to 2.29 mg/L EMPENTHRIN. Using a respiration rate of 0.045 m^3/kg/hr, this inhalation dose is equivalent to 412 mg/kg. In a 21-day inhalation study in rats at lower doses no instance of muscular fibrillation was seen. Irregular respiration and salivation occurred after the first exposure, with a NOAEL at 0.0476 mg/L (13.7 mg/kg bw) and LOAEL at 0.212 mg/L (58 mg/kg bw/day). It is unclear if these might be site-of-contact sensory reactions of oral and nasal mucosa. Suggestion of an inhalation acute NOAEL at 13.7 mg/kg bw is therefore highly conservative.

A safety factor of 1000 to account for intra and inter species variation and for the lack of short-term neurotixicity or developmental neurotoxicity studies (i.e. 10 x 10 x 10) is used.

$NOAEL_{acute}$ = 13.7 mg/kg bw/day

AEL_{acute} = 0.014 mg/kg bw/day

Subchronic, medium-term exposure

For medium term, it is appropriate to use the end points derived from studies using comparable exposure periods. Therefore, there is 2 studies in rats which can be used:

- 13 weeks inhalation study: Above 0.0946 mg/L, salivation, reduced body weight, irregular respiration, alopecia and kidney and liver effects can be observed in rats. The NOAEL is 0.0219 mg/L, what correspond to 6,3 mg/kg/day.

- 26 weeks oral study: Above 100 mg/kg bw/day there are mostly effects on the kidneys, liver and hypersalivation. The NOAEL is 10 mg/kg/day, corrected to 3 mg/kg/day according 30% oral absorption.

The oral study was therefore chosen for deriving the AEL because it leads to a smaller AEL than with the inhalation study.

An assessment factor of 1000 (i.e. 10 x 10 x 10 to account for intra, inter species variability and for the lack of short-term neurotoxicity or developmental neurotoxicity studies) is suitable.

$NOAEL_{subchronic}$ = 3 mg/kg bw/day (corrected for 30% oral absorption)

$AEL_{subchronic}$ = 0,003 mg/kg bw/day

Chronic, long-term exposure

Since there is no long-term study, the NOAEL of the 26 weeks oral study will be used with an additional assessment factor of 2 for the extrapolation of subchronic to chronic.

Adding 3 additional assessment factor of 10 for intra and inter species variability and an additional for the lack of carcinogenicity and neurotoxicity data, we obtain a total assessment factor of 2000.

$NOAEL_{subchronic}$ = 3 mg/kg bw/day (corrected for 30% oral absorption)

$AEL_{chronic}$ = 0,0015 mg/kg bw/day

Dietary risk

In case of a future intended use that could lead to food contamination, ADI and ARfD are determined below.

- *ARfD, Acute reference dose*

The 28 days oral study in rats will be used. The adverse effects above 100 mg/kg bw are salivation and liver and kidney increase. The NOAEL is 30 mg/kg bw.

An assessment factor of 1000 (i.e. 10 x 10 x 10 to account for intra, inter species variability and for the lack of short-term neurotoxicity or developmental neurotoxicity studies) is suitable.

$NOAEL_{acute}$= 30 mg/kg bw

ArfD = 0.03 mg/kg bw/d

- *ADI, acceptable daily intake*

As for the $AEL_{chronic}$, the NOAEL of the 26 weeks oral study will be used with an additional assessment factor of 2 for the extrapolation of subchronic to chronic.

Adding 3 additional assessment factor of 10 for intra and inter species variability and an additional for the lack of carcinogenicity and neurotoxicity data, we obtain a total assessment factor of 2000.

$NOAEL_{subchronic}$ = 10 mg/kg bw/day

ADI = 0,005 mg/kg bw/day

Summary

	$AEL_{long-term}$	**$AEL_{medium-term}$**	**$AEL_{short-term}$**	**ARfD**	**ADI**
NOAEL (study)	10 mg/kg bw/day (oral 13 & 26 wk rat, 13 wk dog)	10 mg/kg bw/day (oral 13 & 26 wk rat, 13 wk dog)	13.7 mg/kg bw/day (inhalation 21 day rat)	30 mg/kg bw/day (28 day oral rat)	10 mg/kg bw/day (oral 13 & 26 wk rat, 13 wk dog)
Interspecies variation	10	10	10	10	10
Intraspecies variation	10	10	10	10	10
Quality of Database (justification)	10 (lack of long-term toxicity & carcinogenicity)	10 (lack of short-term neurotoxicity & DNT)	10 (lack of acute neurotoxicity & DNT)	10 (lack of acute neurotoxicity & DNT)	10 (lack of long-term toxicity & carcinogenicity)
Extrapolation from medium-term to long-term	2	1	1	1	2
Total Assessment Factor	2000	1000	1000	1000	2000
Oral absorption	30%	30%	n/r	n/r	n/r
HH reference value	**0.0015 mg/kg bw/d**	**0.003 mg/kg bw/d**	**0.014 mg/kg bw/d**	**0.03 mg/kg bw/d**	**0.005 mg/kg bw/d**

2.2.1.3 Exposure assessment

The active substance ***EMPENTHRIN*** and the representative product, Vaporthrin® Mothproofer, are both manufactured and formulated outside the EU. Consequently, no direct contact with the active substance will occur and the only potential direct exposure to EMPENTHRIN will be from using the product. Vaporthrin® Mothproofer is to be marketed exclusively for the amateur/non-professional user. The packaging and design of the product (i.e., the Vaporthrin® Mothproofer is housed within a childproof plastic case, which in turn is individually wrapped in a hermetically-sealed envelope) would exclude use by professional operators on economic and practical grounds. Appropriate risk assessments have been conducted for the non-professional user only.

2.2.1.3.1 INDUSTRIAL EXPOSURE: Production/Formulation of active substance

The active substance ***EMPENTHRIN*** and product (Vaporthrin® Mothproofer) are not manufactured or formulated within the EU, so potential exposure to professional users will not occur in the EU. Vaporthrin is designed specifically for use by the non-professional/amateur user, so professional users will not use this product.

Conclusion : There is no concern for industrial workers

2.2.1.3.2 NON-PROFESSIONAL EXPOSURE from the use of the biocidal product

When amateur/non-professionals use the Vaporthrin® Mothproofer for the control of clothes moth they are assumed to wear no Personal Protective Equipment (PPE). Exposure calculations are detailed within Section 3 of Document IIB. When the Vaporthrin® Mothproofer units are placed in a closet (0.667 m^3), airborne EMPENTHRIN residues will result, and exposure to these airborne residues may occur. The TNsG describe a use scenario for strips and cassettes placed in closets or other sealed areas, which forms the basis of this exposure assessment. Dermal exposure is assumed to be negligible, as the product is supplied as a "ready-to-use" cassette and the unit is hung in its entirety in the closet after removal from the sealed envelope.

Five Vaporthrin® Mothproofers units are used per closet to be in accordance with RIVM factsheet (which considers a closet volume of 1.5m^3) and with the efficacious dose of 1383.33 mg a.s./m^3.

It will last for 6 months from the moment it is taken out of its wrapping.

The mixing & Loading scenario includes cutting and distributing the cassette among the clothes by an adult. (See details in Document IIB)

Inlahation acute (internal) dose estimated by ConsExpo is : 0.00385 mg/kg.

The application scenario estimates exposure concentrations of EMPENTHRIN when an adult open the wardrobe. (See details in Document IIB)

Table 2.2-1:Predicted exposures by inhalation

Intended use (PT)	**Exposure scenario**	**a.s**	**Acute exposure Inhalation Estimated internal exposure [mg/kg bw/day]**			**Chronic exposure Inhalation Estimated internal exposure [mg/kg bw/day]**		
PT18 (Insecticide)	Residential indoor use (strip or cassette used in closed areas)	500 mg per unit (20 – 22% of the total weight)	Adult **0.0019**	Child **0.005**	Toddler **0.011**	Adult **0.0019**	Child **0.005**	Toddler **0.011**

2.2.1.3.3 INDIRECT EXPOSURE as a Result of Use (Secondary Exposure)

The active substance may adhere on all materials in the wardrobe, such as clothes or bed linen.

No experimental data provides the average concentration of EMPENTHRIN detected in the clothes or bed linen. The scenario worst-case, according to which the total amount of EMPENTHRIN from the cassette will deposit on wardrobe's tissues, is presented in document IIB. For Toddlers, a scenario for oral exposure during hand-to-mouth contact was added.

Estimated internal exposure (Adult)= **0.0104 mg/kg/d**

Estimated internal exposure (Child)= **0.0144 mg/kg/d**

Estimated internal exposure (Infant)= **0.0182 mg/kg/d**

N.B. Indirect exposure via food : Since exposure to food from the use pattern is not expected, a dietary risk assessment was not undertaken. However, for possible future product authorisations (and the possibility of food or feed contamination), ADI and/or ARfD values have been determined and agreed by the WG : ARfD = 0.03 mg/kg bw.d & ADI = 0.005 mg/kg bw.d.

2.2.1.4 Combined Exposure

Since Mixing & Loading occurs only 2 times per year, it will be negligible compared to other exposures and will therefore not be taken into account in the calculation of combined exposure.

Table 2.2-2:Predicted combined exposure

	Application phase	Secondary exposure	**Combined exposure**

	Exposure via inhalation (mg/kg/d)	Exposure via contact with clothes (mg/kg/d)	**(mg/kg/d)**
Adult	0.0019	0.0104	**0.0123**
Child	0.005	0.0144	**0.0194**
Toddler	0.011	0.0182	**0.0292**

2.2.1.5 Risk characterisation

The risk characterisation is in general based on the assumption that the products are used according to the conditions for normal use.

2.2.1.5.1 Industrial Workers in production/formulation

There is no concern for industrial workers in the production and formulation of the active substance.

2.2.1.5.2 Human health risk for non-professional users (Primary exposure)

Tier 1 :

- **No PPE**

- Inhalation uptake estimated by ConsExpo **(for Mixing & Loading and for Application phase)**

Table 2.2-3**:** Primary exposure for non-professional users PT18

		Estimated Internal Exposure (mg/kg bw/day)	Relevant **NOAEL/LOAEL** [mg/kg.bw day] - Reference Value **$AEL_{chronic}$**	**AF MOE_{ref}**	**MOE**	**Exposure /AEL**
M&L	Adult	**0.00385**	NOAELacute= 13.7 AELacute= 0.014	1000	MOE_{acute} = 3558	TER_{acute} = 0.275
Application Phase	Adult	**0.0019**	$NOAEL_{subchronic}$ = 3 (corrected for 30% oral absorption) **$AEL_{chronic}$ = 0.0015**	2000	$MOE_{chronic}$ = 1579	$TER_{chronic}$ = 1.27
	Child	**0.005**		2000	$MOE_{chronic}$ = 600	$TER_{chronic}$ = 3.3
	Toddler	**0.011**		2000	$MOE_{chronic}$ = 273	$TER_{chronic}$ = 7.3

Conclusion: ***For Mixing & Loading, the risk is acceptable for adults without personal protective equipment.***

But, the risk for inhalation exposure when opening the wardrobe is unacceptable for adults, children and toddlers.

2.2.1.5.3 Human health risk from indirect exposure as a result of use (Secondary exposure)

Tier 1 : **Worst case owing to the lack of data about EMPENTHRIN concentration on wardrobe's tissues.**

Table 2.2-4**:** Secondary exposure for non-professional users PT18

	Estimated Internal Exposure (mg/kg bw/day)	Relevant **NOAEL/LOAEL** [mg/kg.bw day] - Reference Value **$AEL_{chronic}$**	**AF MOE_{ref}**	**MOE**	**Exposure /AEL**
Adult	**0.0104**	$NOAEL_{subchronic}$ = 3 (corrected for 30% oral absorption) **$AEL_{chronic}$ = 0.0015**	2000	$MOE_{chronic}$ = 288	$TER_{chronic}$ = 6.9
Child	**0.0144**		2000	$MOE_{chronic}$ = 208	$TER_{chronic}$ = 9.6
Toddler	**0.0182**		2000	$MOE_{chronic}$ = 165	$TER_{chronic}$ = 12.1

Conclusion: ***The risk for dermal (and oral for toddlers) exposure during contact with clothes or bed linen is unacceptable.***

2.2.1.5.4 COMBINED EXPOSURE

Exposure via inhalation and exposure via contact with tissues can occur simultaneously. Therefore, a calculation of combined exposure is justified.

Since Mixing&Loading occurs only 2 times per year, it will be negligible compared to other exposures and will therefore not be taken into account in the calculation of combined exposure.

Table 2.3.1.4-1**:** Combined exposure for non-professional users PT18

	Estimated Internal Exposure (mg/kg bw/day)	Relevant **NOAEL/LOAEL** [mg/kg.bw day] - Reference Value **$AEL_{chronic}$**	**AF MOE_{ref}**	**MOE**	**Exposure /AEL**
Adult	**0.0123**	$NOAEL_{subchronic}$ = 3 (corrected for 30% oIl yral absorption)	2000	$MOE_{chronic}$ = 244	$TER_{chronic}$ = 8.2
Child	**0.0194**		2000		

		$AEL_{chronic}$ = 0.0015		$MOE_{chronic}$ = 155	$TER_{chronic}$ = 12.9
Toddler	**0.0292**		2000	$MOE_{chronic}$ = 103	$TER_{chronic}$ = 19.5

<u>Conclusion</u>: The risk for combined exposure is unacceptable.

2.2.2 Environmental Risk Assessment

2.2.2.1 Fate and distribution in the environment

Hydrolysis as a function of pH

Hydrolysis of EMPENTHRIN was tested in aqueous sterile buffer solutions at pH 4, 7 and 9 and revealed a relatively fast hydrolysis with degradation half-lives of 12.56, 12.48 and 9.53 days at pH 4, 7 and 9 respectively and at 12 °C.

A major degradation product (U-1) with a structure consistent to a stable rearrangement product of EMPA was identified. No experimental data on the fate and behaviour of this metabolite is available, however a qualitative assessment predicts that this molecule will not be persistent or toxic in the environment.

Since the U-1 metabolite is formed through the cleavage of the ester linkage, it is fair to assume that an acid is simultaneously formed with the alcohol. This acid, chrysanthemic acid (d-c/t-CRA) is then further degraded to t-COOH-CA, which will then further degrades to CO_2. None of the former two molecules were detected in the hydrolysis study, but this was probably due to the positioning of the radiolabel. D-c/t-CRA and t-COOH-CA are considered persistent (P) and very persistent (vP) in the aquatic environment, but not toxic or bioaccumulative.

Photolysis in water

Aqueous photolysis will contribute largely to the degradation of EMPENTHRIN in water, with a half-life of 1.6 days in distilled water and even smaller half-lives in natural waters.

Photo-oxidation in air

The chemical half-life of EMPENTHRIN in the troposphere was estimated to be 0.32 hours in reaction with ozone and 0.691 hours in reaction with hydroxyl radicals, which leads to believe in a quick degradation of any EMPENTHRIN emitted to air.

Biodegradation

According to OECD guideline 302C, EMPENTHRIN is not inherently and thus not readily biodegradable.

No simulation tests are available for the substance in seawater or water/sediment systems.

An aerobic degradation study in soil concluded that EMPENTHRIN and its degradation products are rapidly degradable in soil with an estimated half-life of 11.3 days for EMPENTHRIN at the environmental relevant temperature of 12 °C. Amongst the identified metabolites were d-c/t-CRA and t-COOH-CA, but none of the detected metabolites are to be considered as major.

Mobility

According to an adsorption test performed compliant to OECD guideline 121, EMPENTHRIN revealed a large tendency to adsorb to soil material with a Koc of 5012 (log Koc = 3.70).

Bioaccumulation

According to a bioaccumulation study the lipid normalised BCF_{fish} is equal to 881.

2.2.2.2 Effect assessment

2.2.2.2.1 Aquatic compartment (including sediment)

From the available short term toxicity data for the three trophic levels in the aquatic environment (fish, invertebrates and algae), the lowest determined effect concentration was that determined for *Oncorhynchus mykiss*. This concentration of 1.7 µg L^{-1} was divided by an assessment factor of 1000 – as no chronic data are available – to reveal an aquatic PNEC of $1.7x10^{-6}$ mg L^{-1}.

In a 30 minute respiration inhibition test it was shown that the inhibitory effect concentration of EMPENTHRIN is larger than its water solubility of 0.111 mg L^{-1}.

From this value a PNEC for STP microorganisms was derived to be 0.0111 mg L^{-1}, using an assessment factor of 10.

One long-term toxicity test on a sediment dweller is available in the form of a 28d spiked-sediment study on *Chironomus yoshimatsui*. The EC_{10} of 1.1 mg/kg_{dwt} derived from this study, together with an assessment factor of 100 and the conversion factor of 4.6 to wet weight, result in a $PNEC_{sediment}$ of $2.39x10^{-3}$ mg kg_{dwt}.

For the metabolite d-t-CRA, three acute toxicity limit tests were made available testing the three trophic levels (fish, daphnids and algae). None of the organisms showed signs of toxicity at concentrations up to 1.6 mg/L. Therefore it was decided that the risk assessment performed on the mother molecule suffices to encompass the potential risk for the environment due to the metabolite.

2.2.2.2.2 Terrestrial environment

Two soil toxicity tests are available for EMPENTHRIN, one on soil micro-organisms testing both nitrogen and carbon transformation, and one on earthworms. The lowest endpoint derived from these tests was the 14d LC_{50} of 160 mg kg_{dwt}^{-1} for earthworms.

However, since EMPENTHRIN has an insecticidal mode of action and no data is available on arthropods (the potential most sensitive species), the $PNEC_{soil}$ should be derived following the EPM-method. This results in a $PNEC_{soil}$ of $1.5x10^{-4}$ mg kg_{wwt}^{-1}.

2.2.2.2.3 Non-compartment specific effects relevant to the food chain

Predicted no effect concentrations for top predators were estimated based on the currently available information.

No data for avian toxicity is available at this moment, so a $PNEC_{oral,\ birds}$ cannot be determined at this time.

For mammals, a repeated dose toxicity study on rats yieled a NOAEL of 10 mg kg_{bw}^{-1} day^{-1}, which then resulted in a $NOEC_{mammal,\ food\ chr}$ pf 200 mg kg_{food}^{-1} and eventually results in a $PNEC_{oral,\ mammal}$ of 2.22 mg kg_{food}^{-1}.

Summary of PNEC values

Compartment	Unit	PEC value
$PNEC_{water}$	mg L^{-1}	$1.7x10^{-6}$
$PNEC_{microorganisms(STP)}$	mg L^{-1}	0.0111
$PNEC_{sediment}$	mg kg_{wwt}^{-1}	$2.39x10^{-3}$
$PNEC_{soil}$	mg kg_{wwt}^{-1}	$1.5x10^{-4}$
$PNEC_{bird}$	mg kg_{food}^{-1}	no data
$PNEC_{mammal}$	mg kg_{food}^{-1}	2.22

2.2.2.3 PBT assessment

	EMPENTHRIN	U-1	d-c/t-CRA	t-COOH-CA
P/vP	Potentially P/vP (aquatic environment)	/	P (aquatic environment)	vP (aquatic environment)
B/vB	/	/	/	/
T	Toxic	/	/	/

EMPENTHRIN

No experimental data for the aquatic environment is available for the assessment of the P-criterion. However, following the screening criteria , EMPENTHRIN is to be considered potentially P or vP in the aquatic environment due to the results of the MITI II test on inherent biodegradability.

For the renewal stage of the substance at the latest, a water/sediment study according to OECD 308, monitoring all isomers and degradation products, will be required in order to make a conclusive P-assessment.

Following a DT_{50} of 11.3 days in soil, EMPENTHRIN is not considered persistent in soil.

The BCF derived from an accumulation test was averaged and normalised to a lipid content of 5 %, resulting in a BCF 881. However, during WG-IV-2017 it was decided that the results of this study alone could not serve to decide on EMPENTHRIN being not bioaccumulative.

The calculated BCF from the log Kow was 40179. Based on this EMPENTHRIN could be considered bioaccumulative, but since this calculation is known to be subject to a lot of uncertainty; and comparison with other substances shows that the calculation makes gross-overestimations; this calculated BCF cannot be regarded as proof of EMPENTHRIN fulfilling the B-criterion either.

Other weight of evidence, such as experimental BCF-values for similar structures being in the same order of magnitude as the experimental BCF derived for EMPENTHRIN, the estimated low BCF for EMPENTHRIN through EPI Suites BCFBAF model and evidence from single and repeated dose toxicity studies in rats where complete elimination of EMPENTHRIN is recorded, are the basis to eventually conclude that EMPENTHRIN is not expected to bioaccumulate.

Following the results of the acute toxicity tests and according to the screening criteria, EMPENTHRIN should be classified as toxic (T).

Since based on the current available information EMPENTHRIN fulfils 2 of the 3 PBT criteria, EMPENTHRIN should be considered **a candidate for substitution**.

U-1

No experimental data is available for this metabolite.

Following QSAR predicitons on biodegradation, U-1 should not be considered persistent (P) based on the P screening criteria

The BCFBAF model calculates a BCF of 5.884 – 7.172 L kg_{wwt}^{-1}, from which it follows that U-1 does not fulfil the B-criterium.

Following ECOSAR predictions, U-1 should neither be considered toxic (T).

d-c/t-CRA

Following the commonly agreed water/sediment total system DT_{50} of 52.9 days, it is concluded that chrysanthemic acid fulfils the P-criterion.

The BCFBAF model calculates a BCF of 3.162 232.2 L kg_{wwt}^{-1}, meaning that d-c/t-CRA is not considered bioaccumulative (B).

Following the results of the aquatic acute limit tests, d-c/t-CRA should not be classified as toxic (T).

t-COOH-CA

Following the commonly agreed water/sediment total system DT_{50} of 101 days, it is concluded that t-COOH-CA should be considered very persistent (vP) in the aquatic environment.

No further experimental data is available for this molecule.

The BCFBAF model calculates a BCF of 367 – 427.8 L kg_{wwt}^{-}, so t-COOH-CA is not considered bioaccumulative (B)

Following ECOSAR predictions, t-COOH-CA should not be considered toxic (T) either.

2.2.2.4 Exposure assessment and risk characterisation

The insecticide product Vaporthrin® Mothproofer (20-22 % w/w EMPENTHRIN is solely used indoors by non-professionals. The product consists of a cellulose rectangle impregnated with EMPENTHRIN enclosed in a plastic surround, which can be hanged in closets to protect clothes against moths.

Due to the indoor use, there will be no direct exposure of any environmental compartment to EMPENTHRIN. The possible emission routes of the product are emission to outdoor air through the ventilation of the house and to wastewater through the cleaning of surfaces.

There is also a possible exposure to soil either through deposition of EMPENTHRIN from the atmosphere or through STP sludge application or both.

The predicted environmental concentrations in the different environmental compartments were calculated using the OECD Emission Scenario Document No.18 (ESD, July 2008) for “Insecticides, acaracides and product to control other arthropods for household and professional uses” and the

Guidance on Biocidal Product Regulation, while also taking into consideration the conclusion on efficacy of the active substance and the decisions made during the WG-IV-2017 and TAB.

A TIER 1 and TIER 2 assessment was done, in which the TIER 1 assessment considers that 2.5 wardrobes per household will be equipped with the efficacious amount of Vaporthrin ® Mothproofer units (i.e. 4.15 units for a standard wardrobe of 1.5 m³), while the TIER 2 assessment follows more the traditional ESD assumption of only a single wardrobe being equipped with the efficacious amount of units.

Compartment	Unit	PEC value	
		TIER 1	**TIER 2**
PEC_{STP}	mg L^{-1}	$1.93x10^{-4}$	$7.71x10^{-5}$
$PEC_{surface\ water}$	mg L^{-1}	$1.91x10^{-5}$	$7.65x10^{-6}$
$PEC_{sediment}$	mg kg^{-1}	$2.10x10^{-3}$	$8.40x10^{-4}$
PEC_{air}	mg m^{-3}	$1.59x10^{-6}$	$6.37x10^{-7}$
PEC_{soil}	mg kg^{-1}	$5.28x10^{-4}$	$2.11x10^{-4}$
$PEC_{groundwater}$	mg L^{-1}	$5.96x10^{-6}$	$2.38x10^{-6}$
$PEC_{oral\ predator}$ (aquatic)	$mg._{kgwet\ fish}{}^{-1}$	3.84	1.54
$PEC_{oral\ predator}$ (terrestrial)	$mg._{kgwet\ earthworm}{}^{-1}$	$6.41x10^{-2}$	$2.56x10^{-2}$

For a quantitative risk assessment the PEC values calculated in the environmental exposure assessment are compared to their respective PNEC values calculated in the effects assessment. The resulting risk characterisation ratios are a means to evaluate the risk for the different environmental compartments and are summarised in the tables below.

Aquatic environment

Compartment	PEC	PNEC	PEC/PNEC	Conclusion
TIER 1 (considering 2.5 wardrobes per household)				
STP	$1.93x10^{-4}$	$1.11x10^{-2}$	$1.74x10^{-2}$	no risk
Surface Water	$1.91x10^{-5}$	$1.70x10^{-6}$	11.26	**RISK**
Sediment	$2.10x10^{-3}$	$2.39x10^{-3}$	0.88	no risk
TIER 2 (considering use in only 1 wardrobe)				
STP	$7.71x10^{-5}$	$1.11x10^{-2}$	$6.95x10^{-3}$	no risk
Surface water	$7.65x10^{-6}$	$1.70x10^{-6}$	4.50	**RISK**
Sediment	$8.40x10^{-4}$	$2.39x10^{-3}$	0.35	no risk

Terrestrial environment

Compartment	PEC	PNEC	PEC/PNEC	Conclusion
TIER 1 (considering 2.5 wardrobes per household)				
Soil after 10 years sludge application	$5.28x10^{-4}$	$1.51x10^{-5}$	3.5 x 10 = 35.05	**RISK**

Groundwater	$5.96x10^{-6}$	0.0001	$5.96x10^{-2}$	no risk
TIER 2 (considering use in only 1 wardrobe)				
Soil after 10 years sludge application	$2.11x10^{-4}$	$1.51x10^{-5}$	1.40 x 10 = 14.02	**RISK**
Groundwater	$2.38x10^{-6}$	0.0001	$1.32x10^{-2}$	no risk

Secondary poisoning

Compartment	PEC	PNEC	PEC/PNEC	Conclusion
TIER 1 (considering 2.5 wardrobes per household)				
fish-eating birds	3.84	N/A	N/A	N/A
fish-eating mammals	3.84	2.22	1.73	**RISK**
worm-eating birds	$6.41x10^{-2}$	N/A	N/A	N/A
worm-eating mammals	$6.41x10^{-2}$	2.22	$2.88x10^{-2}$	no risk
TIER 2 (considering use in only 1 wardrobe)				
fish-eating birds	1.54	N/A	N/A	N/A
fish-eating mammals	1.54	2.22	0.69	no risk
worm-eating birds	$2.56x10^{-2}$	N/A	N/A	N/A
worm-eating mammals	$2.56x10^{-2}$	2.22	$1.15x10^{-2}$	no risk

Based on the available data and the proposed use pattern of ***EMPENTHRIN*** in the Vaporthrin® Mothproofer, **the BE eCA concludes that there are unacceptable risks to the aquatic environment, and more particularly for the surface water.** No risks are expected for the Sewage Treatment Plant or for sediment dwellers.

Risks are also calculated for the terrestrial environment, for soil organisms. No risks are calculated for groundwater.

For fish-eating mammals, risks are calculated for the TIER 1 assessment. However, when considering that the BCF-value calculated from the equation from BPR Vol. IV guidance was used, which is subject to a high degree uncertainty and has been shown to give gross over-estimations in cases with similar molecules; and when considering other calculated BCF-values for EMPENTHRIN, there is no longer a risk calculated for the TIER 1 assessment. The TIER 2 assessment never gives a risk for fish-eating mammals.

No conclusions for fish-eating birds can be made, due to lacking data on toxicity of ***EMPENTHRIN*** to birds.

3 EXCLUSION CRITERIA

3.1 EXCLUSION CRITERIA

3.1.1 Assessment of CMR properties

Criteria (BPR Article 5[1])	Assessment
Active substances which have been classified in accordance with Regulation (EC) No 1272/2008 as, or which meet the criteria to be classified as, carcinogen category 1A or 1B	***Not determined, information is lacking on the carcinogenic properties.***
Active substances which have been classified in accordance with Regulation (EC) No 1272/2008 as, or which meet the criteria to be classified as, mutagen category 1A or 1B	*Active substance is not classified and does not meet the criteria to be classified as Muta. Cat. 1A or 1B.*
Active substances which have been classified in accordance with Regulation (EC) No 1272/2008 as, or which meet the criteria to be classified as, toxic for reproduction category 1A or 1B	*Active substance is not classified and does not meet the criteria to be classified as Repr. Cat. 1A or 1B.*

Conclusion on CMR properties	***Conclusion not possible since information is lacking on the carcinogenic properties.***

3.1.2 Assessment of endocrine disrupting properties

Criteria (BPR Article 5)	**Assessment**
Active substances which, on the basis of the criteria specified pursuant to the first subparagraph of paragraph 3 are considered as having endocrine-disrupting properties that may cause adverse effects in humans	*(The criteria are not yet published)*
Pending the adoption of those criteria[1], active substances that are classified in accordance with Regulation (EC) No 1272/2008 as, or meet the criteria to be classified as, carcinogen category 2 and toxic for reproduction category 2[2].	*Carcinogenic classification not determined, information is lacking on the carcinogenic properties.* *Active substance is not classified and does not meet the criteria to be classified as Repr. Cat. 2.*
Substances such as those that are classified in accordance with Regulation (EC) No 1272/2008 as, or that meet the criteria to be classified as, toxic for reproduction category 2 and that have toxic effects on the endocrine organs[3].	*Active substance is not classified and does not meet the criteria to be classified as Repr. Cat. 2.* *Active substance has not been shown to have toxic effects on endocrine organs.*

Criteria (BPR Article 5)	**Assessment**
Active substances which are identified in accordance with Articles 57(f) and 59(1) of Regulation (EC) No 1907/2006 as having endocrine disrupting properties	*Active substance has not been identified as having endocrine disrupting properties.*

Conclusion on ED properties	*The exclusion criteria in BPR Article 5(1)d are not met.*

3.1.3 PBT Assessment (following Annex XIII to Regulation (EC) No 1907/2006)

3.1.3.1 Assessment of persistence

3.1.3.1.1 Screening

In an inherent biodegradability test according to the modified MITI (II) test, 0% of ***EMPENTHRIN*** was degraded. This could be a marker for possible persistency of the substance.

In a hydrolysis study (according to OECD 111) the half-life of ***EMPENTHRIN*** in neutral freshwater was 4.41 days at 25 °C test temperature (12.48 days at 12 °C). Photolysis half-life in distilled water was 1.6 days at 25 °C test temperature. In river- and seawater the photolysis half-lives were 4.8 hours and 2.1 hours respectively.

According to BIOWIN v4.10 the prediction for BIOWIN 2 (Non-Linear Model Prediction) is "Biodegrades fast" with a probability of 0.8128 and the prediction for BIOWIN 3 (Ultimate Biodegradation Timeframe) is "Weeks-Months" with a value of 2.5209. According to the screening criteria according to the REACH guidance (Table C.1-2), the BIOWIN screening does not warrant giving a P assignment to EMPENTHRIN.

No simulation tests are available for the substance in seawater or water/sediment compartments.

An aerobic degradation study in soil concluded that EMPENTHRIN and its degradation products are rapidly degradable in soil with an estimated half-life of 11.3 days for EMPENTHRIN at the environmental relevant temperature of 12 °C.

Conclusion: According to the P screening criteria, EMPENTHRIN should be considered **potentially P or vP** in the aquatic environment following the results of the MITI II test (OECD 302C).

A conclusive assessment of the persistency of the substance is however required at the latest at the renewal stage. To this end, a water/sediment degradation study of the active substance, monitoring all isomers and degradation products, following OECD 308 guideline will be required.

Metabolites

Due to cleavage of the ester bond during degradation of EMPENTHRIN, the first two metabolites formed are an alcohol, EMPA or a rearrangement product named U-1, and chrysanthemic acid (d-c/t-CRA).

In the hydrolysis study, the U-1 metabolite was formed at maximum concentration of 61.8 %, making this a major metabolite for the aquatic environment. Following the cleavage of the ester bond, it is logical to assume an equal amount of d-c/t-CRA would be formed, even though it is not detected in the hydrolysis study, due to the positioning of the radiolabel not following that side of the molecule. Then d-c/t-CRA is further degraded to t-COOH-CA

- For **U-1** no experimental data for degradation are available, but QSAR calculations on ready biodegradability using BioWin vs.4.1 resulted in a probability of 0.9140 for fast biodegradation according to Biowin 2, an ultimate biodegradation timeframe of 3.0847 (*weeks*) in Biowin 3 and a prediction of readily degradable (0.5846) according to Biowin 6. Following this prediction and according to the P-screening criteria, U-1 is not considered to be persistent.
- For **d-c/t-CRA** the QSAR BioWin vs.4.1 screening gives a calculation of 0.3869 for Biowin 2, 2.9799 for Biowin 3 and 0.2788 for Biowin 6. Following the screening criteria no conclusion can be made on the persistency of d-c/t-CRA with these predictions (the Biowin 3 ultimate biodegradation timeframe suggests weeks instead of months)
- For **t-COOH-CA** BIOWIN estimation resulted in a biodegradation probability of 0.5808 in Biowin 2 (*biodegrades fast).*. In Biowin 3 the ultimate biodegradation timeframe was predicted at 3.3668 (*weeks*) and Biowin 6 concluded *readily biodegradable* (0.6006). According to the screening criteria t-COOH-CA should not be considered to be persistent based on these predictions.

Following the aerobic soil degradation study, none of these metabolites are to be considered as major in the soil compartment.

3.1.3.1.2 Assessment

P Criteria	Assessment
T1/2 > 60 days in marine water, or	**EMPENTHRIN:** no experimental data **U-1:** no experimental data. **d-t/c-CRA:** no experimental data **t-COOH-CA:** no experimental data
T1/2 > 40 days in fresh- or estuarine water, or	**EMPENTHRIN:** no experimental data **U-1:** no experimental data. **d-t/c-CRA:** $DT_{50\text{-total system}}$ = 52.9 d (12 °C) **t-COOH-CA:** $DT_{50\text{-total system}}$ = 101 d (12 °C)
T1/2 > 180 days in marine sediment, or	**EMPENTHRIN:** no experimental data **U-1:** no experimental data. **d-t/c-CRA:** no experimental data **t-COOH-CA:** no experimental data
T1/2 > 120 days in fresh- or estuarine sediment, or	**EMPENTHRIN:** no experimental data **U-1:** no experimental data. **d-t/c-CRA:** $DT_{50\text{-total system}}$ = 52.9 d (12 °C) **t-COOH-CA:** $DT_{50\text{-total system}}$ = 101 d (12 °C)
T1/2 <= 120 days in soil.	**EMPENTHRIN:** DT_{50} = 11.3 days (12 °C) **metabolites:** no major metabolites

vP Criteria	Assessment
T1/2 > 60 days in marine-, fresh- or estuarine water water, or	**EMPENTHRIN:** no experimental data **U-1:** no experimental data. **d-t/c-CRA:** $DT_{50\text{-total system}}$ = 52.9 d (12 °C) **t-COOH-CA:** $DT_{50\text{-total system}}$ = 101 d (12 °C)
T1/2 > 180 days in marine-, fresh- or estuarine sediment, or	**EMPENTHRIN:** no experimental data **U-1:** no experimental data. **d-t/c-CRA:** $DT_{50\text{-total system}}$ = 52.9 d (12 °C) **t-COOH-CA:** $DT_{50\text{-total system}}$ = 101 d (12 °C)
T1/2 > 180 days in soil.	**EMPENTHRIN:** DT_{50} = 11.3 days (12 °C) **Metabolites:** no major metabolites

Conclusion on P / vP properties	**EMPENTHRIN** No experimental data for the aquatic environment is available for the assessment of the P-criterion. However, following the screening criteria , EMPENTHRIN is to be considered potentially P or vP. For the renewal stage of the substance at the latest, a water/sediment study according to OECD 308, monitoring all isomers and degradation products, will be required in order to make a conclusive P-assessment. Following a DT_{50} of 11.3 days in soil, EMPENTHRIN is not considered persistent in soil. **U-1:**

	No experimental data is available. Does not fulfil the P screening criteria **d-c/t-CRA:** Fulfils the P-criterion following an aquatic DT_{50} of 52.9 days. **t-COOH-CA:** Fulfils the vP-criterion following an aquatic DT_{50} of 101.0 days.

3.1.3.2 Assessment of bioaccumulation

3.1.3.2.1 Screening

The log octanol-water partitioning coefficient (Log K_{ow}) for EMPENTHRIN was determined at 6.30 at 20 °C, which would indicate, according to the screening criteria, that EMPENTHRIN is a **possible B**-substance, because it is larger than the cut-off value of 4.5.

Metabolites

The octanol-water partitioning coefficient for the metabolites was estimated using EPISUITE vs4.1:

	U-1	**d-t/c-CRA**	**t-COOH-CA**
Log K_{ow} (estimate)	3.49	0.35	1.80

Following these estimates, none of the metabolites should be considerd B or vB according to the screening criterium.

3.1.3.2.2 – Weigth of evidence

Following the screening-assessment for the B-criterium, EMPENTHRIN could be considered as a possible B-substance.

For EMPENTHRIN, an accumulation test is available, in which a BCF-value, normalised to a lipid content of 5 %, of 881 L/kg_{wwt} was derived. However, during the WG-IV-2017 it was decided that the reliability index of 3 should be assigned to this study and that therefore the results could not be used as stand-alone to evaluate the B-criterium, but as part of a Weight-of-Evidence assessment.

It is true that when the BCF is calculated through the parabolic equation provided in the BPR Volume IV guidance, a much higher BCF of 40179 is calculated. However, the BPR guidance itself states that this mathematical equation has a much higher degree of uncertainty. In a statement provided by the applicant for the WG-IV-2017, a comparison was made for a number of substances between BCF-values estimated through the equation and experimental BCF-values. This comparison demonstrates that the equation appears to make gross-overestimations. (see screenshot Table 1 below).

Table 1. Comparison of estimated and experimental BCF values

Compounds [a)]	log K_{ow}	Equation 1	Equation 2	Experimental
Lambda-Cyhalothrin	7.0	45709	1063	2240
Cypermethrin	6.5	43652	970	597
Bifenthrin	6.4	42073	200	6090
Permethrin	6.1	35645	497	558
Cyfluthrin	6.0	33113	216	719
Fenpropathrin	6.0	33113	233	359
Empenthrin	6.4	42073	261	365

a) Cited from "D. A. Laskowski, in Reviews of Environmental Contamination and Toxicology, Vol. 174 (2002) 49 - 170"[4)]

Additionally, the EPI Suite BCFBAF model was used to estimate the BCF for EMPENTHRIN. This resulted in a BCF of 367 according to the traditional regression based method; and a BCF of 427.8 according to the Arnot-Gobas method. When then comparing the BCF derived from the accumulation study to the BCF estimated through EPI's BCFBAF model, the study-BCF appears to be backed by the outcome given by the programme.

A further line of investigation is comparing to similar structures. When looking at BCF-values derived for similar structures to EMPENTHRIN, such as imiprothrin (144), d-allethrin (1300), phenothrin (1623) and transfluthrin (1783), these values are all in the same order of magnitude of the experimental derived BCF for EMPENTHRIN (881), with BCFs ranging from 144 to 1783.

And finally, looking at the results of the single and repeated dose toxicity tests in rats (cfr. Doc IIA §3.1), it can be seen that there was almost a complete elimination of EMPENTHRIN via urine and faeces after only a couple of days. This serves as further evidence that EMPENTHRIN is not expected to bioaccumulate.

3.1.3.2.3 Assessment

B Criteria	Assessment
BCF > 2000	**EMPENTHRIN:** Based on the weight-of-evidence, EMPENTHRIN is not considered to bioaccumulate. **U-1:** no experimental data is available. The BCFBAF model calculates a BCF of 5.884 – 7.172 L kg_{wwt}^{-1} **d-c/t-CRA:** no experimental data is available. The BCFBAF model calculates a BCF of 3.162 232.2 L kg_{wwt}^{-1} **t-COOH-CA:** no experimental data is available. The BCFBAF model calculates a BCF of 367 – 427.8 L kg_{wwt}^{-1}

vB Criteria	Assessment
BCF > 5000	**EMPENTHRIN:** Based on the weight-of-evidence, EMPENTHRIN is not considered to bioaccumulate **U-1:** no experimental data is available. The BCFBAF model calculates a BCF of 5.884 – 7.172 L kg_{wwt}^{-1} **d-c/t-CRA:** no experimental data is available. The BCFBAF model calculates a BCF of 3.162 232.2 L kg_{wwt}^{-1} **t-COOH-CA:** no experimental data is available. The BCFBAF model calculates a BCF of 367 – 427.8 L kg_{wwt}^{-1}

Conclusion on B / vB properties	**EMPENTHRIN:** Following the weight of evidence, EMPENTHRIN is not considered B or vB **U-1 - d-c/t-CRA - t-COOH-CA:** Following the screening criterium and following the BCFBAF estimated BCF, none of the metabolites should be considered B or vB

3.1.3.3 Assessment of toxicity

3.1.3.3.1 Screening

The lowest short term aquatic toxicity values for EMPENTHRIN are as follows:

- 96h LC_{50} for fish: 0.0017 mg/L
- 48h EC_{50} for *Daphnia*: 0.02 mg/L
- 72h EC_{50} for algae: 0.078 mg/L

According to the screening criteria, when the short term aquatic toxicity is below 0.01 mg/L then the T-criterion for the substance is definitely fulfilled and when it is below 0.1 mg/L the T-criterion is fulfilled. EMPENTHRIN should thus be classified as **toxic** according to the screening criteria.

No long-term toxicity data are available.

Metabolites

- **U-1**: no experimental data for toxicity is available. A QSAR estimation using the ECOSAR program predicts a 96h LC_{50} in fish of 2.718 mg/L, a 48h EC_{50} in daphnids of 0.405 and a 72h EC_{50} in green algae of 28.677. Following these predictions and the screening criteria, U-1 should not be considered toxic.
- **d-t/c-CRA:** Experimental data is available for d-t-CRA in the form of acute toxicity limit tests performed on the three trophic levels:
  - 96h LC_{50} for fish: >1.9 mg/L
  - 48h EC_{50} for *Daphnia*: >1.8 mg/L

– 72h EC_{50} for algae: >1.6 mg/L

Following this, d-t-CRA should not be considered toxic according to the screening criteria.

- **t-COOH-CA:** no experimental data is available, however the ECOSAR program predicts acute toxicity values for fish, daphnids and algae for this structure to be well above 1 mg/L, which means that according to the screening criteria this metabolite should not be considered T.

3.1.3.3.2 Assessment

T Criteria	Assessment
NOEC/EC10 (long-term) < 0.01 mg/L for marine or freshwater organisms, or	not available
substance meets the criteria for classification as carcinogenic (category 1A or 1B), germ cell mutagenic (category 1A or 1B), or toxic for reproduction (category 1A, 1B or 2) according to the CLP Regulation, or	Not determined, information is lacking on the carcinogenic properties.
there is other evidence of chronic toxicity, as identified by the substance meeting the criteria for classification: specific target organ toxicity after repeated exposure (STOT RE category 1 or 2) according to the CLP Regulation.	No

Conclusion on T properties	**EMPENTHRIN:** According to the screening criteria, EMPENTHRIN should be classified as toxic (T). **U-1:** No experimental data is available. Following ECOSAR predictions, U-1 should not be considered T. **d-c/t-CRA:** According to the screening criteria, d-c/t-CRA should not be classified as toxic (T). **t-COOH-CA:** No experimental data is available. Following ECOSAR predictions, t-COOH-CA should not be considered toxic (T).

3.1.3.4 Summary and overall conclusions on PBT or vPvB properties

EMPENTHRIN:

Based on the assessment described in the subsections above **EMPENTHRIN is to be considered as potentially P or vP in the aquatic environment and toxic (T).**

For the renewal stage of the substance at the latest, a water/sediment study according to OECD 308, monitoring all isomers and degradation products, will be required in order to make a conclusive P-assessment.

U-1:

The metabolite U-1, a stable rearrangement product of EMPA, the alcohol of the pyrethroid ester, does not fulfil any of the PBT (screening) criteria.

d-t/c-CRA:

Following a whole system DT_{50} derived from a water/sediment degradation study, chrysanthemic acid must be considered persistent in the aquatic environment.

t-COOH-CRA:

Following a whole system DT_{50} derived from a water/sediment degradation study, t-COOH-CRA must be considered very persistent in the aquatic environment.

	EMPENTHRIN	**U-1**	**d-c/t-CRA**	**t-COOH-CA**
P/vP	Potentially P/vP (aquatic environment)	/	P (aquatic environment)	vP (aquatic environment)
B/vB	/	/	/	/
T	Toxic	/	/	/

Since EMPENTHRIN potentially fulfils two of the 3 PBT criteria, it must be concluded, that based on the current information, EMPENTHRIN needs to be considered as a **candidate for substitution**.

3.2 SUBSTITUTION CRITERIA

[Include an assessment if the active substance meets any of the following conditions:]

Substitution criteria (BPR, Article 10)	**Assessment**
One of the exclusion criteria listed in Article 5(1) is met but AS may be approved in accordance with Article 5(2)	*n.a.*
The criteria to be classified, in accordance with Regulation (EC) No 1272/2008, as a respiratory sensitiser is met	*n.a.*
The acceptable daily intake, acute reference dose or acceptable operator exposure level, as appropriate, is significantly lower than those of the majority of approved active substances for the same product-type and use scenario	*The AEL factors of* EMPENTHRIN *are lower than those of the majority of approved active substances for PT 18 (delthamethrin, cyhalothrin, permethrin, cypermethrin). But they are lower for Fipronil.*

Substitution criteria (BPR, Article 10)	**Assessment**
Two of the criteria for being PBT in accordance with Annex XIII to Regulation (EC) No 1907/2006 are met	EMPENTHRIN *should be considered potentially persistent or very persistent (P orvP) in the aquatic environment.* EMPENTHRIN *should be considered toxic (T) according to the screening criteria*
There are reasons for concern linked to the nature of the critical effects which, in combination with the use patterns, amount to use that could still cause concern, such as high potential of risk to groundwater, even with very restrictive risk management measures	*n.a.*
The AS contains a significant proportion of non-active isomers or impurities.	*n.a.*

Conclusion on substitution criteria	*One of the substitution criteria in BPR Article 10(1)a-f is met.*

3.3 ASSESSMENT OF LONG-RANGE ENVIRONMENTAL TRANSPORTATION AND IMPACT ON ENVIRONMENTAL COMPARTMENTS

	Assessment
The active substance or a degradation product is a persistent organic pollutant (POP) listed in Annex I of EC 850/2004	*n.a.*
Assessment of long-range transport potential (LRTAP): • Vapour pressure <1000 Pa and • half-life in air > 2 days or • Monitoring data in remote area showing that the substance is found in remote regions or • Result of multi media modelling	• *Vapour pressure of EMPENTHRIN is 0.014 Pa well below the cut-off value of 1000.* • *Estimation through AOPWIN (vs1.9) shows that half-life of EMPENTHRIN in air is well below the criterion:* o *T1/2 in reaction with OH-radicals: 0.691 hours* o *T1/2 in reaction with ozone: 0.32 hours*
The active substance or a degradation product is vP/vB or T?	*Based on screening data, EMPENTHRIN is considered toxic. EMPENTHRIN is potentially vP in the aquatic environment. Also one of EMPENTHRIN degradation products, t-COOH-CA, is considered vP in the aquatic environment. Nor EMPENTHRIN or any of its degradation products are considered vB.*

Conclusion on LRTAP/POP asessment	*Due to the rapid degradation in the atmosphere, EMPENTHRIN is not considered to pose a risk for LRTAP.*

4 DECISION

4.1 BACKGROUND TO THE PROPOSED DECISION

The outcome of the assessment for ***EMPENTHRIN*** in product-type 18 is specified in the BPC opinion following discussions at the meeting of the Biocidal Products Committee (BPC-23). The BPC opinion is available from the ECHA website.

In view of the conclusions of the evaluation, it is concluded that biocidal products containing ***EMPENTHRIN*** as an active substance for the use as insecticide may not be expected to meet the criteria laid down in point (b)(iii), (b)(iv) and (c) of Article 19(1). Consequently, it is proposed that ***EMPENTHRIN*** shall not be approved and included in the Union list of approved active substances in product type **18**.

4.2 REQUIREMENT FOR FURTHER INFORMATION

Not relevant.

4.3 UPDATING THIS ASSESSMENT REPORT

This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information submitted in relation with Regulation (EU) No 528/2012.

APPENDIX 1 : LISTING OF END POINTS

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

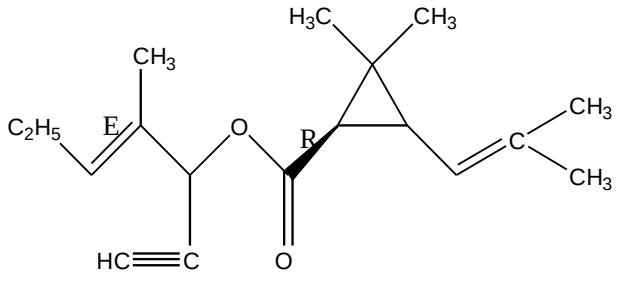
Active substance (ISO Common Name)	EMPENTHRIN
Function (*e.g.* fungicide)	Insecticide

Rapporteur Member State	Belgium

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	IUPAC: 1-ethynyl-2-methylpent-2-enyl 2,2-dimethyl-3-(2-methylprop-1-enyl) cyclopropanecarboxylate
Chemical name (CA)	CAS: Cyclopropane carboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propenyl)-,1-ethynyl-2-methyl-2-pentenyl ester
CAS No	54406-48-3
EC No	-
Other substance No.	Also known as S-2852, S-2852F, S-2852-Forte
Minimum purity of the active substance as manufactured (g/kg or g/l)	94,6 % (w/w) min. racemic mixture containing all possible isomers in the same ratio
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Information on impurities in the technical material is confidential – see Document III-A (confidential data folder). There are no impurities of toxicological concern.
Molecular formula	$C_{18}H_{26}O_2$
Molecular mass	274.40 g/mol

Structural formula



Physical and chemical properties (Annex IIA, point III, unless otherwise indicated)

Melting/freezing point (99.0% purity)	Freezing point determined to be less than -20 ± 0.5 °C		
Boiling point (state purity)	295.5ºC (102.7 –104.4 kPa corrected) (Purity not stated)		
Temperature of decomposition	245 ºC		
Appearance (state purity)	Pale yellow transparent liquid , no odour		
Relative density (state purity)	0.931 (20.8°C)		
Surface tension	Not relevant : water solubility below 1 mg/L		
Vapour pressure (in Pa, state temperature)	0.0154 Pa (25°C) 0.01 Pa (20°C)		
Henry's law constant (Pa m^3 mol^{-1})	3.187 Pa m3 mol-1		
Solubility in water (g/l or mg/l, state temperature)	0.861 mg/L (20°C, pH 5.84-6.45)		
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	solubility > 250 g/L (20°C) for: n-heptane, dichloromethane , methanol, acetone, toluene, ethyl acetate, n-octanol		
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	Not relevant		
Partition coefficient (log P_{OW}) (state temperature)	log Pow = 6.30 (20 °C) log Pow = 4.76 (25 °C)		
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)		25 ºC	40 ºC
	pH 4	4.44 day	22.3 hr

	pH 7	4.41 day	20.4 hr
	pH 9	3.37 day	21.7 hr
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	Not applicable since the chemical structure does not contain any acidic protons or basic centres		
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	UV/VIS, IR, 1H-NMR and MS all gave spectra consistent with the structure of "EMPENTHRIN"		
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	Not determined (exposure to surface water is not expected to occur from the proposed use in wardrobes to control moths)		
Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2)	Not determined		
Flammability	Not flammable : not a solid or a substances which produce flammable gases on contact with water. Auto-flammability/auto ignition temperature = 266 ± 5°C Flash point = 146 ± 2°C		
Explosive properties	Not explosive		

Classification and proposed labelling (Annex IIA, point IX.)

with regard to physical/chemical data	None
with regard to toxicological data	Acute oral tox cat. 4 H302, STOT (SE) 2 Nervous System H371, GHS07, GHS08, Warning **Undetermined for carcinogenicity (data gap)**
with regard to fate and behaviour data	none
with regard to ecotoxicological data	Aquatic Acute 1 H400, Aquatic Chronic 1 H410 GHS09, Warning

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	Non-validated method is based on Gas chromatography with hydrogen flame ionisation detection.
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	Confidential information.

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	**Waiving not accepted.** Substance can reach the STP and will then also come into contact with soil.
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Non-validated method is based on GC-MS using electron impact (EI) as ionisation method. LOQ = 0.0002 mg/m^3
Water (principle of method and LOQ) (Annex IIA, point 4.2)	Non-validated method is based on Gas chromatography with ECD detection. LOQ = 2.44 µg/L
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	A monitoring method is not applicable since the substance is classified in category 4 of acute oral toxicity.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	A monitoring method is not applicable since the proposed use in wardrobes to control moths will not lead to exposure of food or feed of plant origin.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	A monitoring method is not applicable since the proposed use in wardrobes to control moths will not lead to exposure of animal food and feed.

Chapter 3: Impact on Human Health

Absorption, distribution, excretion and metabolism in mammals (Annex IIA, point 5.1)

Rate and extent of oral absorption:	30% absorbed
Rate and extent of dermal absorption	10% absorbed EMPENTHRIN has a molecular weight of 274 and log P_{ow} >5; values similar to other pyrethroids. These physico-chemical values strongly suggest dermal penetration is substantially less than 10%, as is seen for other pyrethroids a specific dermal absorption study to refine dermal absorption estimates below 10% is not scientifically justified.
Rate and extent of inhalation absorption:	100%
Distribution:	Widely distributed
Potential for accumulation:	Rapid elimination, absence of cumulative toxicity, and thorough depletion from tissues suggest there is no potential for accumulation.
Rate and extent of excretion:	Elimination essentially complete within 3 days, mostly in faeces.
Metabolism in animals	Absorbed rapidly, degraded to more than 20 metabolites in urine and faeces
Toxicologically significant compounds (animals, plants and environment)	Parent (metabolites mostly lack the functional pyrethroid core).

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral	1680 mg/kg	Acute toxicity oral, Cat. 4
Rat LD_{50} dermal	>2000 mg/kg	Not classified
Rat LC_{50} inhalation	>4610 mg/m^3	Not classified
Skin irritation	non irritant	Not classified
Eye irritation	non irritant	Not classified
Skin sensitization (test method used and result)	no skin sensitising potential (maximisation test & Buehler)	Not classified

Repeated dose toxicity (Annex IIA, point 5.3)

Short term

Species / Target / critical effect	Rat (21-28 days study) / symptoms of neurotoxity, increased liver and kidney weights.
Lowest relevant oral NOAEL / NOEL	30 mg/kg bw/day (28 days rat)
Lowest relevant dermal NOAEL / NOEL	n.a.
Lowest relevant inhalation NOAEL / NOEL	47.6 mg/m^3 (13.7 mg/kg bw/d) (21 days rat)

Subchronic toxicity

Species / Target / critical effect	Rat / Dog (13-26 weeks study) / Salivation, increased liver and kidney weights.
Lowest relevant oral NOAEL / NOEL	10 mg/kg bw/day (26 week rat / 13 week dog)
Lowest relevant dermal NOAEL / NOEL	n.a.
Lowest relevant inhalation NOAEL / NOEL	21.9 mg/m^3 (6.3 mg/kg bw/d) (13 week rat)

Genotoxicity (Annex IIA, point 5.4)	No evidence of genotoxicity in 3 *in vitro* studies.

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect	No information, since no 2-years study was conducted.
Lowest relevant NOAEL / NOEL	not derived
Carcinogenicity	The carcinogenic waiver did not contain enough scientific evidence to proof that EMPENTHRIN is not carcinogenic.

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect	No effect on reproductive endpoints seen
Lowest relevant reproductive NOAEL / NOEL	500 mg/kg bw/day
Developmental target / critical effect	No effects on development below maternal toxicity seen
Lowest relevant developmental NOAEL / NOEL	150 mg/kg bw/day

Neurotoxicity / Delayed neurotoxicity (Annex IIA, point 5.7)

Acute Neurotoxicity NOAEL 90-Day Neurotoxicity NOAEL	EMPENTHRIN exhibits a NOAEL in adult mammals of 10 mg/kg or greater in this dossier, with the corresponding LOAELs based largely on clinical observations of excessive salivation and tremor. Therefore the most sensitive signs indicative of neurotoxicity have already been observed, and a full neurotoxicology study of EMPENTHRIN is not scientifically justified.

Other toxicological studies (Annex IIA, point 5.8)

None

Medical data (Annex IIA, point 5.9)

Evaluation of 3 years of medical records of employees involved in packing hundreds of tons of pyrethroid products per year, including 34-50 tons of EMPENTHRIN per year, found no effect on body weight, visual and auditory acuity, chest x-ray, blood pressure, urinalysis (protein and glucose) and biochemistry.

Summary (Annex IIA, point 5.10)	**Value**	**Study**	**Safety factor**
Acute AEL	0.014 mg/kg bw/day	21-day inhalation study in rats	1000
Medium-term AEL	0.003 mg/kg bw/day	26 weeks oral study in rats	1000
Long-term AEL	0.0015 mg/kg bw/day	26 weeks oral study in rats	2000
ADI	0.005 mg/kg bw/day	26 weeks oral study in rats	2000
ARfD (acute reference dose)	0.03 mg/kg bw/day	28 days oral study in rats	1000

Acceptable exposure scenarios (including method of calculation)

Professional users	Manufacture and formulation: The active substance, EMPENTHRIN, and the representative product, Vaporthrin® Mothproofer, are neither manufactured nor formulated within the EU. Professional use: There are no professional uses of Vaporthrin® Mothproofer products, which are sold exclusively for the residential market.
Non-professional users	<u>Residential indoor use</u> 5 units (2500 mg) used for a wardrobe volume of 1.5 m^3 so concentration is estimated to be 1.07 mg/m^3 (ConsExpo 4.1) Adult (acute and chronic inhalation) = 0,0019 mg/kg bw/day Child (acute and chronic inhalation) = 0,005 mg/kg bw/day Toddler (acute and chronic inhalation) = 0,011 mg/kg bw/day

Indirect exposure as a result of use (secondary exposure)	Settings for exposure caused by contact with tissues: - The wardrobe volume is 1.5 m^3. -The total amount of EMPENTHRIN can adhere to wardrobe's clothes: 2500 mg for 6 months. - Such wardrobe contain approximatively 50 pieces of clothes. - We wear the same suit once every 3 months. Therefore only 1250 mg adheres to 50 clothes. - The body surface in contact with clothes/bed linen is 50% of the total body surface (HEEG 17). - A dislodgeable amount of 30%. - A dermal absorption of 10%. - A toddler put his hands in his mouth 60 minutes per day. - His hands account for 10% of his body surface. - An oral absorption of 30%. Estimated internal exposure: Adult: 0.0104 mg/kg bw/d Child: 0.0144 mg/kg bw/d Toddler: 0.0182 mg/kg bw/d

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 4: 22.3 hr at 40 °C 4.44 days at 25 °C
	pH 7: 20.4 hr at 40 °C 4.41 days at 25 °C
	pH 9: 21.7 hr at 40 °C 3.37 days at 25 °C
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Distilled water: DT_{50} of 1.6 days River water: DT_{50} of 4.8 hrs Sea water: DT_{50} of 2.1 hrs
Readily biodegradable (yes/no)	No
Biodegradation in seawater	No data are available
Non-extractable residues	Not determined
Distribution in water / sediment systems (active substance)	EMPENTHRIN was found to highly adsorb to organic carbon in soil with a K_{oc} of 5012. EMPENTHRIN is immobile and will remain dominantly in soil.
Distribution in water / sediment systems (metabolites)	No data are available

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralization (aerobic)	No data are available
Laboratory studies (range or median, with number of measurements, with regression coefficient)	Estimated DT_{50} (25 °C, aerobic): 4 d Recalculated to 12 °C, DT_{50}: 11.3 d
Field studies (state location, range or median with number of measurements)	No data are available
Anaerobic degradation	No data are available

Soil photolysis	No data are available
Non-extractable residues	No data are available
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	No metabolite > 10 % in aerobic laboratory study
Soil accumulation and plateau concentration	No data are available

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

Ka , Kd Ka_{oc} , Kd_{oc}	K_{oc}: 5012 (HPLC method)
pH dependence (yes / no) (if yes type of dependence)	Not expected from structural considerations

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

Direct photolysis in air	Not determined
Quantum yield of direct photolysis	Not determined
Photo-oxidative degradation in air	According to the method of Atkinson: DT_{50} of 0.32 hrs in reactions with O_3 DT_{50} of 0.691 hrs in reaction with $OH^{\cdot}$
Volatilization	

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	No monitoring data available
Surface water (indicate location and type of study)	No monitoring data available

Ground water (indicate location and type of study)	No monitoring data available
Air (indicate location and type of study)	No monitoring data available

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 h	LC_{50}	1.7 µg L^{-1}
Invertebrates			
Daphnia magna	48 h	LC_{50}	20 µg L^{-1}
Algae			
Pseudokirchneriella subcapitata	72 h	E_bC_{50} E_rC_{50}	78 µg L^{-1} > 82 µg L^{-1}
Microorganisms			
Activated sludge	30 min	EC_{50}	> 111 µg L^{-1}

Effects on earthworms or other soil non-target organisms

Acute toxicity to *Eisenia fetida* (Annex IIIA, point XIII.3.2)	14d LC_{50} > 160 mg/kg_{dwt}
Reproductive toxicity to (Annex IIIA, point XIII.3.2)	No data available

Effects on soil micro-organisms (Annex IIA, point 7.4)

Nitrogen mineralization	28d $EC_{50,\ standard}$ >256.41 mg/kg_{dwt} 28d $NOEC_{standard}$ = 16.15 mg/kg_{dwt}
Carbon mineralization	28d $EC_{50,\ standard}$ >256.41 mg/kg_{dwt} 28d $NOEC_{standard}$ = 128.21 mg/kg_{dwt}

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	Acute oral LD_{50}	1680 mg/kg bw (rat)
	Acute dermal LD_{50}	>2000 mg/kg bw (rat)
	Acute inhalation LD_{50}	>4610 mg/m^3 (rat)

Acute toxicity to birds (Annex IIIA, point XIII.1.1)	No data available
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	No data available
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	No data available

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	No data available
Acute contact toxicity	No data available

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	No data available
Acute contact toxicity	No data available
Acute toxicity to	No data available

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	40179.08 L/kg (calculated)
Depuration time (DT_{50}) (DT_{90})	Not determined
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not determined

Chapter 6: Other End Points

Not applicable, no other end points

APPENDIX 2 : LIST OF INTENDED USES[1]

Object and/or situation	**Member State or Country**	**Product name**	**Organisms controlled**	**Formulation**		**Application**			**Applied amount per treatment**	**Remarks:**
				Type	Conc. of as	method kind	number min max	interval between applications (min)	g as/m^3	
(a)			(c)	(d-f)	(i)	(f-h)	(k)			(m)
Protection of stored clothing and other textiles	EU	Vaporthrin® Mothproofer	Common clothes moth *Tineola bisselliella*	VP	500 mg a.s. per unit	Natural vapourisation of active substance from impregnated strip	Use as required*	-	1.348 g/m^3 3 units/m^3	2 units recommended to treat volume of 0.667 m^3

VP = Vapouriser

[1] adapted from: EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998

APPENDIX 3 : LIST OF STUDIES

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012.

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
	IIIA5.3/01	1985	Basic Potency of Vaporthrin and Dursban against fabric pests Report No. BBE-50-0017 Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Anon.	IIIA2.6	Not stated	Manufacturing process of Vaporthrin. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Anon.	IIIA2.8/01	Not stated	Active ingredient and inert ingredients of Vaporthrin technical material. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Anon.	IIIA3.12	2002	Safety Data Sheet Vaporthrin TG. Issue date 28 August 2002	N	N/A
Anon.	IIIA3.14	2002	Safety Data Sheet Vaporthrin TG. Issue date 28 August 2002	N	N/A
Anon.	IIIA3.3.1/01 IIIA3.3.2/01 IIIA3.3.3/01	Not stated	Physical and chemical properties of S-2852 Forte. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Anon.	IIIA3.3.1/02 IIIA3.3.2/02	Not stated	Physico-chemical properties of Vaporthrin technical material. Unpublished	Y (New/First)	Sumitomo Chemica

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
	IIIA3.3.3/02				l Co. Ltd.
Anon.	IIIA3.7	Not stated	Solubility of Vaporthrin in various solvents. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Anon.	IIIA4.2/01	Not stated	Analytical method for « «EMPENTHRIN" " in water. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Anon.	IIIA5.7.1/02	1992	Vector Resistance to Pesticides. Fifteenth Report of the WHO Expert Committee on Vector Biology and Control, TRS 818, 1992 Non-GLP, published	N	N/A
Anon.	IIIA5.7.1/03	2000	Guidelines for preventing and managing insecticide resistance in the peach-potato aphid, Myzus persicae Insecticide Resistance Action Group, February 2000 Non-GLP, published	N	N/A
Anon.	IIIA6	1991	Overview of Toxicology of « «EMPENTHRIN" " (Vaporthrin). Report No. Not stated. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Anon.	IIIA6.2xii IIIA 6.3.2xii IIIA 6.4.2xii	2001	Cypermethrin (α-, β-, θ, ζ-Cypermethrin) Handbook of Pesticide Toxicology Ch 58 Pyrethroid Chemistry and Metabolism. Vol. 2. 2nd Edn. p1268. Academic Press; San Diego.	N	N/A
Anon.	IIIA8	2002	Safety Data Sheet Vaporthrin TG. Issue date: 28 August 2002	N	N/A
Anon.	IIIA9	2002	Safety Data Sheet Vaporthrin TG. Issue date: 28 August 2002	N	N/A

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
	IIIA5.3/07	1985	Summary of efficacy tests for the use of « «EMPENTHRIN" " and Vaporthrin mothproofing strips in museum pest control. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
ATSDR	IIIA6.2iii IIIA 6.3.2iii IIIA 6.4.2iii	2003	Toxicological Profile for Pyrethrins and Pyrethroids" Available at: http://www.atsdr.cdc.gov/toxprofiles/tp155.pdf.	N	Public
	IIIA7.4.1.1/03	1990	Acute Flow-through Toxicity of Vaporthrin to Bluegill (Lepomis macrochirus). ABC Laboratories, Inc, Columbia, Missouri Report Number: 37785. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA7.4.1.1/01	1990	Acute Flow-through Toxicity of Vaporthrin to Rainbow Trout (Oncorhynchus mykiss). ABC Laboratories, Inc, Columbia, Missouri Report Number: 37786. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Brogdon, W.G., & McAllister, J.C.	IIIA5.7.1/04	1998	Insecticide Resistance and Vector Control Emerging Infectious Diseases; Vol. 4 No. 4, December 1998. http://www.cdc.gov/ncidod/EID/vol4no4/brogdon.htm Non-GLP, published	N	Public
	IIIA7.4.1.2	1990	Acute flow-through toxicity of Vaporthrin to Daphnia magna. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA7.1.1.1.1	2003	Hydrolysis of [pentenyl-1-14C]-Vaporthrin (VEP) at pH 4, 7 and 9. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.

Author (s)	**Section No / Reference No**	**Year**	**Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
	IIIA6.4.1/ 02	1989	S-2852F (Vaporthrin) oral toxicity study in Beagle dogs. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Eadsforth, C., Bragt, P., van Sittert,N.	IIIA6.2iv IIIA 6.3.2iv IIIA 6.4.2iv	1988	"Human dose-excretion studies with pyrethroid insecticides cypermethrin and alphacypermethrin: relevance for biological monitoring". Xenobiotica 18(5): 603-14 Published	N	N/A
EC	IIIA6.2ix IIIA 6.3.2ix IIIA 6.4.2ix	2002b	Deltamethrin 6504/VI/99-final European Commission, Health and Consumer Protection Directorate-General, Directorate E. 17 October 2002 http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1197Published	N	Public
EC	IIIA6.2vii IIIA 6.3.2vii IIIA 6.4.2vii	2004	alpha-Cypermethrin SANCO/4335/2000 final European Commission, Health and Consumer Protection Directorate-General, Directorate E. 13 February 2004. http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=937Published	N	Public
EC	IIIA6.2viii IIIA 6.3.2viii IIIA 6.4.2viii	2002a	beta-Cyfluthrin 6841/VI/97-final European Commission, Health and Consumer Protection Directorate-General, Directorate E 2 December 2002 http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1022Published	N	Public
EC	IIIA6.2x IIIA 6.3.2x IIIA 6.4.2x	2000	Esfenvalerate 6846/VI/97-final European Commission, Health and Consumer Protection Directorate-General, Directorate E. 30 November 2000 http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1286Published	N	Public

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
EC	IIIA6.2xi IIIA 6.3.2xi IIIA 6.4.2xi	2001	lambda-cyhalothrin 7572/VI/97-final European Commission, Health and Consumer Protection Directorate-General, Directorate E. 25 January 2001 http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1509	N	Public
	IIIA3.1.3	2012	Vaporthrin PAI: Evaluation of Relative Density. GLP. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA.3.7	2012	Vaporthrin PAI: Evaluation of Solvent Solubility. GLP. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.10	2012	Vaporthrin PAI: Evaluation of Thermal Stability. GLP. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.14	2012	Evaluation of Viscosity. GLP. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.3.2	2012	Vaporthrin PAI: Determination of Physical State, Colour and Odour. GLP. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.5	2013	Vaporthrin PAI: Development and Validation of an Analytical Method, and Evaluation of the Water Solubility. GLP. Unpublished	Y (New/First)	Sumitomo Chemica

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
					l Co. Ltd.
	IIIA3.9	2013	Vaporthrin PAI: Determination of Octanol:Water Partition Coefficient. GLP. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA2.7	2006	Analysis results of recent batches of Vaporthrin. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA2.8/02	2006	Analysis results of recent batches of Vaporthrin. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.2.1	2013	Henry's Law Constant for Sumitomo Chemical Vaporthrin® («EMPENTHRIN") – Calculated Method. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA7.4.1.4	2001	Toxicity of Vaporthrin to Activated sludge in a Respiration Inhibition test. *GLP, Unpublished*	Y (New/First)	Sumitomo Chemical Co. Ltd.
Hashimoto, T. et. al.	IIIA5.3/10	1999	Evaluation of the acaricidal efficacy of sixteen chemicals to three species of house dust mite, *Dermatophagoides farinae*, *Tyrophagus putrescentiae* and *Blomia tropicalis*, by filter paper contact method Med. Entomol. Zool., Vol. 50 No. 4, p349-354 Published	N	N/A

Author (s)	**Section No / Reference No**	**Year**	**Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
	IIIA6.1.1/01	1989a	Acute oral toxicity of Vaporthrin in rats. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.1.2/01	1989b	Acute dermal toxicity study of Vaporthrin in rats. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.1.1/02	1989c	Acute oral toxicity study of Vaporthrin in mice. Testing laboratory:	Y	Sumitomo Chemical Co. Ltd.
	IIIA6.1.2-02	1989d	Acute dermal toxicity study of Vaporthrin in mice. Testing laboratory:	Y	Sumitomo Chemical Co. Ltd.
	IIIA7.4.2	1980	Bioaccumulation test of (RS)-1-ethynyl-2-methyl-2-pentenyl (1R)-cis,trans-chrysanthemate. (Translation). Unpublished.	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA7.4.1.3	2002	Vaporthrin – Toxicity to the freshwater green alga, *Pseudokirchneriella subcapitata.* GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.1.1-03	1982a	Acute oral toxicity study of S-2852 Forte in rats	Y	Sumitomo Chemica

Author (s)	**Section No / Reference No**	**Year**	**Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
					l Co. Ltd.
	III6.1.3-02	1982b	Acute oral toxicity study of S-2852 in rats. Testing laboratory:	Y	Sumitomo Chemical Co. Ltd.
	IIIA 6.1.2-03	1982c	Acute dermal toxicity of S-2852 Forte in rats. Testing laboratory:	Y	Sumitomo Chemical Co. Ltd.
	IIIA6.3.3-02	1984	Subacute inhalation toxicity of the fume of S-2852 Forte in rats.	Y	Sumitomo Chemical Co. Ltd.
IARC	IIIA6.10[1]	1999	IARC Scientific Publications No. 147. Species differences in thyroid, kidney and urinary bladder carcinogenesis. Consensus report. International association for Research on cancer. Lyon, France. Published	N	N/A
ICH	IIIA6.5[iii]	1998	ICH Harmonised tripartite guideline: Duration of chronic toxicity testing in animals (rodent and nonrodent toxicity testing) S4 Current *Step 4* version. Available at: http://www.ich.org/LOB/media/MEDIA497.pdf Published	N	Public
ILSI	IIIA6.8[i]	In Press	A Tiered Approach to Life Stages Testing for Agricultural Chemical Safety Assessment CRC Critical Reviews in Toxicology	N	N/A
	IIIA6.2/01	1989	Metabolism of S-2852F in rats: A single oral administration study.	Y (New/First)	Sumitomo Chemica

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
					l Co. Ltd.
	IIIA6.2/02	1990	Metabolism of S-2852F in rats: repeated oral administration study. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA7.3.1	2006	« «EMPENTHRIN" " – Stability in air. Unpublished	N	Sumitomo Chemical Co. Ltd.
	IIIA.6.1.4e-02 IIIA.6.1.4s-02	1980	Primary eye and skin irritation tests of S2852 forte in rabbits.	Y	Sumitomo Chemical Co. Ltd.
	IIIA6.6.3/01	1994	*In vitro* gene mutation test of Vaporthrin in V79 Chinese hamster cells. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.1.5/01	1989	Skin sensitisation test of Vaporthrin in guinea pigs (by maximisation method) GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.1.3/01	1989	Acute inhalation toxicity study of Vaporthrin in rats. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.3.3/01	1989	Three week inhalation toxicity study of Vaporthrin in rats. GLP, Unpublished	Y	Sumitomo

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
				(New/First)	Chemical Co. Ltd.
	IIIA6.4.3/01	1990	Three month inhalation toxicity study of Vaporthrin in rats. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.6.1/01	1989	Reverse mutation test of Vaporthrin in bacterial systems. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.8.1/02	1992	Rat teratology study with S-2852F. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Lumley, C., Walker S.	IIIA6.5[ii]	1986	A Critical Appraisal of the Duration of Chronic Animal Toxicity Studies. Regul. Toxicol. Pharmacol 6, 66-72 Published	N	N/A
Morita, T. et al	IIIA5.3/06	1987	Application of a new type of pyrethroidal compound for the moth on ethnographic textiles Proceedings of ICOM meeting 1987 Report No. BBE-71-0024 Published	N	N/A
	IIIA6.8.1/01	1993	Rabbit teratology study with S-2852F. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.4	2001	UV/VIS, IR, NMR and Mass Spectra of Vaporthrin Technical material. GLP, Unpublished	Y (New/First)	Sumitomo Chemica

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
					l Co. Ltd.
	IIIA6.6.2	1989	Mutagenicity test on Vaporthrin (S-2852F) in an *in vitro* cytogenetic assay measuring chromosomal aberration frequencies in Chinese Hamster Ovary (CHO) cells. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA7.1.1.2.2	1990	The biodegradability of Vaporthrin (S-2852 Forte). Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.1.4 e/01	1988a	Primary eye and skin irritation tests with Vaporthrin in rabbits. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.1.4s /01	1988b	Primary eye and skin irritation tests with Vaporthrin in rabbits. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA7.2.1	1981	Degradation of S-2852F in Soil.	Y	Sumitomo Chemical Co. Ltd.
Naumann, K.,	IIIA5.4.1	1990	Synthetic pyrethroids insecticides:Structures and properties. Ch 7 Molecular Neurotoxicology p156 – 178. Springer Verlag. Published	N	N/A
	IIIA6.4.1/ 01	1991	Subchronic toxicity study in rats. GLP, Unpublished	Y	Sumitomo Chemica

Author (s)	**Section No / Reference No**	**Year**	**Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
				(New/First)	l Co. Ltd.
	IIIA3.1.2	1989	Determination of boiling point/boiling range of Vaporthrin. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.2	1990	Vapour pressure determination of Vaporthrin. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Ray, D.	IIIA6.2[i] IIIA 6.3.2[i] IIIA 6.4.2[i]	2001	"Pyrethroid Insecticides: Mechanisms of Toxicity, Systemic Poisoning Syndromes, Paresthesia, and Therapy" (in) Kreiger R (ed) "Handbook of Pesticide Toxicology", 2nd Edn. p1289-1303. Academic Press: San Diego Published	N	N/A
Ray, D., Fry, J.	IIIA6.9[ii]	2005	A reassessment of the neurotoxicity of pyrethroid insecticides. Pharmacol Therapeut., online preprint Dec 2005. Published	N	N/A
Ray, D.E.	IIIA6.9[i]	2001	"Pyrethroid Insecticides: Mechanisms of Toxicity, Systemic Poisoning Syndromes, Paresthesia, and Therapy" (in) Kreiger R (ed) "Handbook of Pesticide Toxicology", 2nd Edn. p1289-1303. Academic Press: San Diego Published	N	N/A
Ross, J., Driver, J., Cochran, R., Thongsinthusak, T, Krieger, R.	IIIA6.2[v] IIIA 6.3.2[v] IIIA 6.4.2[v]	2001	"Could pesticide toxicology studies be more relevant to occupational risk assessment?". Ann. Occup. Hyg. 45(1001):S5-S17. Published	N	N/A

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
	IIIA6.8.1/04	1985	A teratology study in rabbits with S-2852F. Testing laboratory:	Y	Sumitomo Chemical Co. Ltd.
	IIIA4.2/06	1989	Method Validation for the Analysis of Vaporthrin («EMPENTHRIN") in Aquatic Test Water. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Scott, R., Ramsey, J.	IIIA6.2[vi] IIIA 6.3.2[vi] IIIA 6.4.2[vi]	1987	"Comparison of the *in vivo* and *in vitro* percutaneous absorption of a lipophilic molecule (cypermethrin, a pyrethroid insecticide). J.Invest.Dermatol. 89(2) 142-146. Published	N	N/A
Senbo, S. et. al.	IIIA5.3/09	1991	Insecticidal activity of a synthetic pyrethroid, «EMPENTHRIN" Japanese Society of Environmental Entomology and Zoology, Vol. 3 No. 2, p75-80 Published	N	N/A
Shafer, T.J., Meyer, D.A., Croftton, K.M.	IIIA6.9[iii]	2005	Developmental Neurotoxicity of Pyrethroid Insecticides: Critical Review and Future Research Needs. Environmental Heath perspectives. Vol. 113, No. 2 123 – 136. February 2005. Published	N	N/A
	IIIA6.7.1	1993	Effect of S-2852F on the Induction of Placental Glutathione S-Transferase in Liver Medium-Term Bioassay for Carcinogenesis.	Y	Sumitomo Chemical Co. Ltd.
	IIIA3.1.3	1989	Specific gravity of Vaporthrin Technical grade. Unpublished	Y (New/First)	Sumitomo Chemica

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
					l Co. Ltd.
	IIIA3.10	1989	Thermal stability of Vaporthrin technical grade by differential thermal analysis. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA4.1/01	1991a	Analytical methods for the determination of Vaporthrin Technical grade. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA4.1/02	1991b	Analytical methods for the determination of Vaporthrin Technical grade. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA4.1/03	1991c	Analytical methods for the determination of Vaporthrin Technical grade. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA4.2/02	1989	Determination of aerial concentration of Vaporthrin. Part 1: Analytical method for the determination of Vaporthrin trapped in silica gel by gas chromatography-mass spectrometry. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.12	2005	Review on medical examination of factory workers exposed to pyrethroids Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Staetz, C.A.	IIIA5.7.1/05	2004	Insecticide Mode of Action Classification: A Key to Insecticide Resistance Management (v.3.3.2)	N	N/A

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
			Insecticide Resistance Action Committee (IRAC International), 2004 Non-GLP, published		
	IIIA6.1.5-02	1980	Dermal sensitization test of S2852 forte in guinea pigs.	Y	Sumitomo Chemical Co., Ltd.
	IIIA4.1/04	1982	Analytical method for the determination of S-2853F technical preparations. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.4.1/03	1988	Twenty-six week oral toxicity study of S-2852 Forte in rats. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.3.1	1986	Four week oral toxicity study of S-2852F in rats. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA7.4.1.1/02	1986	The Acute Toxicity of S-2852 Forte to Carp (*Cyprinus Carpio*). Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA7.1.1.1.2	1981	Photolysis of « «EMPENTHRIN" " in Water. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
	IIIA7.1.3	2001	Estimation of the adsorption coefficient of Vaporthrin on soil using high performance liquid chromatography (HPLC). GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.1.1	2007	Determination of physico-chemical properties. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.11	2007	Determination of physico-chemical properties. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.12/01	2007	Determination of physico-chemical properties. GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Weil, C., McCollister D.	IIIA6.5[i]	1963	Relationship between Short- and Long-Term Feeding Studies in Designing an Effective Toxicity Test. Agricultural and Food Chemistry 6, 484-491. Published	N	N/A
	IIIA6.8.2/01	1987a	S-2852F: Reproductive function and fertility study in the rat. (Segment I). GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA6.8.2/02	1987b	S-2852F: Peri and postnatal study in the rat. (Segment III). GLP, Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
	IIIA6.8.1/03	1987c	Teratology study in the Rat S-2852F (Segment II), [BBT-71-0027]	Y	Sumitomo Chemical Co. Ltd.
	IIIA4.2/03	2006	Vaporthrin («EMPENTHRIN") validation of an analytical method for determination of residues in air. GLP. Unpublished	Y	Sumitomo Chemical Co. Ltd
Woollen, B., Marsh, J, Laird, W., Lesser, J.	IIIA6.2[ii] IIIA 6.3.2[ii] IIIA 6.4.2[ii]	1992	"The metabolism of cypermethrin in man: differences in urinary metabolite profiles following oral and dermal administration". Xenobiotica 22(8) 983-991. Published	N	N/A
	IIIA3.5	1990	Water solubility of Vaporthrin. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA3.9	1990	Partition coefficient of Vaporthrin. Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA5.3/03	1982	Insecticidal efficacy of mothproofing strip containing Vaporthrin against adult casemaking clothes moth (*Tinea pellionella*) Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
	IIIA5.3/05	1983	Insecticidal efficacy of mothproofing strips containing Vaporthrin against adult casemaking clothes moth and webbing clothes moth Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.

Author (s)	**Section No / Reference No**	**Year**	**Title.** **Source (where different from company)** **Company, Report No.** **GLP (where relevant) / (Un)Published**	**Data Protection Claimed (Yes/No)**	**Owner**
[redacted]	IIIA5.3/04	1983	Effect of mothproofing strip impregnated with Vaporthrin® against eggs and larvae of casemaking clothes moth (*Tinea pellionella*) Unpublished	Y (New/First)	Sumitomo Chemical Co. Ltd.
Yoshida, K. *et al*	IIIA5.3/02	1984	Practical application of « «EMPENTHRIN" " as a mothproofer of textile Sen-I Gakkaishi Vol. 40, pp254-262 Report No. BBE-40-0019 Published	N	N/A
	IIIA5.3/08	2005	Evaluation of an anti moth cassette Not published	Y (New/First)	Sumitomo Chemical Co. Ltd.

N/A = Not applicable