Document I

CYPERMETHRIN

CAS no. 52315-07-8

Evaluation report according to Regulation 528/2012
Arysta LifeScience Benelux sprl, Belgium

For use in insecticides (PT 18)

Rapporteur Member State: Belgium

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Applicant: Arysta LifeScience Benelux sprl, Belgium

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I.1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Introduction

This evaluation report and the supporting Documents II-A, II-B, II-C, IIIA and III-B review the use of an existing biocidal active substance, Cypermethrin cis:trans/40:60, as an insecticide (product type 18), according to the procedures of Regulation 528/2012 concerning the placing of biocidal products on the market.
This evaluation report was prepared by the BE Competent Authority: The Federal Public Service, Health and Environment; DG 5 environment; Risk Management Office.

The Applicant of Cypermethrin cis:trans/40:60 is Arysta Life Science Rue de Renory, 26 B-4102 Ougrée, Belgium. The dossier, including original test reports and study summaries were submitted to the BE CA on 30th March 2006 and this were accepted as complete for evaluation on 30^{h} June 2006.
For Cypermethrin cis:trans/40:60 and the representative product Cypermethrin 100g/l EW the risks to human health and the environment and risks from physico-chemical properties as well as its efficacy and possible unacceptable effects like occurrence of resistance, have been assessed in accordance with the provisions laid down in the Directive 98/8/CE and in the regulation 528/2012 for the use as an insecticide (product type 18) as applied for by the applicant.

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. The information in this report is, at least partly, based on information that is protected under the provisions of Directive 98/8/EC. This report shall not be used to support any authorisation/registration outside the context of that Directive, e.g. in other countries, unless the applicant has demonstrated legitimate access to the information on which this report is based.

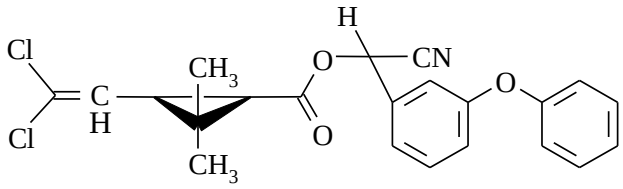
I.2. OVERALL SUMMARY AND CONCLUSIONS

2.1. General substance information

2.1.1. Identification of the active substance

CAS-No.	*52315-07-8*
EINECS-No.	*257-842-9*
Other No. (CIPAC, ELINCS)	*CIPAC 332*
IUPAC Name	*(RS)-α-cyano-3 phenoxybenzyl-(1RS)-cis, trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate*
Common name, synonym	*Cypermethrin, Cypermethrin cis:trans/40:60*
Molecular formula	$C_{22}H_{19}Cl_2NO_3$

Structural formula



Molecular weight (g/mol) *416.3*

Isomer ratio *Cis:trans 40:60*

Cis I	23.3%
Cis II	16.8%
Total Cis Isomers	40.1%
Trans I	35.8%
Trans II	24.1%
Total Trans Isomers	59.9%

2.1.2. Isomeric composition

Cypermethrin cis:trans isomer ratio 40(±5) :60(±5).

The cypermethrin molecule has 3 chiral centers giving rise to 8 stereoisomers, four pairs of enantiomers – two cis (CIS I & CIS II) and two trans (TRANS I & TRANS II). Each enantiomeric pair is racemic – i.e. 50:50 mix of each enantiomer. See Table 1.2

Table 1.2 Overview of the eight isomers of cypermethrin

	C.A. denomination of the isomers	CAS n°		Most common Cis-Trans ratios	
1	[1R-(1α(S*),3α)]	65731-84-2	cis-II	40% min	48% max
2	[1S-(1α(R*),3α)]	72204-43-4			
3	[1R-(1α(R*),3α)]	65731-83-1	cis-I		
4	[1S-(1α(S*),3α)]	72204-44-5			
5	[1R-(1α(S*),3β)]	65732-07-2	trans-II	60% max	52% min
6	[1S-(1α(R*),3β)]	83860-31-5			
7	[1R-(1α(R*),3β)]	66841-24-5	trans-I		
8	[1S-(1α(S*),3β)]	83860-32-6			

Additional information regarding cypermethrin identification is available in the confidential annex folder.

2.1.3. Physico-chemical properties

Cypermethrin cis:trans/40:60 is a yellow/brown viscous liquid with a mild chemical odour (technical active substance) and a low vapour pressure (6 x 10^{-7} Pa at 25 ºC). Therefore, volatilisation is not expected to significantly contribute to the dissipation of cypermethrin cis:trans/40:60 in the environment. The compound has a low water solubility (<9 µg/L; 4µg/l used for environmental assessment) but is moderately soluble in organic solvents and is highly lipophilic (log P_{ow} = 5.3–5.6)

2.1.4. Identification of the products

2.1.4.1. Cypermethrin 100 g/L EW

Trade name(s)	Cypermethrin 100 g/L EW, 'EXIT 100'	
Manufacturer´s development code number(s)	[redacted]	
Ingredient of preparation	Function	% Content
Cypermethrin cis:trans/40:60	Active ingredient	10% w/v (100 g/L)
	Details of co-formulants are presented in the confidential annex (see point B2.2).	
Physical state of preparation	Liquid	
Nature of preparation	Bulk Liquid (EW)	

2.1.5. Classification and Labelling

2.1.5.1. Proposal for the classification and labelling of the active substance

Current Classification	**as in EU CLP regulation 1272/2008**
GHS Pictograms	GHS07 GHS09
Signal Word	Warning
Hazard Class and Category Codes	Acute Tox. 4 STOT SE3 Aquatic acute 1 Aquatic chronic 1
Hazard Statement Codes	H332 Harmful if inhaled H302 harmful if swallowed H335 May cause respiratory irritation H400 Very toxic to aquatic life H410 Very toxic to aquatic life with long lasting effects
Precautionary Statement Codes	P261 Avoid breathing vapours/spray P314 Get medical advice/attention if you feel unwell P501 Dispose of content in accordance with local/national regulation

	P273 Avoid release to the environment P391 Collect spillage

Proposed Classification	**as proposed by the BE CA (as in EU CLP regulation 1272/2008 2nd ATP)**
GHS Pictograms	 GHS08 GHS09
Signal Word	Warning
Hazard Class and Category Codes	Acute Tox. 4 STOT RE2 STOT SE3 Aquatic acute 1 (M = 100) Aquatic chronic 1 (M = 1000)
Hazard Statement Codes	H332 Harmful if inhaled H302 harmful if swallowed H373 May cause damage to organs through prolonged or repeated exposure H335 May cause respiratory irritation H400 Very toxic to aquatic life H410 Very toxic to aquatic life with long lasting effects

Justification for the proposal

The classification of Cypermethrin cis:trans/40:60 was agreed at the 29th ATP and appears in Annex I of former Directive 67/548/EEC containing the list of harmonised classifications and labelling for substances.

Currently, Cypermethrin *cis:trans/40:60* has a harmonised classification as listed in Annex VI table 3.1. to Regulation (EC) No 1272/2008.

No new scientific information/data is available that may affect the classification of the active substance. Nevertheless, in CLP-Regulation (EC) No 1272/2008 the guidance values are modified for 'specific target organ toxicity following repeated exposure'. Because of the change in guidance values, the clinical effects of neurotoxicity observed in both animals and humans, and the liver toxicity observed in animals, **classification/labelling of the active substance 'cypermethrin'** for repeated-dose toxicity according to the criteria (modified guidance values) in CLP-Regulation (EC) No 1272/2008 2nd ATP is justified: **STOT RE2; H373. May cause damage to organs through prolonged or repeated exposure.**

For the environment part of the classification, M-factor has been introduced as part of the classification and are needed in order to classify mixture or products. No M-factor exist in current harmonized classification and these need to be set. The above proposed M factor results from the data set available for the CLH proposal which include in addition to the data available for the CAR, data belonging to other industry to which Arysta Life Science has no access and are not part of this CAR. In the CLH proposal , the lowest EC_{50} values for Cypermethrin are between > 0.001 < 0.01 mg/L for fish (0.00283 mg/L); > 0.001 < 0.01 for crustacean (0.0047 mg/L) and > 0.01 < 0.1 mg/L for algae (>0.033 mg/L), chronic NOEC values between >0.0001<0.001 for fish (0.00025 mg/L), > 0.00001 < 0.0001 mg/L for crustacean (0.00004 mg/L) and > 0.01

mg/L for algae (≥0.033mg/L). A mesocosm study produces values NOAEC > 0.00001< 0.0001mg/L for macrozoobenthos community and periphyton .

Based on the lowest LC_{50} (fish), cypermethrin should be classified as **Aquatic Acute Category 1 and an M factor of 100 is proposed.**

NOEC values for cypermethrin are available for all trophic levels. The lowest acceptable NOEC is -0.00004 mg/L (obtained for invertebrates). Cypermethrin fulfills criteria for classification as **Aquatic Chronic Category 1.**

The lowest NOEC is between 0.00001 mg/l and 0.0001 mg/l and Cypermethrin is considered not rapidly degradable, therefore an M factor of 1000 for chronic toxicity is proposed.

A proposal for the new classification and labelling has been prepared but still has to be validated by ECHA.

2.1.5.2. Proposal for the classification and labelling of the preparation Cypermethrin 100 g/L EW

Current Classification and proposed classification by the BE CA	**as in Directive 1999/45/EEC**	
Class of danger	Xn:	Harmful
	N:	Dangerous for the environment
R phrases	R22:	Harmful if swallowed
	R38:	Irritating to skin
	R43:	May cause sensitisation by skin contact
	R50/R53:	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S phrases	S 2:	Keep out of the reach of children
	S 13:	Keep away from food, drink and animal feeding stuff
	S 20/21:	When using, do not eat, drink or smoke
	S 23:	Do not breathe the gas, fumes, vapours, spray
	S 24:	Avoid contact with skin
	S 29/35:	Do not empty into drains; dispose of this material and its container in a safe way
	S 36/37:	Wear suitable protective clothing and gloves
	S51:	Use only in well-ventilated areas
	S61:	Avoid release to the environment. Refer to special instructions/safety data sheets

Classification	**as proposed by the BE CA (EU CLP regulation No 1272/2008, 2nd ATP)**
GHS pictograms	GHS08 GHS09
Signal Word	Warning
Hazard Class and Category Codes	Acute Tox. (oral) 4 Skin sens 1 STOT RE2 Aquatic acute 1 Aquatic chronic 1
Hazard Statement Codes	H302 Harmful if swallowed H317 May cause an allergic skin reaction H373 May cause damage to organs through prolonged or repeated exposure H400 Very toxic to aquatic life H410 Very toxic to aquatic life with long lasting effects
Precautionary Statement Codes	P260 Do not breathe vapours/spray P262 Do not get in eyes, on skin, or on clothing P314 Get medical advice/attention if you feel unwell P273 Avoid release to the environment P391 Collect spillage P501 Dispose of content in accordance with local/national regulation
Additional statement on the Label	THE PRODUCT CONTAINS cypermethrin. May cause paraesthesia.

Justification for the proposal (according to the criteria of CLP Regulation EC No 1272/2008)

Based on actual data on the formulation or comparable formulation, the results of acute toxicology studies on the formulation or comparable formulations, Cypermethrin 100 g/L EW must be classified as Acute tox. (oral) 4 and as Skin sens. 1.

According to the criteria of CLP Regulation EC No 1272/2008 and based on actual data on the formulation, no classification for skin irritation is justified.

In addition, Cypermethrin 100 g/L EW (10% cypermethrin cis:trans/40:60) must be classified as STOT RE2 derived from the application of the CLP calculation method. (The justification for classifying the active substance as STOT RE2 is provided in DocIIA section 1.5).

Cypermethrin 100 g/L EW (10% cypermethrin cis:trans/40:60) must be classified as Aquatic Acute Cat.1 and Aquatic chronic cat1if M factor of 100 and 1000 are used respectively.

Based on the toxicological properties of cypermethrin and other pyrethroids and Human data (section 3.11 of the DOCIIA), the following sentence is highly advised on the label: “THE PRODUCT CONTAINS cypermethrin. May cause paraesthesia.”.

2.1.6. Methods of analysis

Adequate methodology exists for the determination of the active substance in the technical active substance

(as manufactured), the formulated product and in soil/sediment, water, air, animal tissues (bovine milk, liver, kidney, muscle fat and hen eggs) and in food/feedingstuffs (oilseed rape and wheat). Full details of the analytical methodology is given in Document IIIA, Section 4.2.

2.2. Effectiveness against target organisms

2.2.1. Field of use envisaged / Function

Product Type 18: Insecticides.

2.2.2. Organism(s) to be controlled and products, organisms or objects to be protected

According to the applicant, products containing CYPERMETHRIN (in spray formulations) are intended to be used by professionals (Pest Control Operators) as a broad spectrum insecticide against crawling and flying insects, including cockroaches, ants, fleas, bedbugs, flies, mosquitoes, moths and wasps nests for mainly indoor use as a surface spray on walls and floors and also for outdoor use on paths and patios and around the edges of buildings.

Efficacy studies has been provided against flies, cockroaches, ants and fleas (see section 2.2.4)

The outcome of the evaluation is that efficacy of CYPERMETHRIN could be claimed against cockroaches and fleas in indoor application.

2.2.3. Effects on target organisms

CYPERMETHRIN cis:trans/40:60 is a synthetic pyrethroid with contact and stomach action. It acts by preventing the transmission of impulses along the nervous system of the insect. It is thought that this is achieved by blocking the sodium channels in nerve membranes, thus preventing action potentials passing down the nerve axon. Typically, this intoxication results in a rapid "knockdown". The affected insect shows uncoordinated movements and finally dies.

2.2.4. Efficacy studies with Cypermethrin 100 g/L EW

For the purpose of listing the active for PT 18 in the list of approved active substances, the applicant has provided several studies on the efficacy of CYPERMETHRIN against house flies, German and Oriental cockroaches, garden ants and cat fleas. All efficacy studies have been performed in indoor conditions.
To assess and to support the efficacy of CYPERMETHRIN, the applicant submitted 3 simulated use bioefficacy trials with the formulated product Cypermethrin 100 g/L EW (Brand product = EXIT 100), an oil/water emulsion, used as followed: 2.5ml/0.5l/10m^2 (25 mg CYPERMETHRIN/m^2 – 0,05% a.i.) or 5ml/0.5l/10m^2 (50 mg CYPERMETHRIN/m^2 – 01% a.i.). Summaries of the results are presented in Table 2.1

Table 2.1 Summary of the studies submitted

Test Product	Test Organism	Test Method	Test results	Reference
Cyperkill 10 Formulated	***Musca domestica***	Lab study On plywood or glazed ceramic tiles	**Regardless the surface type** 24h:	Doc^t B5.10(01)

product – Liquid Emulsifiable Concentrate with 10% w/w cypermethrin	Adult – mixed sex	<u>Application rate:</u> 16.66 mg/m^2	$KD_{100\%}$ < 15 min $Mortality_{24h}$ = 100% <u>3 months:</u> $KD_{100\%}$ < 20 min $Mortality_{24h}$ = 100%	JH Cole (1992) **Supportive study**
	Blatella germanica Adult - ♂♂	Lab study On plywood or glazed ceramic tiles <u>Application rate:</u> 33.33 mg/m^2	**Glazed ceramic tiles** <u>24h:</u> $KD_{100\%}$ < 30 min $Mortality_{24h}$ = 100% <u>3 months:</u> $KD_{100\%}$ < 30 min $Mortality_{24h}$ = 100% **Plywood tiles** <u>24h:</u> $KD_{100\%}$ < 15 min $Mortality_{24h}$ = 92% <u>3 months:</u> $KD_{100\%}$ < 60 min $Mortality_{48h}$ = 92%	
Exit 100 Formulated product - oil in water emulsion with 10% w/w Cypermethrin	***Blatella germanica*** 30♂,30 non gravid ♀, 20 large nymphs and 20 small nymphs	Simulated use trial On hard surfaces <u>Application rate:</u> 25 mg/m^2	$KD_{30\ min}$ = 91.1% KD_{24h}= 100% $Mortality_{72h}$= 98.4%	Doc^t B5.10(02) L. Senior (2006) **Key study**
		Simulated use trial On hard surfaces <u>Application rate:</u> 50 mg/m^2	$KD_{30\ min}$ = 85.8% KD_{24h}= 100% $Mortality_{72h}$= 97.7%	
	Blatta orientalis 30♂, 30 non gravid ♀, 20 large nymphs and 20 small nymphs	Simulated use trial On hard surfaces <u>Application rate:</u> 25 mg/m^2	$KD_{30\ min}$ = 66.3% KD_{24h}= 100% $Mortality_{72h}$= 78.9%	
		Simulated use trial On hard surfaces <u>Application rate:</u> 50 mg/m^2	$KD_{30\ min}$ = 57.6% KD_{24h}= 100% $Mortality_{72h}$= 83.8%	
Exit 100 Formulated product - oil in water emulsion with 10% w/w Cypermethrin	***Ctenocephalides felis*** Mixed age and mixed sex	Simulated use trial On hard surfaces <u>Application rate:</u> 25 mg/m^2	KD_{24h}= 100% $KT_{50} \leq$ 30 min $Mortality_{48h}$= 99.5% $Mortality_{72h}$= 100%	Doc^t B5.10(03) L Senior (2006) **Key study**
		Simulated use trial On hard surfaces <u>Application rate:</u> 50 mg/m^2	KD_{24h}= 97.9% $KT_{50} \leq$ 30 min $Mortality_{48h}$= 100%	
Exit 100 Formulated product - oil in water emulsion	***Lasius niger*** Only workers	Simulated use trial On hard surfaces <u>Application rate:</u> 25 mg/m^2	$KD_{30\ min}$ = 30.4% KT_{50} = 2h $Mortality_{196\ h}$ = 88.1%	Doc^t B5.10(04) L Senior (2006)

with 10% w/w Cypermethrin		Simulated use trial On hard surfaces Application rate: 50 mg/m^2	$KD_{30\ min}$ = 40.8% KT_{50} = 1h $Mortality_{196\ h}$ = 81.2%	**Key study**

The first study showed that CYPERMETHRIN is effective indoor against mixed age/mixed sex cockcroaches (*Blattella germanica* and *Blatta orientalis*) when used at 5ml/0.5l/10 m2 – 50 mg a.i./m2 – 0.1% a.i.. Tests were performed on different types of hard surfaces. Test results showed that 100% knock-down was achieved within 24h regardless the cockroach species. 97.7% and 83.8% mortality was achieved within 72h against *Blattella germanica* and *Blatta orientalis* respectively.

The second study showed that CYPERMETHRIN is effective indoor against adult cat fleas (*Ctenocephalides felis*) when used at maximum 5ml/0.5l/10 m2 – 50 mg a.i./m2 – 0.1% a.i.. Tests were performed on different types of hard surfaces. Test results showed that 100% knock-down was achieved within 24h regardless the product concentration. 100% mortality was achieved within 48h.

The last one showed that CYPERMETHRIN is not sufficiently effective against garden ants (*Lasius niger*) when used at 5ml/0.5l/10 m2 – 50 mg a.i./m2 – 0.1% a.i.. Tests were also performed on different types of hard surfaces. Test results showed that 81.2% knock-down/mortality was achieved in 196h.

Besides these 3 simulated use bioefficacy trials, the applicant submitted a laboratory study from 1992. Considering its age, this study is only taking into account as a supportive study. For a purpose of clarity, a summary is also presented in Table 2.1.

Efficacy of CYPERMETHRIN could be claimed against cockroaches and fleas. CYPERMETHRIN must be used at application rates between 25 and 50 mg a.i./m^2.

Only results of studies performed in indoor conditions were submitted,. Therefore, additional studies will be needed at the Product Authorisation Stage to assess the efficacy of CYPERMETHRIN-based products intended to be used in outdoor conditions.

Overall, the Belgian CA concludes that the data demonstrated the effectiveness of the products containing CYPERMETHRIN to a sufficient degree for inclusion in the list of approved active substances.

2.2.5. Development of resistance.

Resistance to pyrethroid insecticides has been reported for a number of pests both in agriculture and public health. Strategies such as alteration of insecticides with different modes of action and avoidance of over frequent use are standard practises in agriculture and should be applied also to biocidal uses of cypermethrin *cis:trans*/40:60.

As all efficacy studies seem to have performed in UK, if the applicant wants to use the product in other countries, it is necessary to give new information on the effect of product on a local population of insects

2.3. Risk characterisation for human health

2.3.1. Hazard identification

Cypermethrin possesses three chiral carbon atoms and is therefore a racemic mixture of 8 isomers (four *cis*- and 4 *trans*-isomers). The technical products commonly available contain more than 92% cypermethrin and the ratio *cis*- to *trans*-isomers varies from 48/52 to 40/60.
A R configuration at the cyclopropane C-1 position is essential for neurotoxicity; the corresponding 1-S enantiomer is non-toxic. The configuration of the α-cyano group also influences toxicity: a S configuration of the α-cyano carbon is a potent mammalian toxicant, whereas the α-R enantiomers are essentially non-toxic. Thus, the active components of cypermethrin are 1R *cis* α S and 1R *trans* α S, e.g. approximately 25% of the mixture.

2.3.2. Hazard identification of active substance cypermethrin *cis:trans*/40:60

In this Section, summaries and evaluation of data presented in Doc.III-A6, Toxicological and metabolic studies of the CA-Report are reported as far as possible in summary tables. This data were discussed and approved for the inclusion of cypermethrin in the list a of approved active substance for the PT 8. Since no new data were provided for the PT 18 evaluation, this section has not been revised.

ADME

Absorption of cypermethrin cis:trans/40:60 from the gastro-intestinal tract of the rat is rapid but incomplete. Urinary and faecal excretion was similar at the low dose (3 mg/kg bw) for both the cyclopropyl and phenyl ring radiolabels but at the higher dose (50 mg/kg bw) faecal excretion predominated, especially in the males. This suggests that the absorption of cypermethrin is being saturated at the high dose. At the low dose 51.3 to 52.8% of the dose was absorbed by the male rats and 43.6 to 57.6% in case of the females. At the high dose level, 28.7 to 31.5% of the dose was adsorbed in male rats and 38.4 to 42.7% in the case of the females. For the estimation of oral absorption, a conservative approach is adopted. Different values were adopted for animals and humans, based on the low dose (3 mg/kg bw) data of the Needham study (2006). For **animals**, an oral absorption value of **44%** is adopted for deriving systemic NOAELs (PODs for the AELs are closer to the low dose rather than the high dose). For the estimation of **human** systemic exposure, an oral absorption value of **57%** is adopted.

Distribution. Following repeated daily oral dosing of 3 mg [^{14}C-phenyl]-cypermethrin/kg bw, the levels of radioactivity in inguinal and peri-renal fat rose by 6-7 times in the female rats, and by >10 times in the males. The lowest levels of radioactivity were seen in the brain and spinal cord. The tissue residues were rapidly cleared following the cessation of dosing, with the levels of radioactivity in the plasma falling by approximately 30 times over a 7 day period (for both males and females), and the levels in the fat falling by 2-7 times: in males in peri-renal fat (2-fold), and in females in brown fat (7-fold).

Excretion. The excretion was rapid being virtually complete by 72 h following a single oral dose of [^{14}C-cyclopropyl]- or [^{14}C-phenyl]-cypermethrin at a dose of 3 or 50 mg/kg bw. Urinary and faecal excretion was similar at the low dose for both radiolabels, but at the higher dose level faecal excretion predominated, especially in the males.

Metabolism. Hydrolytic cleavage of the ester bond and elimination of the *cis*- and *trans*-cyclopropanecarboxylic acid and 3-phenoxybenzyl moieties in the free and conjugated form is known to be a major route of metabolism in mammals, including humans. The cyclopropane carboxylic acid moiety is mainly and rapidly excreted as the glucuronide conjugate, with only limited hydroxylation of the methyl

groups attached to the cyclopropane ring. The 3-phenoxybenzyl moiety is mainly converted to 3-phenoxybenzoic acid which is further metabolised to a hydroxyl derivative (3-(4'-hydroxyphenoxy)benzoic acid) and conjugated with glucuronic acid or sulphate. The major route of excretion of metabolites is via the urine. In faeces, most of the radioactivity is unchanged compound. The metabolism of cypermethrin cis:trans/40:60 is stereoselective with a preference for the *trans*-isomers (human and animal data).

Dermal absorption. The *in vivo* dermal absorption study in rats provided the most reliable dermal absorption data. The dermal absorption of cypermethrin determined in rats *in vi*vo resulted in an absorption of 7.6% and 12.7% of the applied dose for the concentrate (500 g/L) and spray dilution (25 mg/L). For the assessment of the human internal dermal exposure, a value of 13% is used.
Absorption by inhalation. Pyrethroïds are rapidly absorbed in humans following inhalation exposure, but no estimates are available regarding how much of an inhaled dose is absorbed for cypermethrin. Consequently, in the risk characterisation a value of 100% absorption is used following inhalation exposure.

Acute toxicity

The oral toxicity of cypermethrin cis:trans/40:60 varies with the type of vehicle used and the isomer ratio. In general, aqueous suspensions were the least toxic and non-polar solutions the most toxic. The acute toxicity of the racemic mixture is also determined by the isomer ratio, with the cis-isomer found the most toxic (WHO, 1989). Oral LD_{50} values vary from 250 mg/kg (in oil) to >5000 mg/kg (in aqueous solutions). Inhalation LC_{50} = 3281 mg/m^3 (4h, aerosol, rat). Nevertheless, the toxic responses in all species were found to be qualitatively similar. The clinical signs observed after oral and inhalation exposure were indicative for an action on the central nervous system and consisted of salivation, ataxia, splayed gait, hyper-excitability to auditory stimuli, tremors, convulsions, choreoathetosis. These neurotoxic signs, better known as CS-syndrome, appear within 1 hour after dosing and survivors recover within 10-12 days. Transient facial sensory symptoms can appear after cypermethrin exposure. Abnormal facial sensations (burning sensations, tingling, tightness or numbness on the face) are reported in open literature, e.g. in health surveys (workers engaged in packaging cypermethrin), cross sectional surveys (field operators, spraymen). Cypermethrin cis:trans/40:60 was found of low dermal toxicity in the rat with clinical signs characterised by dyspnea, ruffled fur, curved and ventral body position. Dermal LD_{50} > 2000 mg/kg bw (rat).

In conclusion, cypermethrin *cis:trans*/40:60 is of moderate acute oral and inhalation toxicity, but of low dermal toxicity.

Irritation

Cypermethrin *cis:trans*/40:60 is slightly irritant to the rabbit skin and eye, but does not require classification. Acute toxicity and repeated dose toxicity studies performed with rats revealed that cypermethrin cis:trans/40:60 has a respiratory irritation potential. Respiratory tract irritation caused by cypermethrin is characterised by cough, mild dyspnoea, sneezing, and rhinorrhea. This is confirmed with human data. Case reports reported shortness of breath, dyspnea, wheezing, cough, congestion, nasal discharge, burning eyes, after exposure (inhalation) of cypermethrin with the development of significant pulmonary dysfunction (still complaining of cough, congestion, wheezing) 7 months post-exposure.

Sensitisation

Cypermethrin *cis:trans*/40:60 was not found to be a skin sensitizer by animal testing (LLNA). However, there are indications, from both animals and humans, that *technical cypermethrin* may have a mild skin sensitising potential. Results from preliminary experiments performed with technical cypermethrin (50:50) in rats indicated that technical cypermethrin had a weak skin sensitising potential. In addition, skin sensitisation (contact sensitivity and eczema) in humans is occasionally reported.

Respiratory sensitization is a recent endpoint introduced by GHS/CLP regulation. The toxicological effect of these active substance were discussed and approved for the inclusion of cypermethrin as an approved active substance for PT8. No new data were provided for the PT18 assessment and the Human Health effects were not subjected to revision. Consequently, there is no data available to draw a conclusion for this endpoint.

Short/Medium-term toxicity

The medium-term *dermal* toxicity of cypermethrin cis:trans/40:60 was studied in a 21-day dermal toxicity study in rabbits. This resulted in irritation of the skin and was associated with systemic effects such as focal liver necrosis. NOAEL = 20 mg/kg bw/d.

The medium-term *oral* toxicity of cypermethrin cis:trans/40:60 was studied in rats and dogs. The central nervous system and the liver were detected as the target tissue/organ. Neurotoxicity was characterised by clinical signs including piloerection, nervousness and uncoordinated movements, ataxia, splayed gait and hyperesthesia. In the dog, clinical signs of neurotoxicity were observed at 37.5 mg/kg bw/d in a 90-day study (NOAEL = 12.5 mg/kg bw/d). In the rat, clinical signs of neurotoxicity were observed at 80 mg/kg bw/d in a 90-day study (NOAEL = 20 mg/kg bw/d). In rats, neurotoxicity was confirmed by histopathology by peripheral nerve damage. (not in dogs). In addition, body weight was reduced, liver weight increased, and rats presented signs of anemia. In the open literature liver toxicity was characterised by inhibition of the rat liver ATPase activity. The oxidative stress induced by cypermethrin cis:trans/40:60 in the cerebral and hepatic tissues was evidenced by enhanced lipid peroxidation. Additionally, a decrease in delayed type hypersensitivity, leucopenia and immunotoxicity were observed when rats were dosed cypermethrin orally for 90 days at doses of 40 mg/kg bw/d (NOAEL = 10 mg/kg bw/d.

NOAEL medium-term = NOAEL (90-days, oral, dog) = 12.5 mg/kg bw/d.

Long-term toxicity

The long-term *oral* toxicity of cypermethrin cis:trans/40:60 was studied in rats. The effects were in line with those observed in the medium-term studies. The central nervous system, liver, and kidneys were detected as the target tissues/organ. Hepatotoxicity was characterised by increased liver weight associated with microsomal enzyme activity induction, but not associated with histological lesions. Increased kidney weight was associated with an increase in blood urea.

NOAEL long-term = NOAEL (2-year, oral, rat) = 5 mg/kg bw/d.

Carcinogenicity

Cypermethrin cis:trans/40:60 was tested in a combined chronic toxicity / carcinogenicity study in the rat. The overall results revealed no effect of cypermethrin cis:trans/40:60 treatment (0.05, 0.5, 5, 50 mg/kg bw/d, orally) on the number and type of tumours.

Genotoxicity

Cypermethrin cis:trans/40:60 was found negative for genotoxic effects in *in vitro* bacterial and mammalian cell test systems (bacterial reverse gene mutation assay, mammalian gene mutation assay in L5178Y mouse lymphoma cells, mammalian chromosomal aberration study on CHO-cells). *In vivo*, cypermethrin cis:trans/40:60 did not produce micronuclei in the immature erythrocytes of the mouse bone marrow micronucleus assay (single oral dose), and was, therefore considered negative for mutagenicity.

Overall, the open literature provides inconsistent evidence of genotoxicity *in vitro* as well as *in vivo*. The data reported on the genotoxicity of cypermethrin cis:trans/40:60 are rather inconsistent, depending on the genetic system or the assay used. Most of these studies were not performed according to accepted guidelines. Additionally, they lack reliablility because of procedural flaws such as deviating route of administration, single versus repeated exposure, other sampling times, no use of positive controls, no 2nd or 3rd confirming experiments, no data about reaching the target organ. Nevertheless, the modest or marginal increases in DNA damage reported in some studies in peripheral lymphocytes or other cells indicate, at least to a limited extent, potential genetic hazards posed by cypermethrin cis:trans/40:60, and emphasize the need and the importance of protective measures and safety regulations to minimize exposure to cypermethrin cis:trans/40:60.

Although the genotoxicity studies on cypermethrin cis:trans/40:60did not exclude a potential for DNA damage, the global weight-of-evidence suggests that cypermethrin cis:trans/40:60 should not be considered a genotoxicant, and thus, no DPD classification as a Category 3 mutagen is warranted, nor a CLP classification is foreseen.

In addition, there was no evidence of carcinogenicity. Also in other repeated-toxicity studies, there was no evidence of proliferative lesions, which would possibly occur if cypermethrin cis:trans/40:60 would display aneuploidogenic or polyploidogenic properties *in vivo.*

Reproductive and developmental toxicity

The teratogenicity studies involving oral administration of cypermethrin cis:trans/40:60 during organogenesis at dosages up to 70 mg/kg bw/d in rats and up to 120 mg/kg bw/d in rabbits were without adverse effects upon the progress and outcome of gestation.

A three-generation study involving administration of the substance in the diet of the rat showed that cypermethrin cis:trans/40:60 exerts no effect on the different reproduction parameters or on the survival of the offspring. $NOAEL_{parental}$= 10 mg/kg bw/d; $NOAEL_{reproductive}$= 50 mg/kg bw/d; $NOAEL_{developmental}$= 10 mg/kg bw/d.

According to the open literature, cypermethrin cis:trans/40:60 induced functional impairments at the neurotransmitter receptor levels in neonatal rats. However, since the multigeneration reproduction study in rats was without any indication of persistent effects in the offspring, which were also exposed to cypermethrin cis:trans/40:60 neonatally, it is suggested that receptor binding changes are not predicitive or causally related to the behavioural changes. Moreover, the most vulnerable phase for humans during the brain growth spurt is prenatal and not post-natal as in rodents. Therefore, exposure of the human fetus will be limited by maternal pharmacokinetics as well as maternal toxicity. The decreased male fertility seen in the rat and rabbit as demonstrated in the open literature appeared to be an indirect effect as it was caused at cypermethrin cis:trans/40:60 doses inducing clear general toxicity.

Based on the available data provided in the original dossier, there were no evidence giving rise to concern for an additional risk for the newborn or young humans that should trigger further investigations. According to results available to a similar substance, the WGIV 2016 concluded that the applicant should provide a DNT study on cypermethrin six months before approval date of the active substance.

Neurotoxicity

Cypermethrin has a neurotoxic potential. Repeated oral dosing of adult laying hens with 1000 mg/kg cypermethrin cis:trans/40:60 produced no immediate or delayed signs of poisoning, nor any histopathological lesions in the nervous system. However, the hen sciatic nerve is not suitable for studying pyrethroid-induced nerve damage. In contrast with hens, rats treated with a single dose of cypermethrin cis:trans/40:60 (60 mg/kg

bw) showed behavioral changes indicating a broad neurological activity of cypermethrin. A NOAEL was observed at 20 mg/kg bw. The clinical signs observed are characteristic for the acute poisoning with a type II pyrethroid: choreoathetosis accompanied by salivation (CS syndrome). In the rat, cypermethrin cis:trans/40:60 also produces epileptic activity during repeated administration. The neurotoxic effect of cypermethrin cis:trans/40:60on peripheral nerves (axons, endoneurium) was highly correlated with exposure time. Cypermethrin cis:trans/40:60 exerts its toxicity by opening the voltage-gated sodium channel slowly for extended times, leading to a prolonged sodium current in the target neurons. Furthermore, the decrease in the Na^+, K^+-ATPase pump activity is involved in the paroxysmal epileptic activity induced by cypermethrin cis:trans/40:60. Cypermethrin cis:trans/40:60 also inhibits $GABA_A$ receptors.

In addition, to the above result the BPC Working Group IV 2016, requested that a DNT study is added to the CAR no later than six month before inclusion. This study should be provided in order to address the concerns raised by EFSA during the evaluation of another cypermethrin which are critical for the settings of reference value.

The post-approval data for Cypermethrin PT18 was provided by the applicant, Arysta Life Science Benelux sprl, via R4BP3 on 29.11.2019, containing 2 neurotoxicity studies:
- [redacted]. *Cypermethrin: Oral (Gavage) Screening Study of Reproduction/Development Toxicity in the Rat. (OECD 421).*
- [redacted] *Cypermethrin: Oral (Gavage) Study of Developmental Neurotoxicity in the Rat (OECD 426).*

In both studies, clinical effects were observed on parents at dose 5 mg/kg bw/day and more. Salivation, mouth rubbing and paddling of the forelimbs are reported, mainly immediately after administration (by oral gavage).

It was concluded at the WG III 2023 that these effects have to be considered as adverse and that the parental LOAEL is set at 5 mg/kg bw/day.

Regarding the offspring, effects on learning and memory and in the functional observational battery were observed at dose 25 mg/kg bw /day in the OECD 426 study. Since only the top dose was tested, it was agreed to not set a NOAEL, but only a developmental LOAEL of 25 mg/kg bw/day.

Other: Immunotoxicity

Cypermethrin cis:trans/40:60 causes immunosuppression: both the humoral and cell-mediated immune response are impaired by cypermethrin.

Other: Endocrine disruption activity

The estrogenic potential of cypermethrin cis:trans/40:60 based on ER-mediated mechanisms remains equivocal. Contradictory results were revealed in different studies. In summary, the estrogenic and antiandrogenic effect of cypermethrin cis:trans/40:60 (and pyrethroids in general) depend on the assays or cells used. Results indicate that data obtained with high concentrations (> 10 µM) should be interpreted carefully (solubility of test chemical, cell toxicity). Possibly, cypermethrin cis:trans/40:60 is an estrogen-like chemical that might act through signalling pathways other than direct ER binding, and as such, might function as an endocrine modulator. However, at present no definite conclusions can be drawn.

In november 2016 , the criteria for identification of endocrine disrupters are still under discussion for the biocide regulation. The entry into force is foreseen for 2017.

Therefore, eCA suggest to to consider the available studies at the renewal stage of cypermethrin for PT8 or PT18.

2.3.3. Hazard identification of formulation Cypermethrin 100 g/L EW

Dermal absorption

The *in vivo* dermal absorption study in rats performed with the Cypermethrin 500 g/L EC formulation provided the most reliable dermal absorption data. The dermal absorption of cypermethrin determined in rats *in vi*vo resulted in an absorption of 7.6% and 12.7% of the applied dose for the concentrate (500 g/L) and spray dilution (25 mg/L). The solvents used in the EC formulation are considered to be more likely to carry the active substance through the skin due to the more lipophilic nature. Therefore, this can be used as a worst case. For the assessment of the human internal dermal exposure to the biocidal product Cypermethrin 100 g/L EW, a value of **13%** is used, as humans are exposed to a water-based biocidal formulation containing cypermethrin 100 g/L (10% a.s. concentration) or less when applied as a solution (0.1% a.s. concentration in final applied product).

Acute toxicity

The Cypermethrin 100 g/L EW formulation is harmful via the oral route when tested in the rat (LD50 cut-off = 500 mg/kg bw). Clinical symptoms were hunched posture, and/or pilo-erection, uncoordinated movements on day 1 at 300 mg/kg. Dermal and inhalation acute toxicity studies in the rat were performed with the Cypermethrin 250 g/L EC formulation. LD_{50} dermal > 4000 mg/kg bw, with no systemic effects/mortality, nor skin irritation, nor abnormalities noted at necropsy. LC_{50} > 5000 mg/m^3 (aerosol, 4 hours). Body weight was not affected. Clinical observations during exposure included increased respiration rate, hunched posture, pilo-erection and wet fur. There were isolated instances of ataxia, laboured or noisy respiration, heightened sensitivity to external stimuli, and tip-toe gait.

Irritation

In rabbits the Cypermethrin 100 g/L EW formulation caused well-defined erythema and very slight or slight oedema. Scaliness was noted in all 3 animals at 72 hours after exposure. Skin irritation had resolved within 7 days. According to the criteria in Directive 67/548/EEC, the Cypermethrin 100 g/L EW formulation is considered a skin irritant. Nevertheless, the skin reactions observed did not trigger classification/labelling according to the criteria in Regulation EC No 1272/2008. The Cypermethrin 100 g/L EW formulation caused no eye irritation in the rabbit. Irritation of the conjunctivae consisted of redness, chemosis and discharge, but the irritation had completely resolved within 72 hours.

Sensitisation

The Cypermethrin 100 g/L EW formulation is considered a skin sensitizer. The formulation could elicit a stimulation index ≥ 3 in the mouse Local Lymph Node Assay. An EC3 value of 2.8% was calculated.

2.3.4. Effects Assessment, AEL setting

The relevant critical endpoints of cypermethrin cis:trans/40:60 in the toxicological studies are identified as the effect on the central nervous system.

Acute	$LOAEL_{oral}$	=	5 mg/kg bw/day	(rat, DNT study)
Medium-term	$LOAEL_{oral}$	=	5 mg/kg bw/day	(rat, DNT study)

Long-term $NOAEL_{oral}$ = 5 mg/kg bw/day (rat, 2-year)

As there is no indication for route-specific differences in toxicity (not reflected by absorption data) and as cypermethrin cis:trans/40:60 did not elicit any local effects in experimental animals, there is no hindrance for the use of an AEL derived from a NOAEL/LOAEL based on studies using the oral route of administration, i.e. setting the level of internal exposure that is toxicologically acceptable.

Assessment factors: WG III 2023 agreed on assessment factor of 200 (100 for inter & intraspecies and additional 2 for using LOAEL value instead of NOAEL)

Oral absorption: As absorption of cypermethrin *cis:trans*/40:60 by the oral route was found rapid but incomplete, a correction for incomplete absorption from the gastrointestinal tract has to be made in the systemic AEL setting. For the estimation of oral absorption, a conservative approach is adopted. Different values were adopted for animals and humans, based on the low dose (3 mg/kg bw) data of the Needham study (2006). For **animals**, an oral absorption value of **44%** is adopted (agree at TM II 2011) for deriving systemic NOAELs (PODs for the AELs are closer to the low dose rather than the high dose).

In conclusion:

Acute AEL	**=**	**0.011**	**mg/kg bw/d**
Medium-term AEL	**=**	**0.011**	**mg/kg bw/d**
Long-term AEL	**=**	**0.011**	**mg/kg bw/d**

The long-term AEL was not derived with the NOAEL long term but was aligned with the acute and medium term AEL which were lower.

At WG-III-2023 the following values for ADI and ARfD were agreed:

ADI	**=**	**0.025**	**mg/kg bw/d**
ARfD	**=**	**0.025**	**mg/kg bw/d**

2.4. Risk characterisation

The risk characterisation is, in general, based on the assumption that the products are used according to the conditions for normal use. It is furthermore assumed that the recommended PPE and/or RPE will always be worn by professional users.

2.4.1. Human health risk for professionals (Primary exposure)

2.4.1.1. Industrial workers in production/formulation: Formulation of the biocidal product

The active substance is produced in a closed process. The process of production is described in the confidential annex (see doc IIIA 2.6). No relevant exposure is foreseen (DocIIB) and no concern is identified. Outside the EU, no exposure data with respect to this production step are required and therefore, characterization of potential occupational risks is not subject to regulation n°528/2012.

The manufacturing of the biocidal product Cypermethrin 100 g/L EW may be of concern. Consequently, the exposition associated with the formulation of the biocidal product was calculated. This product is produced batch-wise in an enclosed system from manufacture to drumming.

Cypermethrin is transferred to the reactor, via an open manway, using a pneumatic pump from the drum. Therefore inhalation of vaporised cypermethrin could only occur in the workplace when open containers of neat cypermethrin are handled, during the transfer to the vessel or during cleaning and maintenance of equipment. The concentration is limited by the vapour pressure and has been calculated (DOCIIB).

Direct dermal contact with cypermethrin 40:60 is not foreseen. However, incidental contact is possible during transfer of the substance to the mixing vessel and during cleaning and disposal of the containers. The appropriated model for estimating this exposure is Model 7 for mixing and loading.

Table 2.4.1.1.1. Industrial workers in production/formulation (primary exposure) – risk characterisation

Exposure Scenario		Estimated Internal Exposure			Relevant NOAEL/LOAEL [mg/kg.bw day] - Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
		estimated inhalation uptake [mg/kg bw day]	estimated dermal uptake [mg/kg bw]	estimated total uptake [mg/kg.bw day]				
Tier 1 (-PPE)	**Formulation: dilution step**	1.67×10^{-5}	0.449†	0.449†	$NOAEL_{systemic}$: 2.2 mg/kg bw/d long-term AEL: 0.022 mg/kg bw/d	100	4.9	20
Tier 2 (+PPE; gloves)	**Formulation: dilution step**	1.67×10^{-5}	0.045	0.045	$NOAEL_{systemic}$: 2.2 mg/kg bw/d long-term AEL: 0.022 mg/kg bw/d	100	49	2

† Model 7 for mixing and loading, indicative values for dermal exposure: **hand exposure without gloves**

Production and formulation plant workers are expected to be trained and skilled in the main tasks of their occupation and should have experience and skill in the use of personal protective equipment (PPE). It is assumed that engineering controls such as local exhaust ventilation and PPE are available and used.
As such, the use of appropriate PPE including chemical resistant gloves is taken into account for this industrial scenario.

According to the applicant, the product is formulated in only one plant. Also workers are wearing full PPE, not only gloves.

Conclusion: There is concern for industrial workers in the formulation of the biocide Cypermethrin 100 g/L EW.

2.4.1.2. Professional Users of the biocidal product PT18.01

According to the applicant, Cypermethrin 100 g/L EW is used by professional operators by spray application for the control of insects in and around domestic and public buildings and food processing (PT18.01). The product must be diluted in order to obtain a concentration in a.s. of 0.1%. According the recent document, the accurate model is SPRAYING Model 1 (BHHEM, Oct 2015). This model include the Mixing and Loading

phase. The outdoor use is considered similar to the indoor use because the application rate would be the same and the inhalation exposure should be the same or lower.

Table 2.4.1.2.1. Professional users PT18.01 (primary exposure) – risk characterisation

Exposure Scenario		Estimated Internal Exposure			Relevant NOAEL/LOAEL [mg/kg.bw day] - Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
		estimated inhalation uptake [mg/kg bw day]	estimated dermal uptake [mg/kg bw]	estimated total uptake [mg/kg.bw day]				
Tier 1 (no PPE; no RPE)	**spraying** indoor, low pressure spray application (without gloves, without RPE)	*0.0054* Acute exposure	*0.07098*† Acute exposure	*0.0764* Acute exposure	$NOAEL_{systemic}$: 8.8 mg/kg bw/d acute AEL: 0.088 mg/kg bw/d	100	115	0.87
		0.0036 Chronic exposure	0.04667† Chronic exposure	0.0502 Chronic exposure	$NOAEL_{systemic}$: 2.2 mg/kg bw/d long-term AEL: 0.022 mg/kg bw/d	100	43.82	2.28
Tier 2 (use of PPE: chemical resistant gloves; no RPE)	**spraying** indoor, low pressure spray application (with gloves, no RPE)	0.0054 Acute exposure	*0.02670*† Acute exposure	*0.0321* Acute exposure	$NOAEL_{systemic}$: 8.8 mg/kg bw/d Acute AEL: 0.088 mg/kg bw/d	100	274	0.36
		0.0036 Chronic exposure	0.01756† Chronic exposure	0.0211 Chronic exposure	$NOAEL_{systemic}$: 2.2 mg/kg bw/d long-term AEL: 0.022 mg/kg bw/d	100	104	0.96

† Spraying model 1 indicative values for dermal exposure: **hand exposure inside gloves 10.70 mg/min and hand exposure without gloves 181.0 mg/min**

The biocidal formulation Cypermethrin 100 g/L EW did show irritant properties to the skin (but no classification is required according to the criteria of CLP Regulation EC No 1272/2008) and has a skin sensitising potential. Considering the recent guidelines, a qualitative Risk assessment has been performed for professional handling the undiluted product during Mixing and Loading and during the professional spraying of the product.

Description of the local effects:
The product cypermethrin 100g/L EW is classified for Skin Sensitization category 1 according LLNA mouse study. Following the guidance on the biocidal products regulation, local qualitative risk characterization has to be performed. The value of EC3 of the study is 2,8% that trigger classification of the product as skin sens 1B (H317) and potency evaluated as “moderate” according CLP guidance, is also classified as “Medium” hazard category.

Description of the exposures scenarios:
The scenario use is spraying Model 1 (TNsG- Human Exposure to Biocidal Products (2002), Part 2, p. 146). It is described in the DOC IIB.

Secondary exposure has not have been considered since the product is diluted 100 fold. Moreover, the type of application done by PCOs is more a crack/crevice application limiting exposure.

If necessary, local risk characterization has to be taken into account by member States when authorizing products.

Conclusion

Hazard			Exposure							Risk	
Hazard category	Effects in terms of C&L	Additional relevant hazard information	PT	Who is exposed	Tasks, uses, processes	Potential exposures route	Frequency and duration of potential exposure	Potential degree of exposure	Relevant RMM & PPE	Conclusion on risk	Uncertainties attaced to conclusion may increase (↑) or decrease (↓) risk or both (↑↓)
Skin sens 1B (moderate)	H317	Skin Sens 1B (moderate) based on experimental study	18 (professional Users of the biocidal products PT18.01)	PROFESSIONALS	Mixing and Loading follows by spraying indoor, low pressure Mixing and Loading and spray application (with gloves, without RPE) according to human exposure scenario	Dermal, Inhalation	Frequency : 1 task/day Duration : 120 min/task	50 mL/m^2 Of suface treated	with gloves, without RPE	Acceptable: - The biocidal product used is diluted 100X - Used for short duration - Frequency varies with the period of the year. - Used by trained professional (supposed proper use of RMM and PPE)	

Conclusion, risk is acceptable, if professionals respect the following REACH guidance recommendations :

RMM and OC's:

- Containment as appropriate
- Minimize number of staff exposed

- Avoidance of contact with contaminated tools and objects
- Regular cleaning of equipment

Management/supervision in place to check that the RMM's in place are being used correctly and OC's followed

- Training of staff on good practice

- Good standard of personal hygiene

PPE:

- Substance/task appropriate gloves
- Skin coverage with appropriate barrier material based on potential for contact with the chemicals
- Substance/task appropriate respirator
- Face shield
- Eye protection

In addition, it is shown that the active substance, cypermethrin cis:trans/40:60, has a slight skin and eye (but no classification required) and respiratory irritating potential. As such, professional operators must use proper PPE to prevent exposure.

In practice, primary dermal and inhalation exposure of the professional operator will be reduced by the use of PPE (gloves) and RPE (not mandatory according the scenario). Thus, with the assumption that the obligatory PPE is used, a sufficient margin of exposure is maintained and the total internal dose is below the acute AEL. There is also no concern for chronic use of this product since the chronic internal dose is lower than the long-term AEL .

Conclusion: There is no concern for the professional operators (PT18.01), using the biocidal product Cypermethrin 100 g/L EW during spraying indoor, provided appropriate PPE (gloves) is worn.

2.4.2. Human health risk for non professional users (Primary exposure)

The biocidal product, Cypermethrin 100 g/L EW, is not available for non-professional use.

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

Secondary exposure could occur in the residential environment following pest-control measures. These exposures include inhalation of volatilized residues and dermal contact of contaminated surfaces. Hand-to-mouth contact might apply to infants and toddlers on the floor.

Secondary exposure can occur immediately after application of the product (mid-term event), but could also occur as a chronic event.

Adults may be subject to inhalation exposure only, whereas children may be exposed by inhalation and dermal contact (playing on the floor). Toddlers and infants may be additionally exposed via oral ingestion (hand-to-mouth contact). The inhalation exposure is calculated based on the assumption that the indoor air is saturated with cypermethrin vapour. The dermal and hand-to-mount contact are calculated using the computer program ConsExpo.

Table 2.4.3.1. Indirect exposure (secondary exposure)

Exposure Scenario			Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg.bw day] - Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
			estimated inhalation uptake [mg/kg bw day]	estimated dermal uptake [mg/kg bw]	estimated oral uptake [mg/kg bw day]	estimated total uptake [mg/kg.bw day]				
Tier 1 Acute Scenario		**Adult** Inhaling volatilised residues post treatment	1.68×10^{-5}	-	-	1.68×10^{-5}		100	327380	0.00031
	Unintended use	**Child** Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	4.46×10^{-5}	0.00736	-	0.0074		100	743.3	0.13
		Toddler Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	1.02×10^{-4}	0.0176	0.0077	0.0254		100	216.5	0.46
		Infant Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	8.484×10^{-5}	0.022	0.00963	0.0317	$NOAEL_{systemic}$: 5.5 mg/kg bw/d Mid term AEL: 0.055 mg/kg bw/d	100	173.5	0.58
		Child Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	4.46×10^{-5}	0.049	-	0.049		100	112.3	0.89
		Toddler Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	1.02×10^{-4}	0.117	0.0513	0.168		100	32.7	3.05
		Infant Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	8.484×10^{-5}	0.146	0.0641	0.210		100	26.2	3.82

Exposure Scenario			Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg.bw day] - Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
			estimated inhalation uptake [mg/kg bw day]	estimated dermal uptake [mg/kg bw]	estimated oral uptake [mg/kg bw day]	estimated total uptake [mg/kg.bw day]				
Tier 2 (Worst Case) Chronic Scenario		**Adult** Inhaling volatilised residues post treatment	5.8×10^{-6}	-	-	5.8×10^{-6}		100	379310	0.00026
	Unintended use	**Child** Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	1.54×10^{-5}	0.0025	-	0.0026	$NOAEL_{systemic}$: 2.2 mg/kg bw/d Chronic AEL: 0.022 mg/kg bw/d	100	846.2	0.12
		Toddler Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	3.52×10^{-5}	0.00607	0.00265	0.0088		100	250	0.4
		Infant Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	2.93×10^{-5}	0.0075	0.00332	0.0109		100	201.8	0.50
		Child Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	1.54×10^{-5}	0.0169	-	0.0169		100	130.2	0.77
		Toddler Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	3.524×10^{-5}	0.040	0.0177	0.0581		100	37.9	2.64
		Infant Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	2.93×10^{-5}	0.0505	0.022	0.0726		100	30.3	3.3

The AEL mid-term was used in the risk characterisation of secondary exposure because it is estimated that the duration of exposure is more important than a single event, among others considering inhalation exposure. The exposure time would be high, 8 hours for inhalation of the residues and a dermal contact of one hour for children, toddlers and infants playing on the treated floor.

Conclusion: There is no concern for indirect secondary exposure for general public when the product is applied **as a crack and crevice spray application**.

Considering **general surface spray application**, there is a concern for infant and toddler playing on treated floor. The risk for acute and chronic exposure for the product cypermethrin 100 g/L EW is not acceptable for these categories. For adults and children, there is no concern for indirect secondary exposure from the use of cypermethrin cis:trans/40:60 in the biocidal product, cypermethrin 100 g/L EW, as an insecticide PT18.01.

Only a crack and crevice spray application is considered to be safe.

Remark:

1. EXPOSURE FROM INDIRECT EXPOSURE THROUGH FOOD AND FEED

During WG-IV-2016, it has been accepted to that a dietary exposure assessment was not necessary due to the expected use of the substance.

Considering the use of the product, no direct contact with food should normally occur if precautionary measure are observed during the application of the product. The product will be applied only by professional user and they supposed to do it in absence of any food.

The professional will normally use this product in accordance with HACCP principles.

The RMs advises nevertheless a mitigation measure : “do not use/apply directly on or near food, feed or drinks, nor on surfaces or utensils likely to be in direct contact with food, feed or drinks.

The RMs also recommend to assess, at product authorization level, residues in food if it’s seems likely to happen.

2. MEASURES TO PROTECT ANIMALS

Based on the toxicological properties of cypermethrin and other pyrethroids, the following sentence is highly advice on the label: “the biocidal product may be lethal to cats” or “Do not let cats and others pets access treated areas”.

2.5. Risk characterisation for the environment

Cypermethrin possesses three chiral carbon atoms and is therefore a racemic mixture of 8 isomers (four *cis*- and 4 *trans*-isomers). The technical products commonly available contain more than 92% cypermethrin and the ratio *cis*- to *trans*-isomers varies from 50/50 to 40/60. A R configuration at the cyclopropane C-1 position is essential for neurotoxicity; the corresponding 1-S enantiomer is non-toxic. The configuration of the α-cyano group also influences toxicity: a S configuration of the α-cyano carbon is a potent mammalian toxicant,

whereas the α-R enantiomers are essentially non-toxic. Weipung L. *et al* (2005) has shown that in the case of cypermethrin, these enantiomers contributed for almost all the toxicity to aquatic invertebrates (Cerodaphnia dubia or Daphnia magna) which confirms the founding made for mammalian toxicology. Increase content of the active enantiomers decreases the LC_{50}. Linear regression of the LC_{50} values against the content of insecticidally active enantiomers showed close correlation (r^2=0.995) However, Edwards et al, (1987) did not found this relation for the brain toxicity of cypermethrin to fish.
Weipung L. *et al* (2004) showed that isomer selectivity in degradation by bacteria isolates and sediments also occurs. The -cis enantiomers being degraded at slower rate in comparison to the -trans enantiomers. Of the two biologically active enantiomers, 1R-cis α S was relatively persistent compared with the other stereoisomers, whereas 1R *trans* α S was likely the least persistent among all stereoisomers. Therefore, the difference between 1R *cis* α S and 1R *trans* α S in persistence may be compensatory and the overall persistence of the biologically active enantiomers may be similar to the overall trends of all cypermethrin stereoisomers.
Thus in the case of cypermethrin, the active components are 1R cis α S and 1R trans α S, e.g. approximately 25% of the mixture. Less active isomers are 1R cis α R; 1S cis α S ; 1R trans α R and 1S trans α S e.g. approximately 50% of the mixture . Relatively on active isomers are 1S cis α R and 1 S trans α R e.g. approximately 25% of the mixture.

2.5.1. Fate and distribution in the environment

2.5.1.1. Hydrolysis

Cypermethrin cis:trans/40:60 is degraded under alkaline condition at pH9 (1.9 hours at 50°C). Under neutral condition (pH 7) cypermethrin cis:trans/40:60 is slightly degraded(4.73 days at 50°C; > 29 days at 25°C). Cypermethrin cis:trans/40:60 is "relatively-stable" in acidic condition (> 1 year at 50°C). The increase in temperature increase the degradation rate of cypermethrin cis:trans/40:60 at 12°C and pH 9, cypermethrin has a derived DT50 of 1.65 day. The respective values at 12°C for pH7 and pH 4 are 98.8 days and > 7630 days.

2.5.1.2. Photolysis

In water

Cypermethrin cis:trans/40:60 is degraded by photolysis in water. The reaction quantum yield was measured to 0.0308. When irradiated the DT_{50} are 8.85d for the phenoxy- cycle and 7.10d for the cyclopropane cycle of the mother molecule. From the rate constants obtained for irradiated samples and dark controls, the net photolysis rate constant and corresponding half lives were calculated to be 0.0469 d-1 and 14.8 d for 14C phenoxy label and 0.0557 d-1 and 12.4 d for 14C cyclopropane label. The main photolytic degradants was 3-Phenoxybenzoic acid (15%), DCVC acid (18%) and 3-phenoxybenzaldehyde (Max levels were 3%) of applied radioactivity. A further 16 unidentified photolytic degradation products containing < 10% of applied radioactivity at any time point (maximum 5.6% at 7 day sunlight equivalent) were detected.

In air

EPIWIN AOP model gives an indirect half-life of 0.749 day or 17.990h for the photolysis in air (OH) of cypermethrin cis:trans/40:60 and 49 d (indirect Ozone). Due to its low volatility, cypermethrin cis:trans/40:60 is not to be expected to cause global warming or Stratospheric Ozone depletion.

In soil

Light accelerates the degradation of cypermethrin cis:trans/40:60 on a soil surface and in water. However data on distribution of radioactivity and DT50 for cis- and trans isomers indicate that soil photolysis is a minor route of degradation of the active substance.

2.5.1.3. Biodegradability

Ready: cypermethrin cis:trans/40:60 is **not readily biodegradable**

Inherent: Cypermethrin cis:trans 40:60 is **not inherently biodegradable**

Ultimate: Cypermethrin cis:trans 40:60 is **not ultimately biodegradable**

2.5.1.4. Degradation

In water/sediment: Cypermethrin cis:trans/40:60 is degradable in a water/sediment compartment. Degradation of cypermethrin cis:trans/40:60 was effective in both water-sediment systems (DT_{50} values between 2.5 and 9.8 days in total system, respectively 4.7 and 18.5 d; 12°C and 0.5 days, respectively .095d 12°C in the water phase).

The significant metabolites were 3-phenoxybenzoic acid (from the phenoxy label), TDCVC and CDCVC (from the cyclopropyl label). A further unknown metabolite (Unknown 1) was identified at levels >10% in the units dosed with the cyclopropyl label. In both systems there were no other single unidentified metabolites which individually comprised 5% of applied radioactivity at any time point. , The two main degradation products TDCVC and CDCVC have to be considered as persistent with typical DT_{50} values > 40 days.

Aerobic in soil :

Cypermethrin cis:trans/40:60 is metabolised to three extractable metabolites in soil, 3-phenoxybenzoic acid, CDCVC and TDCVC. Further metabolism of cypermethrin cis:trans/40:60 and/or these metabolites lead to bound residues and mineralisation to carbon dioxide. The DT50 values for the degradation of cypermethrin cis:trans/40:60 in the four soils tested is within the range 6 to 24 days following incubation at 20 ± 2°C. In soil PT 102, incubated at 10 ± 2°C, the DT50 value for the degradation of cypermethrin cis:trans/40:60 is 52 days. Cis cypermethrin degrades at lower rates in comparison to trans cypermethrin

Anaerobic in soil:

Cypermethrin cis:trans/40:60 is metabolised to three extractable metabolites 3PBA, CDCVC, TDCVC and carbon dioxide in the total flooded soil system. Their maximum levels were 36.6, 25.8, 33.4 and 28.2% of applied radioactivity, respectively. Further metabolism of cypermethrin cis:trans/40:60 and/or these metabolites resulted in bound residue and mineralisation to carbon dioxide. The DT50 of total cypermethrin is estimated to 46 days at 20°C. The DT_{50} of the isomers for both labels were 58d, 31d, 55d, 34d for the phenoxy cis and trans isomer and the cyclopropyl cis and trans isomers respectively at 20°C. Normalisation to 12°C resulted in DT_{50} of 87.2d for total cypermethrin; 110 d and 58.8 d for the phnoxy cis and trans isomers and 104d and 64.5 d for the cyclopropyl cis and trans isomers respectively.

2.5.1.5. Distribution

2.5.1.5.1. Adsorption/desorption in soils

These results of the soil adsorption/desorption study provided minimum Koc values ranging from 80653 to 574360 for the soil and is minimum 527972 for the sediment. The result of a QSAR (first Qsar of the table 4 TGD part III, page 26) provided a Koc of 2676776 for a log Pow of 5.3 and a Koc of 574360. These values

are indicative of a strong adsorption to the soil particles and sediment.

2.5.2. Effects on environmental organisms

2.5.2.1. Aquatic compartment

Acute toxicity

Cypermethrin shows an acute LC50 (96h) of 2.83µg/L on fish and a 48h acute effect to Daphnia magna of EC50(48h)= 4.71µg/L. However, Cypermethrin cis:trans/40:60 does not show acute toxicity to algae up to the water solubility of the active substance. The inhibition of the microbial activity appears at 163mg/L of a.i.in emulsifier surfactant, which is a concentration far above the water solubility.

Chronic toxicity

A new study has been commissioned by the applicant to further address the chronic toxicity to fish. The result of the new study is available for the PT 18anex I inclusion. The result of the new study shows that hatching success is not impaired at concentration equal or above 0.463µg/L. Fry survival is not impaired at concentration equal or above 0.463µg/L. Total lengths and wet weights shows not statistical differences compared to controls. Therefore it is suggested to derive the NOEC from the study of Taylor 2012.
NOEC Fish = 0.463 µg/L

The most sensitive organism identified in the CAR was invertebrates (Daphnia magna). The lowest NOEC calculated is 0.04µg/L for daphnia.

Effect to other non-target organisms (mesocosm)

No dose response related effect is identifiable after twice application of cypermethrin cis:trans/40:60 in an artificial pond for zooplankton and for emergent insect at 0; 0.0016; 0.005; 0.016; 0.05; 0.2; 1µg/L . An NOAEC of 0.05µg/L was calculated for the macrozoobenthos community. An overall NOAEC of 1 µg/L was calculated for the phytoplankton and of 0.05µg/l for the periphyton. The macrophytes were characterised by an NOAEC of 1.0 µg/L. This study is not considered valid for the risk assessment under PT 8 and therefore not even for PT 18.

2.5.3. Bioaccumulation

Cypermethrin cis:trans/40:60tends to bioaccumulate in water organism with a typical bioaccumulation factor (fish) of 374.4 (±45.35) and a depuration rate of 0.00158 l/h. The short depuration time impairs the relevance of the study. A QSAR (BCFwin ;EPISUITE) provided a BCF of 417 L/Kg (Log POW = 5.45).

2.5.4. Terrestrial compartment

Plant
A vegetative vigor test study showed that single application of cypermethrin as a diluted product on six plant species (both monocotyledonous and dicotyledonous) results in no phytotoxicity unless on one species where slight chlorosis was observed. The design of the test is unsuitable for biocide purpose therefore the result is only supportive for the effects of cypermethrin on the terrestrial compartment.

In the absence of any phytotoxic effects resulting from the use of cypermethrin cis:trans/40:60 in agriculture for decades, the weight of evidence of the historical use of cypermethrin cis:trans/40:60 in agriculture is a reasonable argument for the statement of no phytotoxicity of cypermethrin to plant.

Terrestrial fauna
Cypermethrin cis:trans/40:60 has limited acute effect on terrestrial organisms such as earthworms. The EC50 is found >100mg/Kg.

In a chronic test on earthworms, a NOEC mortality > of 100mg/Kg was determined. A NOEC biomass of 30.8 mg/Kg and a NOEC reproduction of 5.2 mg/Kg where determined in the same study. Based on the measured concentration the NOEC (reproduction) for earthworms is 4mg/kgdw.

In addition to these tests on earthworms, field trials provided information on the effect of 14d apart applications of cypermethrin 100g/L (250ml/ha) on non-target arthropod fauna. No adverse effects were identified on Linyphiidae; Collembolla; Diptera; Braconidae/ Ichneumonidae+ Aphidius Sp.; Gamebird-chick food populations. The observed effects on Carabid and Staphilinid populations were only transient allowing populations to recover within a crop season.

Terrestrial micro organisms
Cypermethrin has moderate effect on soil microorganisms on mineralisation process. A NOEC of 52.0 mg/Kg dry soil was determined.

2.5.5. Toxicity to birds

Cypermethrin cis:trans/40:60 shows oral acute toxicity to bird a dose above 1376mg a.i. /Kg/d or 5620 mg/Kg feed. Chronic effects (21d) investigated up to 1000mg/Kg_{food} don't show any significant results up to 92.0 mg as/Kg_{bw}. There were no treatment-related effects upon reproductive performance at any of the concentrations tested and no treatment-related macroscopic abnormalities were observed in any birds examined at autopsy. The NOEC was set to 1000 mg/Kg_{food}or 92.0 mg as/Kg_{bw}

2.6. Effect assessment :

2.6.1. Pnec settings.

The relevant critical endpoints of cypermethrin cis:trans/40:60in for the environment were identified based on the most sensitive species for the water, sediment and terrestrial compartment and for the STP.

2.6.1.1. PNEC water

The results of the mesocosm study cannot be used to derive the PNEC water. The value of the assessment factor (10) was chosen according to the TGD based on the available dataset. The lowest NOEC calculated is 0.04 µg/l for daphnia. Therefore, using the AF of 10, the PNEC water is 0.004µg/l

PNECwater = 0.004 µg/l

2.6.1.2. PNEC sediment

No study allow for the derivation of a PNEC sed.

Using the equilibrium partitioning method and a value of koc of 575000 to calculate Ksusp-water

PNECsed= 0.050 mg/Kg

2.6.1.3. PNEC in STP

The result of the microbial activity inhibition test is provided as an EC50. According to the TGD, an assessment factor of 100 is applied to the 163mg/l EC50 to derive the PNEC.

PNECstp= 1.63mg/l

2.6.1.4. PNEC soil

Two acute tests on earthworms was provided, which both presented small deficiencies. The study presenting the most conservative value for the earthworms was kept as key study with an LC_{50} of 100mg/Kg $_{dry\ soil}$. A reproduction study with earthworms provided a NOEC of 4.0mg/Kg $_{dry\ soil}$ based on measured concentration.

The field trial on mineralization of nitrogen in soil performed by Servajean, provided a NOEC of 52.0mg/Kg $_{ww}$

Additional studies on plant and non-target arthropods indicated that cypermethrin has minor and transient effect on the evaluated organisms at PPP application rate (250ml/ha) following two sequential applications (14 or 19 days).

According to the TGD, an assessment factor of 50 can be used from the earthworm's acute test, the chronic earthworms test and microbial inhibition test (two NOEC from two trophic levels). However, the result from the study on plant and the tests on non target arthropod which are non key studies does not normally allowed to further lower the AF. However the results of the tests enhance the confidence on the overall picture of the toxicity of cypermthrin on soil and terrestrial organisms. The resulting Pnec is 0.08 mg/Kg dw (equivalent to 0.07 mg/kg ww) soil from the chronic earthworm NOEC reproduction using and AF of 50.

PNECsoil = 0.08mg/Kg$_{soil\ dw}$

2.6.2. Environmental risk in the STP and aquatic compartment (incl. sediment)

STP

Scenario	Einfluent stp kg/d	Pec stp mg/l	Pnec stp= 1,63mg/l PEC/PNEC
Indoor	1,07E-02	4,89E-04	3,00E-04
Indoor , dry	2,85E-04	1,30E-05	7,99E-06
Chemical barrier	1,66E-03	7,59E-05	4,66E-05
Chemical barrier, dry	1,82E-03	8,35E-05	5,12E-05
Cracks and Crevices	2,82E-04	1,29E-05	7,93E-06
Cracks and Crevices, dry	1,31E-05	5,97E-07	3,66E-07
Outdoor wall urban	1,10E+00	5,04E-02	3,09E-02
Outdoor wall rural	1,20E-05	5,49E-07	3,37E-07
Outdoor perimeter urban	7,10E-02	3,25E-03	1,99E-03
Outdoor perimeter rural	5,75E-05	2,63E-06	1,61E-06

Surface Water

Scenario	Elocal water kg/d	Pec surf water mg/l	Pnec water= 0,000004mg/l PEC/PNEC
Indoor	1,07E-02	2,63E-05	6,57E+00
Indoor , dry	2,85E-04	7,00E-07	1,75E-01
Chemical barrier	8,63E-04	2,12E-06	5,30E-01
Chemical barrier, dry	6,74E-05	1,66E-07	4,14E-02
Cracks and Crevices	2,82E-04	6,94E-07	1,73E-01
Cracks and Crevices dry	1,31E-05	3,21E-08	8,02E-03
Outdoor wall urban	1,10E+00	2,71E-03	6,76E+02
Outdoor wall rural	1,20E-05	2,95E-08	7,37E-03
Outdoor perimeter urban	7,10E-02	1,74E-04	4,36E+01
Outdoor perimeter rural	5,75E-05	1,41E-07	3,53E-02

From the table above, we see that risks have been identified for the water compartment for the indoor and outdoor wall scenarios. However, no risks has been identified for the other scenarios for the surface water and for the STP.

Sediment

$PNEC_{sediment}$ can be provisionally calculated using the equilibrium partitioning method. This assumes that sediment-dwelling and water column organisms are equally sensitive to the chemical, and that sediment-dwelling organisms are only exposed via uptake from the water phase.

Based on the equilibrium partitioning method, the following formula

$$PNEC_{sediment} = \frac{Ksusp\text{-}water}{RHOsusp} * PNEC\ water * 1000$$

$$PNEC_{sediment} = \frac{2017.22}{1.15E03} * PNECwater * 1000$$

Local PEC/PNEC for sediment calculated based on PECwater above and a PNECsed of 0.050mg/Kg

According to the TGD, the PEC/PNEC ratio should be increased by a factor 10 since the molecule will bind to the sediment, which lead us to the following PEC/PNEC ratio

		Pecsed	$Pnec_{sed}$= 0,005 mg/kg
Scenario		mg/Kg	**PEC/PNEC**
Indoor	1,25E+04	3,29E-01	6,57E+01
Indoor , dry	1,25E+04	8,75E-03	1,75E+00
Chemical barrier	1,25E+04	2,65E-02	5,30E+00
Chemical barrier, dry	1,25E+04	2,07E-03	4,14E-01
Cracks and Crevices	1,25E+04	8,67E-03	1,73E+00
Cracks and Crevices dry	1,25E+04	4,01E-04	8,02E-02
Outdoor wall urban	1,25E+04	3,38E+01	6,76E+03
Outdoor wall rural	1,25E+04	3,68E-04	7,37E-02
Outdoor perimeter urban	1,25E+04	2,18E+00	4,36E+02
Outdoor perimeter rural	1,25E+04	1,77E-03	3,53E-01

Using the equilibrium partitioning method (epm) with a Koc of 575000, the highest Koc within those derived (see doc IIA), and an additional Af of 10 necessary due to the strong biding of the active to the sediment particles, no risk is identified for the sediment.

Conclusion for the water and sediment compartments:

As regards to the above results, risks have been identified for the water/STP and sediment except for three scenario.

Ground water assessment

Ground water can be contaminated by the application of sludge, slurry or manure on field, grassland and arable land.

The TGD and the ESD for stable and manure allow a first tier estimation of ground water contamination following application of slurry and/or manure on arable land and on grassland. Due to the very low volatility of the active (2.3x10-7 Pa *at 20 °C),* local emission to air is negligible and indirect local emission to air from stp are equal to zero and thus the aerial deposition flux is closed to zero. Therefore it has been neglected in the following. For a first tier approach, the initial concentrations of active substance in soil after 10 years of application for the respective scenario has been used to derive the concentration in pore water. The concentration has to be compared with the threshold value of 0.1µg/l.

Scenario	Elocal water	Csludge	Csludgesoil0	Csludgesoil 10	PEClocalsoil,porew
	kg/d	mg/kg	mg/kg		mg/l
Indoor	1,07E-02	1,36E+02	1,99E-01	1,99E-01	1,97E-05
indoor ,dry	2,85E-04	3,61E+00	5,31E-03	5,31E-03	5,23E-07
Chemical barrier	8,63E-04	1,09E+01	1,61E-02	1,61E-02	1,59E-06
Chemical barrier dry	6,74E-05	8,55E-01	1,26E-03	1,26E-03	1,24E-07
Cracks and crevices	2,82E-04	3,58E+00	5,26E-03	5,26E-03	5,19E-07
Cracks and crevices, dry	1,31E-05	1,66E-01	2,43E-04	2,43E-04	2,40E-08
Outdoor wall urban	1,10E+00	1,40E+04	2,05E+01	2,05E+01	2,02E-03
Outdoor wall rural	1,20E-05	1,52E-01	2,24E-04	2,24E-04	2,20E-08
Outdoor perimeter urban	7,10E-02	9,00E+02	1,32E+00	1,32E+00	1,30E-04
Outdoor perimeter rural	5,75E-05	7,29E-01	1,07E-03	1,07E-03	1,06E-07

The result showed that the pore water concentration is below the threshold value of 0.1µg/L excepted for the outdoor wall urban and for the outdoor perimeter in urban area scenarios.

2.6.3. Environmental risk in the atmosphere (resulting from industrial application)

The very low vapour pressure and Henry law constant suggests that atmospheric concentrations will be negligible (2.92E-12 mg/m^3). A qualitative environmental risk assessment only can be conducted for this compartment in the absence of specific effect data. However, based on the low PEC's, any possible adverse effects, such as ozone formation in the troposphere, is likely to be negligible.

2.6.4. Environmental risk in the terrestrial compartment

The PNEC for the terrestrial compartment is derived from a chronic toxicity study in the earthworm (PNEC = 0.08mg/kg). The terrestrial PEC/PNEC ratios are shown in the table below.

Environmental soil concentration following sludge application (up to 10 years)

Scenario	$Csludge_{soil1}$	$Csludge_{soil\ 10}$	Clocal soil	$Pec/Pnec_{sludge\ soil10}$	$Pec/Pnec_{local\ soil}$
	mg/kg	mg/kg	mg/kg		
Indoor	$1,99E^{-01}$	$1,99E^{-01}$	$1,37E^{-03}$	$2,49E^{+00}$	$1,72E^{-02}$
Indoor ,dry	$5,31E^{-03}$	$5,31E^{-03}$	$3,66E^{-05}$	$6,64E^{-02}$	$4,57E^{-04}$
Chemical barrier	$3,09E^{-02}$	$3,09E^{-02}$	$1,11E^{-04}$	$2,01E^{-01}$	$1,39E^{-03}$
Chemical barrier dry	$3,40E^{-02}$	$3,40E^{-02}$	$8,66E^{-06}$	$1,57E^{-02}$	$1,08E^{-04}$
Cracks and crevices	$5,26E^{-03}$	$5,26E^{-03}$	3,63E-05	$6.58E^{-02}$	$4.53E^{-04}$
Cracks and crevices, dry	$2,43E^{-04}$	$2,43E^{-04}$	$1,68E^{-06}$	$3,04E^{-03}$	$2.10E^{-05}$
Stable and animal housing	N.C.	N.C.	N.C.	N.C.	N.C.
Outdoor wall urban	$2,05E^{+01}$	$2,05E^{+01}$	$1,41E^{-01}$	$2,57E^{+02}$	$1,20E^{+00}$
Outdoor wall rural	$2,24E^{-04}$	$2,24E^{-04}$	$1,54E^{-06}$	$2,80E^{-03}$	$1,31E^{-05}$
Outdoor perimeter urban	$1,32E^{+00}$	$1,32E^{+00}$	$9,11E^{-03}$	$1,65E^{+01}$	$7,72E^{-02}$
Outdoor perimeter rural	$1,07E^{-03}$	$1,07E^{-03}$	$7,38E^{-06}$	$1,34E^{-02}$	$6,25E^{-05}$

The Pec/Pnec ratio calculated for 10 year of sludge application does not show risk for indoor application in dry cleaned areas, in chemical barrier treatments and in cracks and crevices application. Outdoor scenarios shows unacceptable risk in rural areas.

Environmental soil concentration following direct release according to esd.

Scenario	$Pec_{soil,house}$	$Pec_{soil,large\ building}$	$PEC/PNEC_{house}$	$PEC/PNEC_{building}$
	kg/kg ww^{-1}	kg/kg ww^{-1}	/	/
Indoor	n.a	n.a	/	/
Chemical barrier	n.a	n.a	/	/
Outdoor wall urban	n.a	n.a	/	/
Outdoor wall rural	$1,50E^{-06}$	$1,55E^{-06}$	$2.88E^{+01}$	$2.97E^{+01}$
Outdoor perimeter urban	n.a.	n.a.	/	/
Outdoor perimeter rural	$1,66E^{-03}$	$8,11E^{-03}$	$3.20E^{+04}$	$1.56E^{+05}$

The PEC/PNEC ratios calculated for the outdoor use of insecticide is acceptable unless against crawling insects .

2.6.5. Non compartment specific effects relevant to the food chain (primary and secondary poisoning)

			Acute		Short term		
Parameter	**Symbol**	**Unit**	**wall/flying**	**perimeter /crawling**	**wall/flying**	**perimeter /crawling**	**S/D/O ***
INPUT							
Quantity of commercial product	**Q_{prod}**	kg/m²	5,00E-05	5,00E-05	5,00E-05	5,00E-05	S

Dillution factor	**Dill**	-	100	100	100	100	
Fraction of active substance in the commercial product	**F_{AI}**	-	0,01	0,01	0,01	0,01	S
Food Intake rate of indicator species	**FIR/bw**	d-1					P
	Small insect mam		0,68	0,68	0,68	0,68	
	Small herb ,mam		1,39	1,39	1,39	1,39	
	Small,insect, bird		1,04	1,04	1,04	1,04	
	Large herb, bird		0,44	0,44	0,44	0,44	
Local concentration of active substance in soil	**Pec_{soil}**	mg/kg					S
	Kow **Foc** **Koc**		281838 0,02 252455	281838 0,02 252455	281838 0,02 252455	281838 0,02 252455	
Residue value per unit dose	**RUD**	mg/kg					P
	Small insect mam		14	14	5,1	5,1	
	Small herb ,mam		142	142	76	76	
	Small,insect, bird		52	52	29	29	
	Large herb, bird		142	142	76	76	

OUTPUT

Application rate per square meter (ground)	**APPL**	kg/m²	5,00E-09	5,00E-09	5,00E-09	5,00E-09	O
Application rate per square meter (ground)	**T_{appl}**	kg/m²	3,75E-09	5,75E-09	1,25E-08	7,50E-09	O
Bioaccumulation factor in worms	**BCF_{worms}**	-	3382,896	3382,896	3382,896	3382,896	O
Total concentration of the active in the worms	**C_{worms}**	mg/kg	7,65E-07	7,90E-07	5,647E-03	2,752E-02	O
Estimated theoretical exposure	**ETE**	mg/kg/d					O
	med, worms, bird		3,70E-07	3,82E-07	2,73E-03	1,33E-02	
	med, worms, mam		6,75E-07	6,96E-07	4,98E-03	2,43E-02	
	Small insect mam		3,57E-12	5,47E-12	4,34E-12	2,60E-12	
	Small herb ,mam		7,40E-11	1,13E-10	1,32E-10	7,92E-11	
	Small,insect, bird		2,03E-11	3,11E-11	3,77E-11	2,26E-11	
	Large herb, bird		2,34E-11	3,59E-11	4,18E-11	2,51E-11	

The above ETE values can to be compared with the acute toxicity values to rats (indicative) and to dietary toxicity to birds respectively for mammals and birds. For rats, the Acute LD50 is 1950 mg/Kg and for birds, the 21d NOEC dietary toxicity is 92.0 mg/Kg/d. Both values are far below the ETE values**.**

2.7. Water Framework Directive (WFD)

Cypermethrin is introduced as a priority substance in Directive 2013/39/EU, which amends Directive 2000/60/EC and Directive 2008/105/EC as regards priority substances in the field of water policy. Cypermethrin is listed as a priority substance, where no distinction is made between cypermethrin and its individual isomers. Consequently, it has to be investigated if the approval of cypermethrin will undermine the achievement of compliance with the standard laid down in the WFD.

Under this Directive, two types of quality standards are established to ensure good water quality: AA-EQS (annual average environmental quality standard) and MAC-EQS (maximum allowable concentration environmental quality standard).

In the case of cypermethrin the AA-EQS is 8 x 10^{-8} mg/L (inland surface waters, total concentration of all isomers). According to the WFD the arithmetic mean of all measured concentrations over a twelve month monitoring period within a body of water should not exceed this value.

This AA-EQS is 50 times lower than the aquatic Predicted No-Effect Concentration (PNEC) established for cypermethrin (4.x 10^{-6} mg/L). The reason for this difference is based on a difference in the endpoints forming the basis of the AA-EQS and PNECaquatic, and the choice of assessment factor. While for the derivation of the PNECaquatic an assessment factor of 10 was used, the AA-EQS was derived with an assessment factor of 50. The choice of this higher factor is explained by the availability of many low endpoints (EC50s or NOECs) for species from sensitive taxa, which were derived from studies of unassignable reliability or where the exposure concentrations were likely not maintained during the course of the experiments. Additionally, most of the studies used in the WFD is not part of the biocide dossier.
In addition to an AA-EQS, also a MAC-EQS was established for cypermethrin. The MAC-EQS (6x10^{-7} mg/L for cypermethrin) may not be exceeded by any measured concentration at any point of the water body or at any point in time.

Again, this standard is lower than the established aquatic PNEC, this time by a factor of 6. Also here this is a result of the choice of assessment factor, which is more conservative for the EQS-derivation.

Before comparing the calculated aquatic Predicted Environmental Concentrations (PECs) from this evaluation with any quality standard, one should first consider what this PEC represents and if it can be compared with the established standards. In the case of cypermethrin, the aquatic PECs are derived from a daily, local emission and represent a concentration in surface water during an emission period: the emission pattern can be considered as intermittent. Therefore, the comparison between the AA-EQS (annual average environmental quality standard) and the MAC-EQS (maximum allowable concentration environmental quality standard) and the PEC may not be appropriate.

Considering the above and when comparing the lowest calculated PEC (3.21x 10^{-8} x10^{-7} mg/L) with the AA-EQS, it can be concluded that two source of cypermethrin already exceeds the established standard, allowing no more room for other sources of the substance (e.g. plant protection). However, as indicated, the PEC calculated here is the concentration resulting from an emission episode, while the AA-EQS is an annual average. Comparing the two and drawing conclusions merely on these numbers does not seem correct.

Comparing the PECs to MAC-EQS seems more relevant, as this EQS represents a single concentration that may not be exceeded. For cypermethrin, neither of the PECs calculated in the identified safe use scenario for crack and crevice treatment, dry cleaning (5.52×10^{-7} and 3.21×10^{-08} mg/L) exceed this standard.

In conclusion, and based on the fact that at the time of adoption of this opinion no monitoring data for this substance are available, the comparison of the PECs with the EQS values listed for cypermethrin as a priority substance under the WFD alone is not reason enough to prevent the approval of alpha-cypermethrin because approval would undermine the achievement of compliance with the standards laid won in the WFD. However, when monitoring data for this substance become available under the WFD, these should be taken into account at product authorisation level. Where relevant, MSCAs have to inform the Commission as a review of the approval in line with Article 15 of the BPR may be initiated.

2.8. PBT Assessment

The PBT-criteria as laid down in the TGD are as follow:

	PBT-criteria	vPvB-criteria
P	Half-life > 60 d in marine water or 40 d in freshwater* or half-life > 180 d in marine sediment or 120 d in freshwater sediment*	Half-life > 60 d marine or freshwater or >180 d in marine or fresh water sediment
B	BCF > 2000	BCF > 5000
T	Chronic NOEC < 0.01 mg/L or CMR or endocrine disrupting effects	Not applicable

* For the purpose of marine environmental risk assessment half-life data in freshwater (sediment) can be overruled by data obtained under marine conditions.

According to reach criteria on soil, P criteria is half-life >120d and vPvB criteria is >180 d

According to an OECD 308 test (Brice, 2005) cypermethrin cis:trans/40:60 undergo rapid degradation in aquatic environment, freshwater and sediments, with DT 50 <40 days in fresh water (DT50= 0.948 d; 12°C) and < 120 day in sediment (DT50 = 20.7d to 27 d; 12°C). In soil the DT50 is 17.2d (Geom mean ;12°C)

Regarding the metabolites, the two metabolites found in the water sediment study (TDCVC and CDCVC) fulfil the P criteria with DT50> 40day.

Therefore cypermethrin cis:trans/40:60 is **not** considered as **Persistent** (P). However, metabolites of the parent compounds fulfil the P criteria.

Cypermethrin cis:trans/40:60 is not bioconcentrated according to a flow through OECD 305 E test (Szeleczy,1990), with a measured BCF of 373±45 < 2000 L/Kg wwt. The result is further confirmed by BCFwin (EPISUIT) which provide a BCF of 417L/Kg_{wwt}

Cypermethrin cis:trans/40:60 is **not bioaccumulable** (B)

TDCVC and CDCVC metabolite have a Log Pow of 2.672 (calculation based on their smiles code) according to the eq.74 of the TGD, the corresponding BCF is 37.25

TDCVC and CDCVC metabolites does not fulfil the B criteria.

Chronic NOEC of cypermethrin for freshwater organisms are below the threshold value of 0.01mg/L. Cypermethrin cis:trans/40:60 meets the (T) criteria.

Therefore, cypermethrin cis:trans/40:60 should be considered as **toxic** (T)

According to the DAR of cypermethrin, TDCVC and CDCVC metabolites have toxicity values which are 10000x higher than those of cypermethrin. TDCVC and CDCVC metabolites does not fulfil the T criteria

Conclusion: Based on the above considerations, cypermethrin cis:trans/40:60 is not PBT.

2.9. Endocrine disruption, pop

Cypermethrin has been listed as potential endocrine disruptor by the EU Commission. However, actually, there is no data available to the applicant or scientific evidence for endocrine disruption effect of cypermethrin.

Pop/vPvB criteria for cyperkill 250 EC (cypermethrin 250g/L) according to the POP criteria of the Stockholm Convention or the vPvB-and PBT criteria.

		POP/vPvB	PBT	Cypermethrin value (DE evaluation report)	Criteria fulfilled?
Persistence	DT50 water	>2 months (60 days)	> 40 days	<14 days	No
	DT50 soil	> 6 months (180 days)	>120 days	69 days (lab) 56 days (field)	No
	DT50 sediment	> 6 months (180 days)	>120 days	7.3-30.3 days	No
	P criteria fulfilled?				No
Potential for long-range transport in the environment	DT50 Air (direct and indirect phototransformation)	>2 days	-	0.681 day	No
Bioaccumulation	BCF	>5000	>2000	1204	No
Toxicity	NOEC aquatic organisms	-	<0.01 mg/L	NOEC = 0,04 µg as/L (daphnia)	Yes

The active ingredient Cypermethrin does not meet neither POP / vPvP-criteria.

2.10. Exclusion and substitution criteria

The table below summarises the relevant information with respect to the assessment of exclusion and substitution criteria:

Property	Conclusions

CMR properties	Carcinogenicity (C)	**no classification required**
	Mutagenicity (M)	**no classification required**
	Toxic for reproduction (R)	**no classification required**
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	**not P or vP (cyp.)** **P (CDCVC and TDCVC)**
	Bioaccumulative (B) or very Bioaccumulative (vB)	**not B or vB (cyp)** **not B or vB (CDCVC and TDCVC)**
	Toxic (T)	**T criteria fulfilled (cyp)** **Not T (CDCVC and TDCVC)**
Endocrine disrupting properties	active substance is **not considered** to have endocrine disrupting properties	
Respiratory sensitisation properties	**no classification required**	
Concerns linked to critical effects	**the active substance does not fulfils this criterion**	
Proportion of non-active isomers or impurities	Cypermethrin cis:trans/40:60 is 92 % pure. It is composed of 8 main isomers which has their own activity whilst the level of activity of each single isomer differs depending on the configuration of the cyclopropane C-1 and the α-cyano group. A R configuration at the cyclopropane C-1 position is essential for neurotoxicity; the corresponding 1-S enantiomer is non-toxic. The configuration of the α-cyano group also influences toxicity: a S configuration of the α-cyano carbon is a potent mammalian toxicant, whereas the α-R enantiomers are essentially non-toxic. Thus, the more active components of cypermethrin are 1R cis α S and 1R trans α S, e.g. approximately 25% of the mixture. Less active isomers are 1R cis α R; 1S cis α S ; 1R trans α R and 1S trans α S e.g. approximately 50% of the mixture . Relatively non-active isomers are 1S cis α R and 1 S trans α R e.g. approximately 25% of the mixture.	

Consequently, the following is concluded:

Cypermethrin cis:trans/40:60 does not meet the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012.

Cypermethrin cis:trans/40:60 does not meet the conditions laid down in Article 10 of Regulation (EU) No

528/2012, and is therefore not considered as a candidate for substitution. The exclusion and substitution criteria were assessed in line with the "Note on the principles for taking decisions on the approval of active substances under the BPR"[1] and in line with "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[2] agreed at the 54th and 58th meeting respectively, of the representatives of Member States Competent Authorities for the implementation of Regulation 528/2012 concerning the making available on the market and use of biocidal products. This implies that the assessment of the exclusion criteria is based on Article 5(1) and the assessment of substitution criteria is based on Article 10(1)(a, b, d, e and f).

I.3. PROPOSAL FOR THE DECISION REGARDING ANNEX I, IA OR IB INCLUSION

3.1. Background to the proposed decision

The overall conclusion from the evaluation of cypermethrin *cis:trans*/40:60 for use in Product Type 18 (Insecticides), is that it may be possible for Member States to issue authorisations of products containing cypermethrin *cis:trans/40:60* in accordance with the conditions laid down in Article 5(1) b), c) and d) of Dir. 98/8/EC.

Article 10 of the Biocides Directive 98/8/EC addresses the inclusion of an active substance in the Annexes I, IA or IB. For the decision or non-inclusion, it has to be examined if the criteria of article 10 (1) are fulfilled.

As regard to the physico-chemical properties, Cypermethrin *cis:trans*/40:60 is not explosive, not flammable and is stable at room temperature.

Assessed from the documentation for the active substance cypermethrin *cis:trans*/40:60, the proposed application manners and areas of use cypermethrin intended to control insect pests in and around domestic and public buildings including farm building, animal housing and food processing may be sufficient effective for these uses and without unacceptable risk to human health nor to the environment, excepted exposure of toddlers and infants playing on a treated floor.

The estimation of hazards and the exposure assessment for human health for cypermethrin *cis:trans*/40:60 showed the following results:

The active substance, cypermethrin *cis:trans*/40:60, is moderately toxic if swallowed and by inhalation, and of low toxicity if applied to the skin. The neurotoxic signs observed, are known as CS-syndrome. The occurrence of transient peripheral sensory symptoms is independent of skin irritation. Cypermethrin *cis:trans*/40:60 is slightly irritant to the skin and eye, but does not require classification. Animal and human data revealed that cypermethrin *cis:trans*/40:60 has a respiratory irritation potential. Cypermethrin *cis:trans*/40:60 was not found to be a skin sensitiser by animal testing. However, there are indications that *technical cypermethrin* may have a mild skin sensitising potential. Cypermethrin *cis:trans*/40:60 is neurotoxic and toxic to the liver, and alters the immune

[1] See document: Note on the principles for taking decisions on the approval of active substances under the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/c41b4ad4-356c-4852-9512-62e72cc919df/CA-March14-Doc.4.1%20-%20Final%20-%20Principles%20for%20substance%20approval.doc)

2 See document: Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/dbac71e3-cd70-4ed7-bd40-fc1cb92cfe1c/CA-Nov14-Doc.4.4%20-%20Final%20-%20Further%20guidance%20on%20Art10(1).doc)

system by immunosuppression. Cypermethrin *cis:trans*/40:60 is unlikely to be genotoxic or to pose a carcinogenic risk to humans. Cypermethrin *cis:trans*/40:60 is unlikely to pose a teratogenic risk, nor have effects on fertility and developmental parameters to humans. At present, no definite conclusions can be drawn concerning the endocrine disruption activity of cypermethrin *cis:trans*/40:60.

The risk characterisation is focused on the uses the applicant applied for:

The professional use (PT18.01), control of insects in and around domestic and public buildings, including farm buildings, animal housing and food processing by spray application; and the indirect exposure to workers and the general public
This overall conclusion relies on the fact that professional users of the biocidal product will be applying the basic principles of good practice and respect the conditions for the normal use recommended on the label of the product.

The evaluation of the hazards and the environmental exposure for cypermethrin *cis:trans*/40:60 give the following results:

Cypermethrin *cis:trans*/40:60 and the related product are toxic for the aquatic fauna but less toxic for the aquatic plants and algae. The K_{ow} of the active substance, the result of a BCF test and QSAR are such that bioaccumulation could not be excluded. Biomagnifications along the food chain cannot be fully excluded. The impact on sewage treatment plan is not of concern if the product is used in respect of the recommendation. Cypermethrin *cis:trans*/40:60 is characterised by Koc value in soil ranging from 80653 to 574360 ml/g and adsorbs strongly to soil and sediment particles. The active is not biodegradable, not inherently biodegradable and not ultimately biodegradable. However, in natural soil and sediment, the mother molecule is degraded in three major metabolites (3PBA, CDCVC, TDCVC). Further metabolism of cypermethrin *cis:trans*/40:60 and/or these metabolites resulted in bound residue and mineralisation to carbon dioxide.

The actual classification of the active has to be revised due to a change in classification criteria in the 2nd ATP of the CLP regulation (see proposal p 6; this document). Stot RE 2 has to be added.

The new classification has still to be validated by ECHA.

3.2. Proposed decision regarding inclusion in annex

It is proposed that cypermethrin cis:trans/40:60 is listed in the List of Approved substance of the regulation 528/2012 as an active substance in insecticide products (Product Type 18), subject to the following specific provisions:

1. The active substance cypermethrin *cis:trans*/40:60, as manufactured, shall have a minimum purity of 92% w/w.
2. The identity and maximum content of impurities (found in the "Confidential Annexes") must not differ in such a way as to invalidate the assessment for the inclusion of the active substance on the annex I.
3. Products containing cypermethrin *cis:trans*/40:60 may be used as insecticide for the control of insects in domestic and public buildings by spray application, by professional

users only

4. The inclusion regulation should, however, only include the intended uses supported by data and the content shall reflect the conditions and restrictions for the use of cypermethrin *cis:trans*/40:60 as an insecticide proposed in the report.
5. The following particular conditions also apply:
   - The product should be applied only on surface out of reach of children (below 6 years old)
   - Professional should decontaminate the area which could be in contact with children (below 6 years old)
   - Professional should not apply the product more than twice a year in the same building
   - Spray application of the product should not be performed on surfaces in direct contact or above fresh water or were direct emission to fresh water is foreseeable.
   - When performing professional treatment (spraying), operators must wear the appropriate personal protective equipment.
   - Application of the product in food processing industry or kitchen should only be performed in accordance with the HACCP method and principles and/or the ISO norm 22000 (which includes HACCP in ISO 9001)

3.3. Factors to be taken into account by member States when authorising products

1. The following recommendations and risk mitigation measures have been identified for the uses assessed. Authorities should consider these risk mitigation measures when authorising products, together with possible other risk mitigation measures, and decide whether these measures are applicable for the concerned product:

   a. If an unacceptable risk is identified for professional users, safe operational procedures and appropriate organizational measures shall be established. Products shall be used with appropriate personal protective equipment where exposure cannot be reduced to an acceptable level by other means.

   b. If an unacceptable risk is identified for infants and toddlers following secondary exposure in areas following treatment, labels, and where provided, safety data sheets, should indicate that products used in these areas shall be restricted to areas not accessible to infants and toddlers.

   c. An assessment of the risk in food and feed areas may be required at product authorisation where use of the product may lead to contamination of food and feeding stuffs.

   d. A local risk assessment may be required if the product is classified for skin sensitisation.

   e. For products containing cypermethrin the following statement should be added to the label: “The product contains: cypermethrin. May cause paraesthesia.”

   f. Unacceptable risks are identified for surface water and sediment for indoor surface treatment. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures or by

other means, such uses should not be authorised.

g. Unacceptable risks are identified for the sediment for indoor chemical barrier application. Products shall only be authorised if the risk can be mitigated by measures that minimise exposure to sediment (via sewage), for example restricted application to areas that are not normally wet-cleaned or if the risk can be mitigated by other means.

h. Unacceptable risks are identified for soil following outdoor wall application in urban and rural areas and following perimeter application in rural areas. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures or by other means, such uses should not be authorised.

i. Unacceptable risks are identified for surface water, ground water and sediment following outdoor wall and perimeter applications in urban areas. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures or by other means, such uses should not be authorised.

j. Due to the increased sensitivity of cats against pyrethroids a specific assessment and specific risk mitigation measures for pets might be required for product authorisation.

2. Cypermethrin is listed as a priority substance under Directive 2013/39/EU. When monitoring data become available, these should be considered during product authorisation stage.

3.4. Requirement for further information

The information and justifications supplied in accordance with Annex II and Annex III of BPR (reg. 528/2012) has been accepted as sufficient to recommend an inclusion of cypermethrin *cis:trans*/40:60 in Union list of approved substance. Nevertheless, to some extends, the evaluation of the environmental exposure may be revised in order to reduce the Risk Characterisation Ratio. Additional studies will be needed to assess the efficacy of CYPERMETHRIN-based products intended to be used in outdoor conditions.

3.5. Updating the evaluation report

The technical information in this evaluation 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 referred to in articles 4, 6, 12.2 , 13 and 14 of regulation 528/2012 (BPR). Such adaptations will be examined and finalised in connection with any amendment of the conditions for the inclusion of cypermethrin *cis:trans*/40:60 in List of Approved Substances of the BPR.

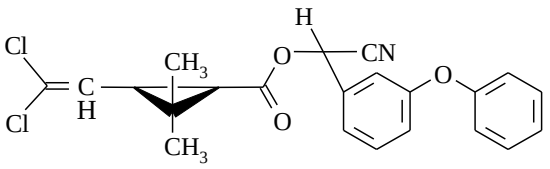
Appendices

APPENDIX 1: LISTING OF ENDPOINTS

Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

Active substance (ISO Common Name)	*Cypermethrin*
Function (*e.g.* fungicide)	Insecticide
Rapporteur Member State	Belgium

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	*(RS)-α-cyano-3 phenoxybenzyl-(1RS)-cis, trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate*
Chemical name (CA)	*cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate*
CAS No	*52315-07-8*
EC No	*257-842-9*
Other substance No.	*Cipac n°: 332*
Minimum purity of the active substance as manufactured (g/Kg or g/l)	*920 g/Kg*
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/Kg)	*See confidential annex*
Molecular formula	$C_{22}H_{19}Cl_2NO_3$
Molecular mass	*416.3*
Structural formula	

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

Melting point (state purity)	*Melting endotherm : onset 41.2°C, peak 47.3°C (98.3%)*
Boiling point (state purity)	*Boiling did not occur: decomposition was observed (98,3%)*
Temperature of decomposition	*Decomposition exotherm starting at 200 ºC*

Appearance (state purity)	*White powder, mild chemical odour (98.3%)* *Yellow to brown viscous liquid/semi-solid, mild chemical odour (96.5%)*
Relative density (state purity)	*D_4^{20} = 1.303 (98.3%)*
Surface tension	*Not applicable (solubility < 1 mg/L)*
Vapour pressure (in Pa, state temperature)	2.3x10-7 Pa *at 20 °C (99.3%)* *6x10-7* Pa at 25°C
Henry's law constant (Pa m^3 mol^{-1})	*H = 0.024 Pa.m³.mol^{-1} at 20°C Log H= -1.6*
Solubility in water (g/l or mg/l, state temperature)	*< 9 µg/L at 20°C (99.5% pure)(value =4µg/L used for the environmental risk assessment)*
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	*Methanol: 248 g/L (20 ºC)*
	Heptane: 57 g/L (20 ºC)
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	*Not applicable, stable in formulated product*
Partition coefficient (log P_{OW}) (state temperature)	*log P_{ow} range of discrete isomer pairs : 5.3 to 5.6 at 25°C (Mean 5.45 used for ecotox in euses)*
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	At 50 ºC: pH4 : DT_{50}>1 year
	pH 7: DT_{50} = 4.73 d
	pH 9: DT_{50} = 1.9 h
	At 12°C:
	pH 4= 7630.5 days
	pH 7 = 98.9 days
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	not applicable, product has very low solubility in water
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	*in methanol, unadjusted pH :* *absorption maxima :* *204 nm, ε = 43217 L.mol-1.cm-1* *278 nm, ε = 2368 L.mol-1.cm-1* *absorption at λ > 290 nm :* *290 nm, ε = 839 L.mol-1.cm-1* *295 nm, ε = 411 L.mol-1.cm-1* *304 nm, ε = 332 L.mol-1.cm-1* *314 nm, ε = 316 L.mol-1.cm-1*
Photostability (DT_{50}) (aqueous, sunlight, state pH) (point VII.7.6.2.2)	pH 4, 20°C : DT_{50} between 12.4 and 14.8 summer sunlight days (net photolysis data calculated from irradiated sample and dark control data)
Quantum yield of direct phototransformation in	0.0308

water at □ > 290 nm (point VII.7.6.2.2)	
Flammability	*Not flammable (no flash point up to 110°C)* *Auto-ignition temperature = 400°C*
Explosive properties	*No potential for explosion*

Summary of intended uses

Field of use/ Product type	**Organisms controlled**	**Application type**	**Number and timing of application**	**Formulated Product**		**Max. Application rate**			**Remarks**
				Type	**Conc. a.s.**	**Conc. a.s. in solution (%)**	**Area of spraying**	**mg a.s./m^2 surface**	
PT18.01	Flying insects, crawling insects, fleas, wasp nests	Spraying (low pressure spray application via hand-held compression sprayers)	1 application/day (duration : 120 minutes)	EW	10%	0.1	100-150 m^2	33.33-50.00	Preventative and remedial treatment, professional users

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

with regard to physical/chemical data	
with regard to toxicological data	GHS08, Warning STOT RE2; H373 May cause damage to organs through prolonged or repeated exposure STOT SE3; H335 May cause respiratory irritation
with regard to fate and behaviour data	
with regard to ecotoxicological data	

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	HPLC with UV detection (280 nm)
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	See Confidential Information document.

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	GC with MS detection, LOQ = 0.05 mg/kg (LOQ = 0.5 µg/kg for sediment)
Air (principle of method and LOQ) (Annex IIA, point 4.2)	GC with MS detection, LOQ = 0.375 µg/m^3
Water (principle of method and LOQ) (Annex IIA, point 4.2)	GC with electron capture detection, LOQ = 0.01 µg/L
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	Not evaluated
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	GC with electron capture detection, LOD = 0.05 mg/kg (oilseed rape) and 0.025 mg/kg (wheat)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	GC with MS detection, LOQ = 0.05 mg/kg (bovine tissue), 0.005 mg/kg (bovine milk), 0.01 mg/kg (hen eggs).

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals (Annex IIIA, point 6.2)

Rate and extent of oral absorption:	Low dose (3 mg/kg bw): 43.6 to 57.6% (♂ 51.3 to 52.8%, ♀ 43.6 to 57.6%) High dose (50 mg/kg bw): ♂ 28.7 to 31.5%, ♀ 38.4 to 42.5%

	For the estimation of oral absorption, a conservative approach is adopted. Different values were adopted for animals and humans, based on the low dose (3 mg/kg bw) data of the Needham study (2006). For **animals**, an oral absorption value of **44%** is adopted for deriving systemic NOAELs (PODs for the AELs are closer to the low dose rather than the high dose). For the estimation of **human** systemic exposure, an oral absorption value of **57%** is adopted.
Rate and extent of dermal absorption:	In vivo dermal absorption (rat): 7.6% of applied dose of undiluted emulsifiable concentrate (500 g/L) and 12.7% of applied dose for spray solution (25 mg/L). For the assessment of the human internal dermal exposure, a value of **13%** is used.
Rate and extent of inhalation absorption	Pyrethroïds are rapidly absorbed in humans following inhalation exposure, but no estimates are available regarding how much of an inhaled dose is absorbed for cypermethrin. For the assessment of the human internal inhalation exposure, a value of 100% is used.
Distribution:	Mainly concentrated in fatty tissues. Lowest levels found in brain and spinal cord.
Potential for accumulation:	accumulation in fat
Rate and extent of excretion:	Virtually complete after 72 hours (27-53% in urine; 43-80% in faeces)
Metabolism in mammals	Major route via hydrolytic cleavage of the ester bond to 3-phenoxybenzoic acid and DCVC acid (cyclopropane carboxylic acid).
Toxicologically significant metabolite	The parent compound is the tox. sign. compound

Acute toxicity (Annex IIIA, point 6.1)

Rat LD_{50} oral	cis:trans/40:60 500 mg/kg bw (groundnut oil) cis:trans/40:60 1732 mg/kg bw (arachis oil) cis:trans/50:50 287 mg/kg bw (10% in corn oil) cis:trans/37:63 250 mg/kg bw (corn oil)
Rat LD_{50} dermal	> 2000 mg/kg bw
Rat LC_{50} inhalation	3281 mg/m^3 (males)
Skin irritation	Slightly irritant, does not require classification
Eye irritation	Slightly irritant, does not require classification

Respiratory irritation	irritant (animal and human data)
Skin sensitization (test method used and result)	cis:trans/40:60 non-sensitiser (LLNA in mouse)

Short term repeated dose toxicity (Annex IIIA, point 6.3-6.4)

Species/ target / critical effect	Neurotoxicity, liver toxicity Rat, oral, 90-days: LOAEL = 80 mg/kg bw/d, NOAEL = 20 mg/kg bw/d Dog, oral, 90-days: LOAEL = 37.5 mg/kg bw/d , NOAEL = 12.5 mg/kg bw/d
Lowest relevant oral NOAEL / LOAEL	Dog, oral, 90-days: NOAEL = 12.5 mg/kg bw/d
Lowest relevant dermal NOAEL / LOAEL	Not required. [Rabbit, 15 doses/ 3weeks: 20 mg/kg bw/d (91/414 DAR for cypermethrin made by the BE CA)]
Lowest relevant inhalation NOAEL / LOAEL	Not required.

Long-term repeated dose toxicity / carcinogenicity (Annex IIIA, point 6.5-6.7)

Species/ target / critical effect	Decreased body weight and food consumption Rat, oral, 2-year: LOAEL = 50 mg/kg bw/d, NOAEL = 5 mg/kg bw/d
Lowest relevant oral NOAEL / LOAEL	Rat, oral, 2-year: NOAEL = 5 mg/kg bw/d
Lowest relevant dermal NOAEL / LOAEL	Not required
Lowest relevant inhalation NOAEL / LOAEL	Not required
Carcinogenicity	
Species/type of tumour	No carcinogenic potential in the rat (NOAEL = 5 mg/kg bw/d)
lowest dose with tumours	Not applicable

Genotoxicity (Annex IIIA, point 6.6)	No genotoxic potential

Reproductive toxicity (Annex IIIA, point 6.8)

Species/ Reproduction target / critical effect	Parental: Decreased bw gain and food intake. Offspring: Reduced litter size and pup weight at parental toxic doses.

	Fertility: Not affected. Rat, 3-generation reproduction study: NOAEL parental = 10 mg/kg bw/d; NOAEL offspring = 10 mg/kg bw/d; NOAEL fertility = 50 mg/kg bw/d
Lowest relevant reproductive NOAEL / LOAEL	NOAEL = 10 mg/kg bw/d
Species/Developmental target / critical effect	No effects at maternal toxic doses Rat, teratogenicity study: NOAEL = 17.5 mg/kg bw/d (maternal toxicity), > 70 mg/kg bw/d (embryotoxicity). Rabbit, teratogenicity study: NOAEL = 120 mg/kg bw/d (maternal toxicity and embryotoxicity).
Lowest relevant developmental NOAEL / LOAEL	NOAEL > 70 mg/kg bw/d

Neurotoxicity / Delayed neurotoxicity (Annex IIIA, point 6.9)

Species/ target/critical effect	Behavioural effects Rat, acute delayed neurotoxicity study: LOAEL = 60 mg/kg bw, NOAEL = 20 mg/kg bw (in corn oil)
Lowest relevant NOAEL / LOAEL.	NOAEL = 20 mg/kg bw

Other toxicological studies

Immunotoxicity	Cypermethrin induces immunosuppression
Endocrine Disruption	At present, no definite conclusions can be drawn

Medical data (Annex IIIA, point 6.12)

.....	Paresthesiae and peripheral sensory phenomena; irritation of respiratory tract

Summary	Value	Study/critical effect	Safety factor/ absorption (%)
Acute AEL	0.011 mg/kg bw/d	Rat, DNT study, neurotox effects	100 44%
Medium-term AEL	0.011 mg/kg bw/d	Rat, DNT study, neurotox effects	100 44%
Long-term AEL	0.011 mg/kg bw/d	Rat, DNT study, neurotox effects	100 44%
ADI	0.025 mg/kg bw/day	Rat, DNT study, neurotox effects	/

ARfD	0.025 mg/kg bw/day	Rat, DNT study, neurotox effects	/

Acceptable exposure scenarios (including method of calculation)

Industrial Formulation of biocidal product	Industrial formulation. Described in detail in Document II-B and II-C. **Of Concern.**
Professional users PT18.01	Spray application by pest control operators (indoor). Described in detail in Document II-B and IIC. Level of personal protection: PPE (gloves and coated coverall) No concern.
Non-professional users	No non-professional use
Indirect exposure as a result of use	Secondary exposure can occur immediately after application of the product (mid-term event), but could also occur as a chronic event. Described in detail in Document II-B and II-C. Acute exposure scenarios: 1° Adult inhaling volatilised residues from treated floor, 2° Children inhaling volatilised residues from treated floor and dermal exposure by playing on the floor, 3° Infant inhaling volatilised residues from treated floor, dermal exposure by playing on the floor, and mouthing hands. No concern when the product is applied as a crack and crevice spray. Of concern for toddler and infant when the product is applied as a general surface spray Chronic exposure scenarios: 1° Adult inhaling volatilised residues from treated floor, 2° Children inhaling volatilised residues from treated floor and dermal exposure by playing on the floor, 3° Infant inhaling volatilised residues from treated floor, dermal exposure by playing on the floor, and mouthing hands. No concern when the product is applied as a crack and crevice spray. Of concern for toddler and infant when the product is applied as a general surface spray

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)	At 50 ºC: pH 4 = > 1 year pH 7 = 4.73 days pH 9 = 1.9 hours
	At 25 ºC: pH 7 > 29 days
	At 12°C: pH 4= 7630.5 days pH 7 = 98.9 days pH 9 = 39.71 hours
DCVC acid	44% max at day 15 pH7 50°
	39% max at day 15 pH9 , 50°C
3-PBA	47% max at 8 hours pH7 ,50°C
	44% max at 8 hours pH7, 50°C
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	*Degradation rate, assuming first order kinetics (expressed as equivalent summer sunlight days) :* irradiated : k = 0.0783 d^{-1}; $t_{1/2}$ = 8.85 d (^{14}C phenoxy) k = 0.0976 d^{-1}; $t_{1/2}$ = 7.10 d (^{14}C cyclopropane) (cis-isomers are degraded 1.3 to 1.7 times faster than trans-isomers) dark control : k = 0.0314 d^{-1}; $t_{1/2}$ = 22.1 d (^{14}C phenoxy) k = 0.0419 d^{-1}; $t_{1/2}$ = 16.5 d (^{14}C cyclopropane) **Net photolysis** k= 0.0469 d^{-1} ; $t_{1/2}$= 14.7d (^{14}C phenoxy) k=0.0557 d^{-1} ; $t_{1/2}$= 12.4d (^{14}C cyclopropane) $\Rightarrow$ sunlight accelerates the rate of degradation *Major photolysis products (> 10% of applied radioactivity) :* DCVC acid (18% after 100 hrs, ^{14}C cyclopropane label); 3-phenoxybenzoic acid (15% after 100 hrs, ^{14}C phenoxy label); 3-phenoxybenzaldehyde (3% after 100 hrs, ^{14}C phenoxy label); in addition, a further 16 unidentified photolytic degradation products (< 10% at any time point) were detected *Proposed degradation pathway :* Photolysis of Cypermethrin proceeds via cleavage of the ester linkage to form DCVC acid and 3-phenoxybenzaldehyde, and subsequent oxidation of

	the CHO group resulting in 3-phenoxybenzoic acid. The DCVC acid is further degraded into unidentified polar compounds and subsequently to CO_2.
Readily biodegradable (yes/no)	No Modified Sturm test: 0.6-1.4% at 33 days Not inherently biodegradable Anaerobic biodeg.: +/-17% at 60 days (indicative)
Inherent biodegradation	No
Ultimate biodegradation	No
Biodegradation in seawater	Not evaluated
Water/sediment study:	
Cypermethrin	
DT50 water	0.5 days (20°±*2*C) 0.948 (12°C)
DT90 water	1.5 days (20°±*2*C)
DT50 sediment	10.9-14.3 days 20.7- 27days (12°C)
DT90 sediment	36.1-47.3 days (20°C)
DT50 whole system	3.5-9.8 days ; 6.6-18.5 days (12°C)
DT90 whole system	11.6-32.7 days (20°C)
Cys-cypemethrin	
DT 50 whole system	12.5-16.9 days; 20°C : 23.7-32 days ; 12°C
Trans -cypermethrin	
DT 50 whole system	11-2.9 days ; 20°C: 2.1-5.5 days ; 12°C
TDCVC	
DT50 whole system	79.9-144.3 days (20°C): 151.5-273.6 days ; 12°C
CDCVC	
DT50 whole system	62.0-187.5 days (20°C): 117.6- 355.6 days ; 12°C
3-PBA	
DT50 whole system	12.9 day (20°C): 24.5 days ; 12°C
Distribution in water / sediment systems (active substance)	After 0 days, water phase: 91-96% AR* After 100 days, water phase: 3-9% AR After 0-3 days, sediment phase: 60-68% AR After 100 days, sediment phase: 3-7% AR
Distribution in water / sediment systems (metabolites)	3-Phenoxybenzoic acid (up to 21% AR in water and 11% in sediment), TDCVC (up to 44% AR in water and 20% in sediment), CDCVC (up to 22% AR in water and 15% in sediment). Unidentified metabolite present (up to 14% AR at day 100)

Mineralization	65.3-68.8 % after 100 days (phenoxy label) 25.1-29.7 % after 100 days (cyclopropyl label)

*AR = Applied radioactivity

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

Mineralization (aerobic)	29-54% AR after 90/120 days (phenoxy label) 49-78% AR after 90/120 days (cyclopropyl label)
Non-extractable residues	24-36% AR after 90/120 days (phenoxy label) 13-16% AR after 90/120 days (cyclopropyl label)
Relevant metabolites	3-Phenoxybenzoic acid, max. 10.2% AR at day 7 (phenoxy label). TDCVC, max. 13.6% AR at day 7, and CDCVC, max 3.9% at day 7 (cyclopropyl label).
DT50 (20ºC)	6-24 days (mean =13.45d)
DT50 (10ºC)	52 days
DT50 (12ºC)	17.2 days (based on the geom.mean)
Laboratory studies (range or median, with number of measurements, with regression coefficient)	Not performed.
Field studies (state location, range or median with number of measurements)	Not performed
Anaerobic degradation	Cypermethrin was metabolised to three extractable metabolites 3PBA, CDCVC, TDCVC and carbon dioxide in the total flooded soil system. Their maximum levels were 35.1, 22.8, 31.2 and 22.8% AR, respectively. Further metabolism of cypermethrin and/or these metabolites resulted in bound residue and mineralisation to carbon dioxide. Max % bound residue for phenoxy label 25.1 % Max % bound residue for cyclopropyl label 9.1% The DT50 (both labels) was 46 days at 20°C and 87.2 at 12°C *Cis-cypermethrin(*phenoxy label)DT_{50}= 58d; 20°C: 110d ; 12°C *Trans-cypermethrin* (phenoxy label) DT_{50}= 31d ; 20°C : 58.8d ; 12°C *Cis –cypermethrin* (cyclopropyl label) DT_{50}= 55d ; 20°C : 104.3d ; 12°C Trans-cypermethrin (cyclopropyl label) DT_{50}= 34d ; 20°C : 64.5 ; 12°C

	Non extractable residues : phenoxy lable 8.2% ;cyclopropyl label 3.3%, Fulvic acid : phenoxy lable 3.9% ; cyclopropyl label 2.1% Humic acid : phenoxy label 7.0%; cyclopropyl label 1.9% Humin: phenoxy label 5.7%; cyclopropyl label 1.9%
Soil photolysis	DT50 (first order, light, assuming equivalent summer sunlight conditions at 30° N) = 29.6d; DT50 (first order, dark) = 43.9d [^{14}C phenoxy] and [^{14}C cyclopropane] labels. Metabolites in irradiated soil samples: carboxamide derivative of cypermethrin (19% AR after 7-9 days continuous irradiation), 3-phenoxybenzoic acid (1.9% AR at day 15) and DCVC acid ((2,2-dichlorovinyl)-2,2- dimethylcyclopropanecarboxylic acid) (2.9% AR at day 15). Bound residue (12.8-21.9 % AR at day 15), mineralisation (5.4-6.2 % AR at day 15) Metabolites in dark samples : 3-phenoxybenzoic acid (23.9% AR at day 15) and DCVC acid (12.7 %AR); carboxamide derivative of cypermethrin (1% AR at day 15). Bound residue (10.6-10.7% AR at day 15), mineralisation (0.2-2.5 % AR at day 15)
Soil accumulation and plateau concentration	No data required

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

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Freundlich adsorption coefficients (K) values could not be determined. Minimum Kd values ranges from 3871 to 8976.Minimum Koc values were between 80653 and 574360 mL/g. QSARkoc: 2.676.776-4.586.002 (log Pow 5.3-5.6)

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

Direct photolysis in air	Not evaluated
Quantum yield of direct photolysis	0.0308
Photo-oxidative degradation in air	Half-life 17.990 hours (indirect photolysis, OH), and 0.749 days based on 24 hr day; 0.5E6 OH/cm^3 0.02326*$\mathbf{10^{-17}}$ cm^3/mol-sec (overall ozone rate constant)
Volatilization	Not expected

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 hours	Mortality	LC_{50} = 2.83 µg/L
Pimephales promelas	28 days (early life stage)	Fry survival, body length/weight	NOEC = 0.463 µg/L
Invertebrates			
Daphnia magna	48 hours	Immobilisation	EC_{50} = 4.71 µg/L
Daphnia magna	21 days	Immobilisation	EC_{50} = 0.35 µg/L NOEC= 0.04 µg/L
Algae			
Selenastrum capricornutum	96 hours	Biomass Growth rate Biomass	96-hour E_bC_{50} = >33 µg/L 96-hour E_rC_{50} = >33 µg/L 96-hour NOEbC = > 33µg/L (value above the water solubility)
Micro organisms			
Activated sludge	3 hours	Respiration inhibition	EC_{50} = 163 mg/L
Outdoor Mesocosm (not relevant for biocide)			
Aquatic invertebrates and algae (natural ecosystem)	105 days	Abundance data	NOEAEC = 0.05 µg/L (all spp.)

Effects on earthworms or other soil non-target organisms

Acute toxicity to *Eisenia foetida* (Annex IIIA, point XIII.3.2)	14-day EC_{50} = >100 mg/Kg substrate

Reproductive toxicity (Annex IIIA, point XIII.3.2)	8-week NOECs: Mortality 100 mg a.s. /Kg $_{\text{dry soil}}$ Biomass 30.8 mg.a.s./Kg $_{\text{dry soil}}$ Reprod. 5.2 mg a.s./Kg $_{\text{dry soil}}$ 4mg/kg dry soil based on measured concentrations

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

Nitrogen mineralization	NOEC = 52.0 mg/Kg dry soil
Carbon mineralization	Not evaluated

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	LD50 (rat, oral) = 1945 mg/Kg
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	Not determined.
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	LC50 (Colinus virginianus, 5d) > 5620 mg a.s./Kg feed or > 1376 mg a.s./Kg bw/d,
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	NOEC (Colinus virginianus, 21 weeks) = 1000 mg a.s./Kg feed or 92.0 mg a.s./Kg bw/d

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

Acute oral toxicity	Not evaluated.
Acute contact toxicity	Not evaluated.

Field trials	Agrochemical field trial in winter wheat, four treatments (control, Cyperkill 10 EC at field rate, Cyperkill 10 EC at drift rate, dimethoate), 4 replicates of one hectare for each treatment. Cypermethrin (2 applications of 25 g a.s./ha at 14 days interval) significantly depleted numbers of Carabidae beetles (adults), Linyphiidae spiders, predatory diptera, Braconidae/ Ichneumonidae + Aphidius sp., other parasitica, gamebird-chick food at 0-4 days after 2nd application. Collembola level increases at 0-4 days after 2nd application (probably due to a decrease of their predators). All the taxonomic groups observed in this study have recovered at 38-40 days after 2nd application. Cypermethrin (2 applications of 0.595 g a.s./ha at 14 days interval, equivalent to drift rate) significantly depleted numbers of Carabidae beetles (adults), Staphylinidae beetles (adults), Linyphiidae spiders, predatory diptera, other parasitica at 0-4 days after 2nd application. Collembola level increases at 0-4 days after 2nd application. All the taxonomic groups observed in this study have recovered at 38-40 days after 2nd application. The effects observed in this study are considered to be acceptable since a full population recovery of non-target arthropods occurred within the same crop-growing season (within 40 days post treatment)

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	Experimental BCF in fish = 373.4±45.35 QSAR BCFwin : BCF = 417 L/Kg
Depuration time	Depuration rate constant 0.00158 l/h
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not evaluated

APPENDIX 2: LIST OF INTENDED USES[3]

Object and/or situation	Member State or Country	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment	Remarks:
				Type	Conc.	method	number	interval between applications (min)	g as/m^3	
(a)			(c)	(d-f)	of as (i)	kind (f-h)	min max (k)			(m)
Flying and crawling insects	EU	Cypermethrin 100 g/L EW.	Cockroaches, ants and fleas	EC	100g/l	Spraying low pressure	1/d, duration 120 minute	/	25-50 mg a.i./m²	

VP = Vapouriser

(a) *e.g.* biting and suckling insects, fungi, molds; (b) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(c) GCPF Codes - GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4); (d) All abbreviations used must be explained
(e) g/kg or g/l;(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench;
(g) Kind, *e.g.* overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated;
(h) Indicate the minimum and maximum number of application possible under practical conditions of use;
(i) Remarks may include: Extent of use/economic importance/restrictions

[3] 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 standard terms and abbreviations

Stand. term / Abbreviation	**Explanation**
A	ampere
ACh	acetylcholine
AChE	acetylcholinesterase
ADI	acceptable daily intake
ADME	administration distribution metabolism and excretion
ADP	adenosine diphosphate
AE	acid equivalent
AF	assessment factor
AFID	alkali flame-ionisation detector or detection
A/G	albumin/globulin ratio
ai	active ingredient
ALD_{50}	approximate median lethal dose, 50%
ALT	alanine aminotransferase (SGPT)
Ann.	Annex
AOEL	acceptable operator exposure level
AMD	automatic multiple development
ANOVA	analysis of variance
AP	alkaline phosphatase
approx	approximate
AR	applied radioactivity
ARC	anticipated residue contribution
ARfD	acute reference dose
as	active substance
AST	aspartate aminotransferase (SGOT)
ASV	air saturation value

Stand. term / Abbreviation	**Explanation**
ATP	adenosine triphosphate
BAF	bioaccumulation factor
BCF	bioconcentration factor
bfa	body fluid assay
BOD	biological oxygen demand
bp	boiling point
BPD	Biocidal Products Directive
BSAF	biota-sediment accumulation factor
BSE	bovine spongiform encephalopathy
BSP	bromosulfophthalein
Bt	*Bacillus thuringiensis*
Bti	*Bacillus thuringiensis israelensis*
Btk	*Bacillus thuringiensis kurstaki*
Btt	*Bacillus thuringiensis tenebrionis*
BUN	blood urea nitrogen
bw	body weight
c	centi- (x 10^{-2})
°C	degrees Celsius (centigrade)
CA	controlled atmosphere
CAD	computer aided design
CADDY	computer aided dossier and data supply (an electronic dossier interchange and archiving format)
cd	candela
CDA	controlled drop(let) application
cDNA	complementary DANN
CEC	cation exchange capacity
cf	confer, compare to
CFU	colony forming units
ChE	cholinesterase

Stand. term / Abbreviation	**Explanation**
CI	confidence interval
CL	confidence limits
cm	centimetre
CNS	central nervous system
COD	chemical oxygen demand
CPK	creatinine phosphatase
cv	coefficient of variation
Cv	ceiling value
d	day(s)
DES	diethylstilboestrol
DIS	draft international standard *(ISO)*
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
dna	designated national authority
DO	dissolved oxygen
DOC	dissolved organic carbon
dpi	days post inoculation
DRP	detailed review paper *(OECD)*
$DT_{50(lab)}$	period required for 50 percent dissipation (under laboratory conditions) (define method of estimation)
$DT_{90(field)}$	period required for 90 percent dissipation (under field conditions) (define method of estimation)
dw	dry weight
DWQG	drinking water quality guidelines
ε	decadic molar extinction coefficient
EC_{50}	median effective concentration
ECD	electron capture detector

Stand. term / Abbreviation	**Explanation**
ED_{50}	median effective dose
EDI	estimated daily intake
EINECS	European inventory of existing commercial substances
ELINCS	European list of notified chemical substances
ELISA	enzyme linked immunosorbent assay
e-mail	electronic mail
EMDI	estimated maximum daily intake
EN	European norm
EPMA	electron probe micro-analysis
ERL	extraneous residue limit
ESPE46/51	evaluation system for pesticides
EUSES	European Union system for the evaluation of substances
F	field
F_0	parental generation
F_1	filial generation, first
F_2	filial generation, second
FBS	full base set
FELS	fish early-life stage
FIA	fluorescence immuno-assay
FID	flame ionisation detector
F_{mol}	fractional equivalent of the metabolite´s molecular weight compared to the active substance
FOB	functional observation battery
f_{oc}	organic carbon factor (compartment dependent)
fp	freezing point
FPD	flame photometric detector
FPLC	fast protein liquid chromatography

Stand. term / Abbreviation	**Explanation**
g	gram(s)
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GEP	good experimental practice
GFP	good field practice
GGT	gamma glutamyl transferase
GI	gastro-intestinal
GIT	gastro-intestinal tract
GL	guideline level
GLC	gas liquid chromatography
GLP	good laboratory practice
GM	geometric mean
GMO	genetically modified organism
GMM	genetically modified micro-organism
GPC	gel-permeation chromatography
GPS	global positioning system
GSH	glutathione
GV	granulosevirus
h	hour(s)
H	Henry's Law constant (calculated as a unitless value)
ha	hectare(s)
Hb	haemoglobin
HC5	concentration which will be harmless to at least 95 % of the

Stand. term / Abbreviation	**Explanation**
	species present with a given level of confidence (usually 95 %)
HCG	human chorionic gonadotropin
Hct	haematocrit
HDT	highest dose tested
hL	hectolitre
HEED	high energy electron diffraction
HID	helium ionisation detector
HPAEC	high performance anion exchange chromatography
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography - mass spectrometry
HPPLC	high pressure planar liquid chromatography
HPTLC	high performance thin layer chromatography
HRGC	high resolution gas chromatography
H_S	Shannon-Weaver index
Ht	haematocrit
HUSS	human and use safety standard
I	indoor
I_{50}	inhibitory dose, 50%
IC_{50}	median immobilisation concentration or median inhibitory concentration 1
ICM	integrated crop management
ID	ionisation detector
IEDI	international estimated daily intake

Stand. term / Abbreviation	**Explanation**
IGR	insect growth regulator
im	intramuscular
inh	inhalation
INT	2-p-iodophenyl-3-p-nitrophenyl-5-phenyltetrazoliumchloride testing method
ip	intraperitoneal
IPM	integrated pest management
IR	infrared
ISBN	international standard book number
ISSN	international standard serial number
IUCLID	International Uniform Chemical Information Database
iv	intravenous
IVF	*in vitro* fertilisation
k *(in combination)*	kilo
k	rate constant for biodegradation
K	Kelvin
Ka	acid dissociation constant
Kb	base dissociation constant
K_{ads}	adsorption constant
K_{des}	apparent desorption coefficient
kg	kilogram
K_H	Henry´s Law constant (in atmosphere per cubic metre per mole)
K_{oc}	organic carbon adsorption coefficient
K_{om}	organic matter adsorption coefficient
K_{ow}	octanol-water partition coefficient

Stand. term / Abbreviation	**Explanation**
Kp	solid-water partition coefficient
kPa	kilopascal(s)
l, L	litre
LAN	local area network
LASER	light amplification by stimulated emission of radiation
LBC	loosely bound capacity
LC	liquid chromatography
LC-MS	liquid chromatography- mass spectrometry
LC_{50}	lethal concentration, median
LCA	life cycle analysis
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
ln	natural logarithm
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level
log	logarithm to the base 10
LOQ	limit of quantification (determination)
LPLC	low pressure liquid chromatography
LSC	liquid scintillation counting or counter
LSD	least squared denominator multiple range test

Stand. term / Abbreviation	**Explanation**
LSS	liquid scintillation spectrometry
LT	lethal threshold
m	metre
M	molar
µm	micrometre (micron)
MAC	maximum allowable concentration
MAK	maximum allowable concentration
MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MDL	method detection limit
MFO	mixed function oxidase
µg	microgram
mg	milligram
MHC	moisture holding capacity
MIC	minimum inhibitory concentration
min	minute(s)
MKC	minimum killing concentration
mL	millilitre
MLT	median lethal time
MLD	minimum lethal dose
mm	millimetre
MMAD	mass median aerodynamic diameter
mo	month(s)
MOE	margin of exposure
mol	mole(s)
MOS	margin of safety

Stand. term / Abbreviation	**Explanation**
mp	melting point
MRE	maximum residue expected
MRL	maximum residue level or limit
mRNA	messenger ribonucleic acid
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MT	material test
MW	molecular weight
n.a.	not applicable
n-	normal (defining isomeric configuration)
n	number of observations
NAEL	no adverse effect level
nd	not detected
NEDI	national estimated daily intake
NEL	no effect level
NERL	no effect residue level
ng	nanogram
nm	nanometre
NMR	nuclear magnetic resonance
no, n°	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NOIS	notice of intent to suspend
NPD	nitrogen-phosphorus detector or detection
NPV	nuclear polyhedrosis virus
NR	not reported

Stand. term / Abbreviation	**Explanation**
NTE	neurotoxic target esterase
OC	organic carbon content
OCR	optical character recognition
ODP	ozone-depleting potential
ODS	ozone-depleting substances
OEL	occupational exposure limit
OH	hydroxide
OJ	Official Journal
OM	organic matter content
Pa	pascal
PAD	pulsed amperometric detection
2-PAM	2-pralidoxime
pc	paper chromatography
PC	personal computer
PCV	haematocrit (packed corpuscular volume)
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PED	plasma-emissions-detector
pH	pH-value
PHED	pesticide handler's exposure data
PIC	prior informed consent
pic	phage inhibitory capacity
PIXE	proton induced X-ray emission
pKa	negative logarithm (to the base

Stand. term / Abbreviation	**Explanation**
	10) of the acid dissociation constant
pKb	negative logarithm (to the base 10) of the base dissociation constant
PNEC	predicted no effect concentration (compartment to be added as subscript)
po	by mouth
POP	persistent organic pollutants
ppb	parts per billion (10^{-9})
PPE	personal protective equipment
ppm	parts per million (10^{-6})
PPP	plant protection product
ppq	parts per quadrillion (10^{-24})
ppt	parts per trillion (10^{-12})
PSP	phenolsulfophthalein
PrT	prothrombin time
PRL	practical residue limit
PT	product type
PT(CEN)	project team CEN
PTDI	provisional tolerable daily intake
PTT	partial thromboplastin time
QA	quality assurance
QAU	quality assurance unit
(Q)SAR	quantitative structure-activity relationship
r	correlation coefficient
r^2	coefficient of determination
RA	risk assessment
RBC	red blood cell
REI	restricted entry interval
RENI	Registry Nomenclature Information System

Stand. term / Abbreviation	**Explanation**
Rf	retardation factor
RfD	reference dose
RH	relative humidity
RL_{50}	median residual lifetime
RNA	ribonucleic acid
RP	reversed phase
rpm	revolutions per minute
rRNA	ribosomal ribonucleic acid
RRT	relative retention time
RSD	relative standard deviation
s	second
S	solubility
SAC	strong adsorption capacity
SAP	serum alkaline phosphatase
SAR	structure/activity relationship
SBLC	shallow bed liquid chromatography
sc	subcutaneous
sce	sister chromatid exchange
SCAS	semi-continous activated sludge
SCTER	smallest chronic toxicity exposure ratio (TER)
SD	standard deviation
se	standard error
SEM	standard error of the mean
SEP	standard evaluation procedure
SF	safety factor
SFC	supercritical fluid chromatography
SFE	supercritical fluid extraction
SIMS	secondary ion mass spectroscopy
S/L	short term to long term ratio

Stand. term / Abbreviation	**Explanation**
SMEs	small and medium sized enterprises
SOP	standard operating procedures
sp	species (only after a generic name)
SPE	solid phase extraction
SPF	specific pathogen free
spp	subspecies
SSD	sulphur specific detector
SSMS	spark source mass spectrometry
STEL	short term exposure limit
STER	smallest toxicity exposure ratio (TER)
STMR	supervised trials median residue
STP	sewage treatment plant
t	tonne(s) (metric ton)
$t_{½}$	half-life (define method of estimation)
T_3	tri-iodothyroxine
T_4	thyroxine
T_{25}	tumorigenic dose that causes tumours in 25 % of the test animals
TADI	temporary acceptable daily intake
TBC	tightly bound capacity
TCD	thermal conductivity detector
TG	technical guideline, technical group
TGD	Technical guidance document
TID	thermionic detector, alkali flame detector
TDR	time domain reflectrometry
TER	toxicity exposure ratio
TER_I	toxicity exposure ratio for initial

Stand. term / Abbreviation	**Explanation**
	exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
tert	tertiary (in a chemical name)
TEP	typical end-use product
TGGE	temperature gradient gel electrophoresis
TIFF	tag image file format
TLC	thin layer chromatography
Tlm	median tolerance limit
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMRC	theoretical maximum residue contribution
TMRL	temporary maximum residue limit
TNsG	technical notes for guidance
TOC	total organic carbon
Tremcard	transport emergency card
tRNA	transfer ribonucleic acid
TSH	thyroid stimulating hormone (thyrotropin)
TTC	2,3,5-triphenylterazoliumchloride testing method
TWA	time weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor (safety factor)
ULV	ultra low volume
UR	unit risk
UV	ultraviolet
UVC	unknown or variable

Stand. term / Abbreviation	**Explanation**
	composition, complex reaction products
UVCB	undefined or variable composition, complex reaction products in biological material
v/v	volume ratio (volume per volume)
vis	visible
WBC	white blood cell
wk	week
wt	weight
w/v	weight per volume
ww	wet weight
w/w	weight per weight
XRFA	X-ray fluorescence analysis
yr	year
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to

Appendix 4: List of studies

Data protection is claimed by the applicant in accordance with Article 12.1(c) (i) and (ii) of Council Directive 98/8/EC for all study reports marked "Y" in the "Data Protection Claimed" column of the table below. These claims are based on information from the applicant. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It was however not possible to confirm the accuracy of this information.

Author(s)	**Section no. / Reference no.**	**Year**	**Title** **Source (where different from company)** **Report no.** **GLP or GEP status (where relevant)** **Published or not**	**Data Protection Claimed Y/N**	**Owner**
Aldana L González de Mejía E., Craigmill A., Tsutsumi V., Armendariz-Borunda J., Panduro A., Rincón A.R.	IIA, 3.5.1	1998	Cypermethrin increases apo A-1 and apo B mRNA but not hyperlipidemia in rats. Toxicology Letters 95: 31-39.		
Amer S.M., Aboul-ela E.I	IIA, 3.6.2	1985	Cytogenetic effects of pesticides. III. Induction of micronuclei in mouse bone marrow by the insecticides cypermethrin and rotenone. Mutat. Res. 155: 135-142.		
Amer S.M., Ibrahim A.A., el-Sherbeny K.M.	UUA, 3.6.1, 3.6.2	1993	Induction of chromosomal aberrations and sister chromatid exchange *in vivo* and *in vitro* by the insecticide cypermethrin. J. Appl. Toxicol. 13: 341-345.		
Anon.	IIA, 2.3.1 (IIIA, 5.2/03)	1980	Determination of toxic values against *Anobium punctatum* larvae. Building Research Establishment, Princes Risborough Laboratory, UK; (CYP/E28). GLP not applicable, unpublished	No	-
Anon	IIA, 2.3.1 (IIIA, 5.2/01).	1981a	Anon. (1981); Determination of toxic values against *Hylotrupes bajulus* larvae. Building Research Establishment, Princes Risborough Laboratory, UK; report no. 80/11 (CYP/E28). GLP not applicable, unpublished.	No	-
Anon.	IIA, 2.3.1 (IIIA, 5.2/02)	1981b	Determination of toxic values against *Hylotrupes bajulus* larvae. Building Research Establishment, Princes Risborough Laboratory, UK; report no. 80/12-15 (CYP/E28). GLP not applicable, unpublished.	No	-

Author(s)	Section no. / Reference no.	Year	Title Source (where different from company) Report no. GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N	Owner
[redacted]	IIA, 4.2.3 (IIIA,7.5.4.1)	1976	Evaluation of the insecticide WL 43467 (cypermethrin) against the honeybee Aphis mellifera Woodstock Laboratory, Shell Research Ltd, report no. WK61/S/BE137 (CYP/T7) Chimac-Agriphar S.A., document no. KII A, 8.3.1.1/01 Not GLP, unpublished	Yes (Exist./First)	Arysta
[redacted].	IIA, 4.1.1.2 (IIIA, 7.1.2.1.2)	2005	Cypermethrin cis:trans/40:60 Evaluation of ultimate anaerobic biodegradability by measurement of biogas production Huntingdon Life Sciences Ltd., report no. HZL 010/053287 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 1.3 (IIIA, 3.1)	2002a	Cypermethrin *cis:trans* 40:60 (purified active substance) : Evaluation of the physico-chemical properties Covance Laboratories Ltd, report no. 40/30-D2149 (CYP/C65) Chimac-Agriphar S.A., document no. KIIA, 2.0/01 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 1.3 (IIIA,3.11)	2002b	Cypermethrin *cis:trans* 40:60 (technical active substance) : Evaluation of the physico-chemical properties Covance Laboratories Ltd, report no. 40/33-D2149 (CYP/C63) Chimac-Agriphar S.A., document no. KIIA, 2.0/02 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA,1.4 (IIIA,4.1(01)) → Confidential Data	2002	Cypermethrin *cis:trans* 40:60 technical active substance : five batch analysis; Covance Laboratories Ltd, report N° 40/29-D2149 (CYP/C66) Chimac-Agriphar S.A., document no. KII A, 1.11/01 GLP, unpublished.	Yes (Exist./First)	Arysta
[redacted]	IIA,1.4 (IIIA,4.1(02)) → Confidential Data	2003	Cypermethrin cis:trans/40:60 (technical active substance) : Five batch analysis – Supplementary analyses Covance Laboratories Ltd, report N° 40/54, (CYP/C76) Chimac-Agriphar S.A., document no. KII A, 1.11/02 GLP, unpublished	Yes (Exist./First)	Arysta

Author(s)	**Section no. / Reference no.**	**Year**	**Title** **Source (where different from company)** **Report no.** **GLP or GEP status (where relevant)** **Published or not**	**Data Protection Claimed Y/N**	**Owner**
[redacted]	IIA, 1.4 (IIIA,4.1(03)) → Confidential Data	2004	Cypermethrin cis:trans/40:60 (technical active substance) : Validation of methods of analysis for the manufacturing impurities <confidential> Covance Laboratories Ltd, report N° 0040/057-D2149 Chimac-Agriphar S.A., document no. KII A, 1.11/03 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.2.	1980	Acute oral LD5 in the rat of CGA 55186 technical. [redacted] Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.9.1, 3.12	2011	Oral (Gavage) Study of Developmental Neurotoxicity in the Rat	Yes	
Batiste-Alentorn M., Xamena N., Velázquez A., Creus A., Marcos R	IIA, 3.6.2	1986	Mutagenicity testing of the pyrethroid insecticide cypermethrin in Drosophila. Mutagenesis 1: 343-346.	No	
[redacted]	IIA, 4.2.1 (IIIA,7.4.1.4)	2002	Cypermethrin – Determination of inhibition of respiration of activated sludge Covance Laboratories Ltd., report no. 40/46 (CYP/T323) Chimac-Agriphar S.A., document no. KII A, 8.7/01 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.6.2	1988	Genotoxic effects of a synthetic pyrethroid insecticide, cypermethrin, in mice in vivo. [redacted]	No	
Bradberry S.M., AGe S.A., Proudfoot A.T., Vale J.A	IIA, 3.11	2005	Poisoning due to pyrethroids. Toixol; Rev. 24: 93-106.	No	
[redacted]	IIA, 3.2 (IIIA, 6.1.3) IIC, 1.2.1	1985	Acute Aerosol Inhalation Toxicity in the Rat of CGA 55186 Tech. (cypermethrin). [redacted] Chimac-Agriphar S.A., document no. KII A, 5.2/01 Non-GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.1.1.2 (IIIA,7.1.2.2. 2)	2005a	[^{14}C]-Cypermethrin cis:trans 40:60: Degradation and retention in water-sediment systems. Covance Laboratories Ltd, Report No. 1669/014-D2149 GLP, unpublished	Yes (Exist./First)	Arysta

Author(s)	Section no. / Reference no.	Year	Title Source (where different from company) Report no. GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N	Owner
[redacted]	(IIA, 4.1.1.3.1 (IIIA,7.1.3, 7.2.3.1)	2005b	[14C]-Cypermethrin cis:trans 40:60: Adsorption/Desorption in soil Covance Laboratories Ltd., report no. 1669/015-D2149 GLP, unpublished.	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.1.3 (IIIA,7.2.2.1)	2006c	[^{14}C]-Cypermethrin cis:trans 40:60: Aerobic soil degradation and metabolism Covance Laboratories Ltd., report no. 1669/012-D2149 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.5.2 IIC, 1.2.1	1977	A 13 week feeding study of WL 43467 (cypermethrin) in dogs. [redacted] Chimac-Agriphar S.A. , doc. No. KII A, 5.3.2.2/01.	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.4 (IIIA,6.4.1 (02))	1977	A 13 week feeding study of WL 43467 (cypermethrin) in dogs [redacted] Chimac-Agriphar S.A., document no. KII A, 5..3.2.2/01 Not GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.1.1.2 (IIIA, 7.1.1.2.2)	2005	Cypermethrin cis:trans/40:60: Assessment of Inherent Biodegradability by measurement of CO_2 evolution Covance Laboratories Ltd., report no. 1699/017-D2149 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIC, 2	2006a	[^{14}C]-Cypermethrin cis:trans 40:60: Degradation and retention in water-sediment systems. Covance Laboratories Ltd, Report No. 1669/014-D2149 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIC, 2	2006b	[14C]-Cypermethrin cis:trans 40:60: Adsorption/Desorption in soil Covance Laboratories Ltd., report no. 1669/015-D2149 GLP, unpublished.	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.1.3 (IIIA,7.2.2.1)	2006c	[^{14}C]-Cypermethrin cis:trans 40:60: Aerobic soil degradation and metabolism Covance Laboratories Ltd., report no. 1669/012-D2149 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.2. IIC, 1.2.1	1993	Acute toxicity of two pyrethroids, permethrin, and cypermethrin in neonatal and adult rats. [redacted]	No	

Author(s)	**Section no. / Reference no.**	**Year**	**Title** **Source (where different from company)** **Report no.** **GLP or GEP status (where relevant)** **Published or not**	**Data Protection Claimed Y/N**	**Owner**
Cantalamessa F., Barili P., Vavagna R., Sabbatini M., Tenore G., Amenta F.	IIA, 3.8.1	1998	Influence of neonatal treatment with the pyrethroid insecticide cypermethrin on the development of dopamine receptors in the rat kidney. Mechanisms of Aging and Development 103: 165-178.	No	
[redacted]	IIA, 3.6.2	1997	*In vivo* induction of sister chromatid exchange in mouse bone marrow following oral exposure to commercial formulations of alpha-cyano pyrethroids. [redacted]	No	
[redacted]	IIA, 3.6.2	2005	*In vivo* cytogenic effects of a commercially formulated mixture of cypermethrin and quinalphos in mice. [redacted].	No	
Chen H., Xiao J., Hu G., Zhou J., Xiao H., Wang X.	IIA, 3.10.2	2002	Estrogenicity of organophosphorus and pyrethroid pesticides. Journal of Toxicology and Environmental Health, part A 65: 1419-1435.	No	
Chen , S., Zhang, S., He, F., Yao, P., Wu, Y., Sun, J., Liu, L., Li, Q.	IIA, 3.9 (IIIA,6.12.4) , 3.11	1991	An epidemiological study on occupational acute pyrethroid poisoning in cotton farmers; British Journal of Industrial Medicine, **48**: 77-81. (CYP/T164) (published) Chimac-Agriphar S.A., document no. KII A, 5.9.3/01 Not GLP, published	No	-
Choi J.-S., Soderlund D.M.	IIA, 3.9.2	2006	Structure-activity relationships for the action of 11 pyrethroid insecticdes on rat $Na_v1.8$ sodium channels expressed in *Xenopus* oocytes. Toxicology and Applied Pharmacology 211: 233-244.	No	
[redacted]	IIA, 3.9.1, 3.12	2010	Oral (gavage), screening study of reproduction/development toxicity in the rat	Yes	
[redacted]	IIB, 2.3 IIIB, 5.10 (01)	1992	Pynosect PCO and Cyperkill 10 – persistence of activity on plywood and tiles against flies and cockroaches. [redacted] GLP not applicable, unpublished.	Yes (New/First)	CAG
Çömelekoğlu Ü., Özge A., Coşkun B.	IIA, 3.9.2	2002	Mode of acute action of cypermethrin on peripheral nerves. Sort communication. J. Appl. Toxicol. 22: 445-447.	No	
Condés-Lara M., Graff-Guerrero A., Vega-Riveroll L.	IIA, 3.9.1	1999	Effects of cypermethrin on the electroencephalographic activity of the rat: a model of chemically induced seizures. Neurotoxicology and Teratology 21: 293-298.	No	

Author(s)	**Section no. / Reference no.**	**Year**	**Title** **Source (where different from company)** **Report no.** **GLP or GEP status (where relevant)** **Published or not**	**Data Protection Claimed Y/N**	**Owner**
[redacted]	IIA, 3.4.1, 3.5.1.	1976	Toxicity studies on the insecticide WL 43467: Summary of results of preliminary experiments. Shell Toxicology Laboratories (Tunstall). Study reference no. TLGR.0104.76 (CYP/T2).	Yes (Exist./First)	Arysta
[redacted]	IIA, 3, 3.1.1	1981	Metabolism of *cis*- and *trans*-cypermethrin in rats. Balance and tissue retention study. [redacted]	No	
Cui Y., Guo J., Xu B., Chen Z.	IIA, 3.6.1	2006	Potential of chlorpyrifos and cypermethrin forming DNA adducts. Mutat. Res. 604: 36-41.	No	
Das R.N., Parajuli S.	IIA, 3.11	2006	Cypermethrin poisoning and anti-cholinergic medication – a case report. Internet Journal of medical Update 1: http:/www. Geocities.com/agnihotrimed/paper06_jul-dec2006.htm	No	
[redacted]	IIA, 3.1	2009	In vivo percutaneous absorption of an EC formulation of [^{14}C] Cypermethrin in rats. [redacted] (GLP, unpublished	Yes (New/first)	Arysta
[redacted]	IIA,1.4.2, IIB, 1.4 (IIIB,4.1)	2005	Validation of an analytical HPLC method for the determination of active substance content in a formulation micro emulsion (ME) containing cypermethrin, Agricultural Research Centre (CRA-W), Gembloux, Belgium; study no. CHIMAC/FO 20830/Ch.3128/2004/109 Chimac-Agriphar SA, document no. KIII A, 5.1.1/01 GLP, unpublished	Yes (New/First)	Arysta
[redacted].	IIB, 5 (IIIB,3.1→3. 10)	2005	Physical and chemical properties and storage stability tests for Cypermethrin 10 ME Agricultural Research Centre (CRA-W), Gembloux, Belgium, report no. Chimac-Agriphar/FO20831/Ch.3128/2004/110 Chimac-Agriphar SA, document no. KIII A, 2.1/01 GLP, unpublished	Yes (New/First)	Arysta
Dési I., varga L., Dobronyi I., Szklenarik G	IIA, 3.10.1	1985	Immunotoxicological investigation of the effects of a pesticide; cypermethrin. Arch. Toxicol., Suppl. 8: 308-309.	No	

Author(s)	**Section no. / Reference no.**	**Year**	**Title** **Source (where different from company)** **Report no.** **GLP or GEP status (where relevant)** **Published or not**	**Data Protection Claimed Y/N**	**Owner**
[redacted]	IIA, 4.2.1 (IIIA,7.4.3.4)	1990	21-Days reproduction test with compound cypermethrin technical in Daphnia magna Pharmatox Beratung und Forschung GmbH, report no. E.H./B.2-7-44-90 (CYP/T143) Chimac-Agriphar S.A., document no. KII A, 8.2.5/01 GLP, unpublished	Yes (Exist./First)	Arysta
Eadsforth C.V. and Baldwin M.K.	IIA, 3.1.1	1983	Human dose-excretion studies with the pyrethroid insecticide, cypermethrin. Xenobiotica 13: 67-72.	No	
ECB	IIC, 1.2.2	2002	Technical Notes of Guidance in support of Directive 98/8/EC of the European parliament and the council concerning the placing of biocidal products on the market, Guidance on exposure estimation, part 3. Final draft.		
ECB	IIC, 1.2.2	2002a	Technical Notes for Guidance: Human exposure to biocidal products – guidance on exposure estimation. Report 2002. http://ecb.jrc.it/biocides		
ECB	IIC, 1.3	2002b	Technical Notes of Guidance in support of Directive 98/8/EC of the European parliament and the council concerning the placing of biocidal products on the market, Guidance on exposure estimation. Final draft.		
ECB	IIC, 1.2.2	2005	Technical Guidance Documents in support of Directive 93/87/EEC on risk assessment for new notified substances and the commission regulation (EC) 1488/94 on risk assessment for existing substances, part 1, chapter 4, human risk characterization, revision document TGD_H_RC_dr_ECB_01.doc.		
EC	IIC, 1.2.2	2006	Guidance for the setting and application of Acceptable Operator Exposure Levels (AOELs). Draft rev. 10, July 7, 2006.	No	
[redacted]	IIA, 3.8.2, 3.10.2	2001	Evaluation of the toxic potentials of cypermethrin pesticide on some reproductive and fertility parameters in the male rats. [redacted]	No	

Author(s)	**Section no. / Reference no.**	**Year**	**Title** **Source (where different from company)** **Report no.** **GLP or GEP status (where relevant)** **Published or not**	**Data Protection Claimed Y/N**	**Owner**
[redacted]	IIA, 3.8.2	2003	Protective effects of isoflavone on some biochemical parameters affected by cypermethrin in male rabbits. [redacted]	No	
[redacted]	IIA, 3.5.1	1993	*In vivo* and *in vitro* studies on the effect of larvin and cypermethrin on adenosine triphosphatase activity of male rats. [redacted]	No	
[redacted]	IIA, 3.8.2	2007	Effects of oral exposure of synthetic pyrethroid, cypermethrin on the behavior of F1-progeny in mice. [redacted]	No	
[redacted]	IIA, 3.6.1	2011	Cypermethrin Technical – L5178Y TK +/- mouse lymphoma assay; Harlan Laboratories Ltd., report no. 41004533, 23 March 2011 (unpublished)	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.2.3 (IIIA,7.5.3.1. 3)	2003	Cypermethrin: Reproduction study with the northern bobwhite quail [redacted] Chimac-Agriphar S.A., document no. KII A, 8.1.3/02 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.6.2	2004	Lymphocyte DNA damage in rats exposed to pyrethroids: effect of supplementation with Vitamins E and C. [redacted]	No	
[redacted]	IIA, 4.2.3 (IIIA,7.5.3.1. 1)	2002	Cypermethrin: A dietary LC50 study with the Northern bobwhite quail [redacted] Chimac-Agriphar S.A., document no. KII A, 8.2.1/01 GLP, unpublished	Yes (Exist./First)	Arysta
Giray B., Gürbay A., Hincal F.	IIA, 3.5.1	2001	Cypermethrin-induced oxidative stress in rat brain and liver is prevented by Vitamin E or allopurinol. Toxicology Letters 118: 139-146.	No	
Giri S., Giri A., Sharma G.D., Prasad S.B.	IIA, 3.6.2	2003	Induction of sister chromatid exchanges by cypermethrin and carbosulfan in bone marrow cells of mice *in vivo*. Mutagenesis 18: 53-58.	No	

Author(s)	Section no. / Reference no.	Year	Title Source (where different from company) Report no. GLP or GEP status (where relevant) Published or not	Data Protection Claimed Y/N	Owner
[redacted].	IIA, 4.1.1.1 (IIIA,7.1.1.1. 2 (02), 7.3.1)	2003	Cypermethrin cis:trans/40:60 (purified active substance): Quantum yield analysis Covance Laboratories Ltd, study number 0040/034 (CYP/M70) Chimac-Agriphar S.A., document no. KII A, 2.9.3/01 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 1.3 (IIIA,3.4)	2004	Cypermethrin *cis:trans* 40:60 (purified active substance) : Evaluation of the spectroscopic properties Covance Laboratories Ltd, report no.: 0040/056-D2149 Chimac-Agriphar S.A., document no. KIIA, 2.5.1.1/01 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIB, 4.2.1 IIB, 3.6 (IIIB, 6.1.3)	2005.	Cypermethrin 250 g/L EC: acute inhalation toxicity (nose only) study in the rat. [redacted] Chimac-Agriphar SA, document no. KIII A, 7.1.3/01.GLP, unpublished.	Yes (New/First)	Arysta
[redacted]	IIA, 3.7	1992	Analysis of carcinogenic activity of some pesticides in a medium-term liver bioassay in the rat. [redacted]	No	
[redacted]	IIA, 3.1.3 IIB, 4.1	2006.	[^{14}C]-Cypermethrin cis:trans 40:60 – Rates of penetration through human skin using a static cell in-vitro system. Covance Laboratories Lt., Study no. 1669/028. GLP, unpublished.	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.1.2 (IIIA,6.2 (02)) IIB, 3.2.1.6 IIC, 1	2006	[^{14}C]-Cypermethrin cis:trans 40:60 – Rates of penetration through human skin using a static cell *in-vitro* system; Covance Laboratories Ltd, Study no. 1669/028 GLP, unpublished	Yes (Exist./First)	Arysta
He F., Sun J., Han K., Wu Y., Yao P., Wang S., Liu L.	IIA, 3.3.3, 3.11	1988	Effects of pyrethroid insecticides on subjects engaged in packaging pyrethroids. British Journal of Industrial Medicine 45: 548-551.	No	
He F., Wang S., Liu L., Chen S., Zhang Z., Sun J.	IIA, 3.11	1989	Clinical manifestations and diagnosis of acute pyrethroid poisoning. Archives of Toxicology 63: 54-58.	No	
Hemming H., Flodström S., Wärngård L	IIA, 3.7	1993	Enhancement of altered hepatic foci in rat liver and inhibition of intercellular communication *in vitro* by the pyrethroid insecticides fenvalerate, flucythrinate and cypermethrin. Carcinogenesis 14: 2531-2535.	No	

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[redacted]	IIA, 3.4 (IIIA,6.4.1 (01)) IIC, 1.2.1	1976	Toxicity studies on the insecticide WL 43467 (cypermethrin): three month feeding study in rats [redacted] Chimac-Agriphar S.A., document no. KII A, 5..3.2.1/01 Not-GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.5.2, 3.7.2 (IIIA,6.8.2) IIC, 1.2.1.	1978	Toxicity studies on the insecticide WL 43467(cypermethrin): A 3 generation reproduction study in rats [redacted] Chimac-Agriphar S.A., document no. KII A, 5.6.1/01 Not GLP, unpublished	Yes (Exist./First)	Arysta
Henderson C., Parkinson G.	IIA, 3.5.1	1981	Subacute dermal toxicity study in rabbits with technical cypermethrin. [redacted] In 91/414 DAR for Cypermethrin, Annex B, prepared by the BE CA.	No	
[redacted]	IIA, 3.1.1	1981	Metabolism of the *cis*- and *trans*-isomers of cypermethrin in mice. [redacted]	No	
[redacted]	IIA, 3.10.1	1999	Comparison of detection sensitivity of immuno- and genotoxicological effects of subacute cypermethrin and permethrin exposure in rats. [redacted]	No	
Inglesfield, C.	IIA, 4.2.3 (IIIA,7.5.1.2 (01)) IIC, 2	1984	Toxicity of the pyrethroid insecticides cypermethrin and WF 85871 to the earthworm, *Eisenia foetida* Savigny Bull. Environ. Contam. Toxicol. (1984) 33:568-570 (CYP/T61) Not GLP, published	No	-
Kakko I., Toimela T., Tähti H.	IIA, 3.9.2	2003	The synaptosomal membrane bound ATPase as a target for the neurotoxic effects of pyrethroids, permethrin and cypermethrin. Chemosphere 51: 475-480.	No	
Kakko I., Toimela T., Tähti H.	IIA, 3.10.2	2004	Oestradiol potentiates in the effects of certain pyrethroid compounds in the MCF7 human breast carcinoma cell line. ATLA 32: 383-390.	No	
Kim I.Y., Shin J.H., Kim H.S., Lee S.J., Kang I.H., Kim T.S., Moon H.J., Choi K.S., Moon A., Han S.Y	IIA, 3.10.2	2004	Assessing estrogenic activity of pyrethroid insecticides using *in vitro* combination assays. Journal of Reproduction and development 50: 245-255.	No	

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[redacted]	IIA, 4.1.1.2 (IIIA, 7.1.1.2.1)	1990	Biodegradation – The modified sturm test Fraunhofer Institute für Umweltchemie und Ökotoxicologie, report no. FEI-001/3-11 (CYP/M50) Chimac-Agriphar S.A., document no. KII A, 7.2.1.3.1/01 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.2.1 (IIIA,7.4.3.2)	2005	Cypermethrin cis:trans/40:60 Fathead Minnow, early Life Stage test [redacted] GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.2.1 (IIIA,7.4.3.2)	2012	Fish early life stage test (*Pimephales promelas*) with cypermethrin [redacted] GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.2 (IIIA, 6.1.1) IIC, 1.2.1	1984a	Acute Oral LD50 in the Rat of CGA 55186 Tech. (cypermethrin) – (administration in oily medium). [redacted] Chimac-Agriphar S.A., document no. KII A, 5.2/01 Non-GLP, unpublished.	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.2 (IIIA, 6.1.2) IIC, 1.2.1	1984b	Acute Dermal LD50 in the Rat of CGA 55186 Tech. (cypermethrin); [redacted] Chimac-Agriphar S.A., document no. KII A, 5.2/01 Non-GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]		1984c	Acute Oral LD50 in the rat of CGA 55186 tech. (cypermethrin) – administration in aqueous medium. [redacted] Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.2.	1984d	Acute Dermal LD50 in the rat of CGA 55186 tech. (cypermethrin) – administration in oily medium. [redacted] Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	Arysta
Kumar S., Gautam A.K., Agarwal K.R., Shah B.A., Saiyad H.N. (	IIA, 3.6.1, 3.6.2	2004	Demonstration of sperm head shape abnormality and clastogenic potential of cypermethrin. J. Environ. Biol. 25: 187-190.	No	

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Laville N., Balaguer P., Brion F., Hinfray N., Casellas C., Porcher J.-M., Aït-Aïssa S	IIA, 3.10.2	2006	Modulation of aromatase activity and mRNA by various selected pesticides in the human choriocarcinoma JEG-3 cell line. Toxicology 228: 98-108.	No	
[redacted]	IIA, 3.9 (IIIA,6.12.1)	1980	Transient Facial Sensory Symptoms following Exposure to Synthetic Pyrethroids: A Clinical and Electro-physiological Assessment; [redacted] Chimac-Agriphar S.A., document no. KII A, 5.9.1/01 Not GLP, published	No	-
Lessenger J.E.	IIA, 3.3.3, 3.11	1992	Five office workers inadvertently exposed to cypermethrin. Journal of Toxicology and Environmental Health 35: 261-267.	No	
[redacted]	IIA, 3.10.2, 3.11	1980	Transient facial sensory symptoms following exposure to synthetic pyrethroids: a clinical and electro-physiological assessment. Neurotoxicology 2: 1-11. (CYP/T38) Chimac-Agriphar S.A. , doc. No. KII A, 5.9.1./01.	No	
Lisi P.	IIA, 3.4.2, 3.11	1992	Sensitization risk of pyrethroid insecticides. Contact Dermatitis 26: 349-350.	No	
[redacted]	IIA, 4.2.1 (IIIA,7.4.1.1)	2006a	Cypermethrin cis:trans/40:60: Acute toxicity to *Oncorhynchus mykiss*; [redacted] GLP, unpublished	Yes (Exist./First)	Arysta
[redacted].	IIA, 4.2.1 (IIIA,7.4.1.2)	2006b	Cypermethrin cis:trans 40:60: Acute toxicity to Daphnia magna. Covance Laboratories Ltd., Report no. 1669/019-D2149 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.2.1 (IIIA,7.4.1.3)	2006c	Cypermethrin cis:trans/40:60: Inhibition of growth to the alga Pseudokirchneriella subcapitata Covance Laboratories Ltd, study no. 1669/020 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.4 IIA, 3.6 (IIIA,6.5,6.7) IIC, 1.2.1	1978	Toxicity studies on the insecticide WL 43467 (cypermethrin): A 2 year feeding study in rats [redacted] Chimac-Agriphar S.A., document no. KII A, 5.5.1/01 Not GLP, unpublished	Yes (Exist./First)	Arysta

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McDaniel, K.L., Moser V.C.	IIA, 3.8 (IIIA,6.9 (02)) IIC, 1.2.1	1993	Utility of a neurobehavioral screening battery for differentiating the effect of two pyrethroids, Permethrin and cypermethrin. Neurotoxicology and Teratology 15: 71-83 Not GLP, published	No	-
McKillop C.M., Brock J.A.C., Oliver G.J.A., Rhodes C.	IIA, 3.2	1987	A quantitative assessment of pyrethroid-induced paraesthesia in the guinea-pig flank model. Toxicology Letters 36: 1-7.	No	
[redacted]	IIA, 3.6.2	2008	Genotoxicity evaluation of Cypermethrin technical by in vivo mouse micronucleus assay. IIBAT – [redacted] Report number 0805303 (unpublished)	Yes (Exist/first)	Arysta
Mukhopadhyay I., Chowdhuri D.K., Bajpayee M., Dhawan A.	IIA, 3.6.2	2004	Evaluation of *in vivo* genotoxicity of cypermethrin in *Drosophila melanogaster* using the alkaline Comet assay. Mutagenesis 19: 85-90.	No	
Nasuti C., Gabbianelli R., Falcioni M.L., Di Stefano A., Sozio P., Cantalamessa F.	IIA, 3.8.1	2007	Dopaminergic system modulation, behavioral changes, and oxidative stress after neonatal administration of pyrethroids. Toxicology 229: 194-205.	No	
[redacted]	IIA, 3.1.1 (IIIA,6.2 (01)), 3.1.4 IIC, 1	2006	[^{14}C]-Cypermethrin-cis:trans 40:60:- Absorption, Distribution and Excretion in the Rat [redacted] GLP, unpublished	Yes (Exist./First)	Arysta
Nehéz M., Lorencz R., Dési I	IIA, 3.6.2	2000	Simultaneous action of cypermethrin and two environmental pollutant metals, cadmium and lead, on bone marrow cell chromosomes of rats in subchronic administration. Ecotoxicol. Environ. Saf. 45: 55-60.	No	
Nishi K., Huang H., Kamita S.G., Kim I.-H., Morisseau C., Hammock B.D.	IIA, 3.1.2	2006	Characterization of pyrethroid hydrolysis by the human liver carboxylesterases hCE-1 and hCE-2. Archives of biochemistry and Biophysics 445: 115-123.	No	

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[redacted]	IIA, 3.5.1, 3.6.2, (IIIA,6.6.1)	1999a	Testing of Cypermethrin cis:trans/40:60 test substance with bacterial reverse mutation assay Toxicology Research Centre Ltd, report no. 98/398-007M (CYP/T310) Chimac-Agriphar S.A., document no. KII A, 5.4.1.1/02 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.5.2 (IIIA, 6.6.4)	1999b	Mouse bone marrow micronucleus test of test substance Cypermethrin cis:trans/40:60 Toxicology Research Centre Ltd, report no. 98/398-013M (CYP/T309) Chimac-Agriphar S.A., document no. KII A, 5.4.2.1/02 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.5.1 (IIIA,6.6.2), 3.6.1	2002	In vitro mammalian chromosomal aberration study of Cypermethrin cis:trans/40:60 Toxicology Research Centre Ltd, report no. 01/569-020C (CYP/T320) Chimac-Agriphar S.A., document no. KII A, 5.4.1.2/01 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted].	IIA, 3.8 (IIIA,6.9 (01)) 3.9.1	1977	Toxicity of Pyrethroid Insecticides: Investigation of the Nerotoxic Potential of WL 43467 (cypermethrin) to Adult Domestic Hens [redacted] Chimac-Agriphar S.A., document no. KII A, 5.7/01 Not GLP, unpublished	Yes (Exist./First)	Arysta
Patel S., Pandey A.K., Bajpayee M., Parmar D., Dhawan A.	IIA, 3.6.2	2006	Cypermethrin-induced DNA damage in organs and tissues of the mouse: evidence from the comet assay. Mutat. Res. 607: 176-183.	No	
Pluijmen M., Drevon C., Montesano R., Malaveille C., hautefeuille A., Bartsch H	IIA, 3.6.1	1984	Lack of mutagenicity of synthetic pyrethroids in *Salmonella typhimurium* strains and in V79 Chinese hamster cells. Mutat. Res. 137: 7-15	No	
Pore M.P.	IIA, 3.4.1	1993	Skin sensitisation test in guinea-pigs with cypermethrin; [redacted] In 91/414 DAR for Cypermethrin, Annex B, prepared by the BE CA.	No	

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Puig M., Carbonell E., Xamena N., Creus A., Marcos R.	IIA, 3.6.1	1989	Analysis of cytogenetic damage induced in cultured human lymphocytes by the pyrethoid insecticides cypermethrin and fenvalerate. Mutagenesis 4: 72-74.	No	
[redacted]	IIA, 3.2	2005	Acute oral toxicity study (acute toxic class method) with cypermethrin in Wistar rats; [redacted] (unpublished).	Yes (Exist./First)	Arysta
Read S.J., Berry, R.W.	IIA, 2.3.1 (IIIA, 5.2/04)	1984	An evaluation of the synthetic pyrethroid cypermethrin in organic solvent and emulsion formulations. The International Research Group on Wood Preservation (working group III), paper prepared for the fifteenth annual meeting, Sweden, May 28 – June 1 1984. Building Research Establishment, UK, report no. IRG/WP/3290 GLP not applicable, published.	No	-
[redacted]	IIA, 3.1.1	1984	The bioaccumulation and biotransformation of *cis, trans*-cypermethrin in the rat. [redacted]	No	
[redacted]	IIA, 3.3, 3.4.1 (IIIA,6.1.5)	2006	Cypermethrin cis:trans/40:60: local lymph node assay in the mouse (individual method) [redacted] GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.2 IIC, 1.2.1	1983	Acute oral toxicity of WL85871 in comparison with WL43467. [redacted]	No	
[redacted]	IIA, 3.9.2	1983	Intoxication with four synthetic pyrethroids fails to show any correlation between neuromuscular dysfunction and neurobiochemical abnormalities in rats. [redacted]	No	
Saito K., Tomigahara Y., Ohe N., Isobe N., Nakatsuka I., Kaneko H.	IIA, 3.10.2	2000	Lack of significant estrogenic or antiestrogenic activity of pyrethroid insecticides in three *in vitro* assays based on classic estrogen receptor α-mediated mechanisms. Toxicological Sciences 57: 54-60	No	

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[redacted]	IIA, 3.8.1	1997	Prenatal exposure to cypermethrin modulates rat NK cell cytotoxic functions. [redacted].	No	
[redacted]	IIA, 3.8.1	1998	Cypermethrin-induced alternation of thymocyte distribution and functions on prenatally-exposed rats. [redacted]	No	
[redacted]	IIA, 3.8.1	1998	Alterations of T cell distribution and functions in prenatally cypermethrin-exposed rats: possible involvement of catacholamines. [redacted]	No	
[redacted]	IIA, 3.2	1980	Acute oral LD50 in the mouse of technical CGA 55186. [redacted] Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.1.1.1 (IIIA,7.1.1.1. 1)	1997	Hydrolysis in water at 3 pH values Dr Krebs Analytik GmbH, report no. PR97/003 (CYP/C52) Chimac-Agriphar S.A., document no. KII A, 2.9.1/01 GLP, unpublished.	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.3.3	1984a	Acute dermal irritation/corrosion study in the rabbit of CGA 55186 technical. [redacted] Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.3.2, 3.3.3	1984b	Acute eye irritation/corrosion study in the rabbit of CGA 55186 technical. [redacted] Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	Arysta
[redacted]	IIB, 2.3 IIIB, 5.10 (02)	2006	Simulated use bioassay to determine the efficacy of formulations against German cockroaches – Interim report. [redacted] GLP not applicable (GEP accredited laboratory), unpublished.	Yes (New/First)	Arysta
[redacted]	IIB,2.3 ; IIIB5.10 (03)	2006	Simulated use bioassay to determine the efficacy of formulations against cat fleas (Ctenocephalides felis); [redacted], December 2006 (unpublished).	Yes (New/First)	Arysta

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[redacted]	IIB,2.3 ; IIIB5.10 (04)	2006	Simulated use bioassay to determine the efficacy of formulations against ants (Lasius niger); [redacted], December 2006 (unpublished).	Yes (New/First)	Arysta
[redacted]	IIA, 4.2.3 (IIIA,7.5.1.1) IIC, 2	2005	Laboratory assessment of the side-effects of cypermethrin, technical grade, on the mineralization of nitrogen Phytosafe s.a.r.l., Report no. 04-99-058-ES GLP, unpublished	Yes (Exist./First)	Arysta
Shono T., Ohsawa K., Casada J.E.	IIA, 3.1.1	1979	Metabolism of *trans*- and *cis*-cypermethrin, and decamethrin by microsomal enzymes. J. Agric. Food Chem. 27: 316-325.	No	
[redacted]	IIA, 3.6.2	2002	Mutagenic potential of cypermethrin in mouse dominant lethal assay. [redacted]	No	
[redacted]	IIA, 3.7	2002	Carcinogenic and cocarcinogenic potential of cypermethrin on mouse skin. [redacted]	No	
[redacted]	IIA, 3.2.1 (IIIA,6.1.4 (02))	1984b	Acute Dermal Irritation / Corrosion Study in the Rabbit of CGA 55186 Tech. (cypermethrin) [redacted] Chimac-Agriphar S.A., document no. KII A, 5.2/01 Non-GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.2.2 (IIIA,6.1.4 (01))	1984a	Acute Eye Irritation / Corrosion Study in the Rabbit of CGA 55186 Tech. (cypermethrin) [redacted] Chimac-Agriphar S.A., document no. KII A, 5.2/01 Non-GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.2.6.2	2011	Earthworm reproduction test with Cypermethrin; Phytosafe s.a.r.l., France, report no. 11-99-064-ES, 30th November 2011 (unpublished).	Yes (Exist./First)	Arysta
Sonawane, K.K.		2007	Analysis and certification of limits for cypermethrin technical. [redacted] report NO. SP 0701 FB 059, GLP, Unpublished	Yes (Exist./First)	Arysta
Stok J.E., Huang H., Jones P.D., Wheelock C.E., Morisseau C., Hammock B.D.		2004	Identification, expression, and purification of a pyrethroidhydrolyzing carboxylesterase from mouse liver microsomes. J. Biol. Chem. 279: 29863-29869	No	

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Suman G., Naravaneni R., Jamil K.	IIA, 3.6.1	2006	In vitro cytogenetic studies of cypermethrin on human lymphocytes. Indian J. Exp. Biol. 44: 233-239.	No	
Sumida K., Saito K., Ooe N., Isobe N., Kaneko H., Nakatsuka I.	IIA, 3.10.2	2001	Evaluation of *in vit*ro methods for detecting the effects of various chemicals on the human progesterone receptor, with a focus on pyrethroid insecticides. Toxicology Letters 118: 147-155.	No	
Sun H., Xu X.-L., Xu L.-C., Song L., Hong X., Chen J.-F., Cui L.-B., Wang X.-R.	IIA, 3.10.2	2007	Antiandrogenic activity of pyrethroid pesticides and their metabolite in reporter gene assay. Chemosphere 66: 474-479	No	
Surrallés J., Xamena N., Creus A., Catalùan J., Norppa H., Marcos R.	IIA, 3.6.1	1995	Induction of micronuclei by five pyrethroid insecticides in whole-blood and isolated human lymphocyte cultures. Mutat. Res. 341: 169-184.	No	
[redacted]	IIA, 4.1.1.1 (IIIA,7.1.1.1.2 (01))	2003a	^{14}C-Cypermethrin : Photodegradation in sterile, aqueous solution Covance Laboratories Ltd., Report N° 40/35 (CYP/M70) Chimac-Agriphar S.A., document no. KII A, 2.9.2/01 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 4.1.1.1 (IIIA,7.2.2.4 (01))	2003b	(^{14}C)-cypermethrin: Photodegradation on a soil surface Covance Laboratories Ltd., Report N° 40/44-D2149 (CYP/M71) Chimac-Agriphar S.A., document no. KII A, 7.1.1.1.2/01 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 1.3 (IIIA,3.10)	2005b	Cypermethrin (technical) physicochemical properties Huntingdon Life Sciences Ltd, report no. CAV002/052564 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 1.3 (IIIA,3.2)	2005a	Cypermethrin (pure) physicochemical properties Huntingdon Life Sciences Ltd, report no. CAV001/052563 GLP, unpublished	Yes (Exist./First)	Arysta

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[redacted]	IIA, 4.1.2 (IIIA,7.4.3.3. 1) IIC, 2	1990	Draft report on flow-through test in rainbow trout to determine the bioaccumulation potential of cypermethrin [redacted] Chimac-Agriphar S.A., document no. KII A, 8.2.3/01 Not GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.10.1	1988	*In vivo* immunosuppression by synthetic pyrethroid (cypermethrin) pesticide in mice and goats. [redacted]	No	
[redacted]	IIA, 3.7.1 (IIIA,6.8.1 (01)) IIC, 1	1978	WL 43467 (Cypermethrin) – Effects upon the progress and outcome of pregnancy in the rat [redacted] Chimac-Agriphar S.A., document no. KII A, 5.6.2.1/01 Not GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.7.1 (IIIA,6.8.1 (02)), 3.8.1 IIC, 1	1984	WL 43467 (Cypermethrin) – Effects upon the progress and outcome of pregnancy in the rabbit [redacted] Chimac-Agriphar S.A., document no. KII A, 5.6.2.2/01 Not GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 3.8.1 IIB, 3.5 (IIIB, 6.1.2) IIB, 4.2.1	1990.	Cyperkill 10 (low cis): acute dermal toxicity test (limit test) in the rat. [redacted] Chimac-Agriphar SA, document no. KIII A, 7.1.2/01. GLP, unpublished.	Yes (New/First)	Arysta
[redacted]		1980	Acute oral LD50 in the rabbit of technical CGA 55186. [redacted] Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	Arysta
Undeğer U., Başaran N.	IIA, 3.6.1	2005	Effects of pesticides on human peripheral lymphocytes *in vitro*: induction of DNA damage. Arch. Toxicol. 79: 169-176.	No	
[redacted]	IIB, 4.2.1 IIB, 3.4, 3.6 (IIIB, 6.1.1)	2005a.	Assessment of acute oral toxicity with cypermethrin 10 g/L ME in the rat (acute toxic class method). [redacted] Chimac-Agriphar SA, document no. KIII A, 7.1.1/01. GLP, unpublished.	Yes (New/First)	Arysta

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[redacted]	IIB, 3.7 (IIIA, 6.2 (01)) IIB, 4.3.1.1	2005b	,. Primary skin irritation/corrosion study with Cypermethrin 10 g/L ME in the rabbit (4-hour semi-occlusive application). [redacted] Chimac-Agriphar SA, document no. KIII A, 7.1.4/01. GLP, unpublished	Yes (New/First)	Arysta
[redacted]	IIB, 3.7 (IIIB,6.2(02)) IIB, 4.3.1.2	2005c.	Acute eye irritation/corrosion study with Cypermethrin 10 g/L ME in the rabbit. [redacted] Chimac-Agriphar SA, document no. KIII A, 7.1.5/01. GLP, unpublished.	Yes (New/First)	Arysta
[redacted]	IIB, 4.4.1 IIB, 3.8 (IIIB, 6.3)	2005d.	Assessment of contact hypersensitivity to Cypermethrin 10 g/L ME in the mouse (Local Lymph Node Assay). [redacted] Chimac-Agriphar SA, document no. KIII A, 7.1.6/01. GLP, unpublished.	Yes (New/First)	Arysta
[redacted]	IIA, 3.5.2, 3.10.1	1992	Immunotoxic responses of cypermethrin, a synthetic pyrethroid insecticide in rats. Short communication. [redacted]	No	
Vijverberg H.P.M., van den Bercken J.	IIA, 3.9.2, 3.11	1990	Neurotoxicological effects and the mode of action of pyrethroid insecticides. Critical Reviews in Toxicology 21: 105-126.	No	
Wagner S.L.	IIA, 3.4.2, 3.11	1994	Allergy from pyrethrin or pyrethroid insecticides. Journal of Agromedicine 1: 39-45.	No	
Wegner R., Sauer C., Lemke M.	IIB, 3.3.2.1	2007a	OECD Guideline I "estimation of emission from preservative treated wood to the environment: laboratory method for wood held in storage after treatment and for wood commodities that are not covered and are not in contact with ground (proposal, version 17.02.2003)- Vacuum pressure treatment. PA Eberswalde, Germany ; report n° 31/05/7632/01, 7th February 2007 (unpublished)	Y	Arysta
Wegner R., Sauer C., Lemke M.	IIB, 3.3.2.2	2007b	OECD Guideline I "estimation of emission from preservative treated wood to the environment: laboratory method for wood held in storage after treatment abd for wood commodities that are not covered and are not in contact with ground (proposal, version 17.02.2003)-Superficial treatment (brushing). PA Eberswalde, Germany ; report n° 31/05/7631/01, 7th February 2007 (unpublished)	Y	Arysta

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Weiping Liu, Jay J Gan, Sangjin Lee Ingeborg Werner	IIA, 4	2004	Isomer selectivity in aquatic toxicity and biodegradation of cypermethrin.	N	
Weiping Liu., Jay J. Gan, Sujie Qin	II A, 4	2005	Separation and aquatic toxicity of enantiomers of synthetic pyrethroid insecticides. *Chirality 17:S127-S133, 2005.* © 2005 Wiley-Liss, Inc.	N	
WHO	IIA, 3.1.2, 3.2	1989	Cypermethrin (EHC 82, 1989); International Programme on Chemical Safety, Environmental Health Criteria 82 – Cypermethrin	No	
[redacted]	IIA, 1.4.3 (IIIA, 4.2c)	2002	Cypermethrin: Validation of an analytical method for the determination and confirmation of residues in surface water Covance Laboratories Ltd, report no. 40/040-D2149 (CYP/C69) Chimac-Agriphar S.A., document no. KII A, 4.2.3/02 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]	IIA, 1.4.3 (IIIA,4.2a)	2003a	Cypermethrin: Validation of an analytical method for the determination and confirmation of residues in soil and sediment Covance Laboratories Ltd, report no. 40/039-D2149 (CYP/C70) Chimac-Agriphar S.A., document no. KII A, 4.2.2/01 GLP, unpublished	Yes (Exist./First)	Arysta
[redacted]		2003b	Cypermethrin: validation of the DFG multi residue method S23 for the determination and confirmation of residues in oilseed rape (seed, oil and straw) and wheat (grain and straw). Covance Laboratories Ltd., report no. 40/037-D2149 (CYP/C67). Chimac-Agriphar S.A., doc. No. KII A, 4.2.1/11.	Yes (Exist./First)	Arysta
[redacted]	IIA, 1.4.3 (IIIA, 4.2d (01))	2003b	Cypermethrin: : Validation of an analytical method for the determination and confirmation of residues in products of animal origin (milk, liver, kidney, muscle, fat and eggs) Covance Laboratories Ltd, report no. 40/041-D2149 (CYP/C68) Chimac-Agriphar S.A., document no. KII A, 4.2.5/01 GLP, unpublished	Yes (Exist./First)	Arysta

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[redacted]	IIA, 1.4.3 (IIIA, 4.2b)	2005	Cypermethrin cis:trans 40:60: Validation of an analytical method for the determination of residues in air Covance Laboratories Ltd, report no 1669/016-D2149 GLP, unpublished	Yes (Exist./First)	Arysta
Woollen B.H., Marsh J.R., Laird W.J.D., Lesser J.E	IIA, 3.1.1, 3.1.3	1992	The metabolism of cypermethrin in man: differences in urinary metabolite profiles following oral and dermal administration. Xenobiotica 22: 983-991.	No	
Wolansky M.J., Gennings C., Crofton K.M.	IIA, 3.9.1	2006	Relative potencies for acute effects of pyrethroids on motor function in rats. Toxicological Sciences 89: 271-277.	No	
[redacted]	IIA, 3.5.2	2003a	Changes in some hematological and biochemical indices of rabbits induced by isoflavones and cypermethrin. [redacted]	No	

[redacted]	IIA, 3.8.2, 3.10.2	2003b	Protective role of isoflavones against the toxic effect of cypermethrin on semen quality and testosterone levels of rabbits. [redacted]	No	
[redacted]	IIA, 3.8.2, 3.10.2	2003b	Protective role of isoflavones against the toxic effect of cypermethrin on semen quality and testosterone levels of rabbits. [redacted]	No	