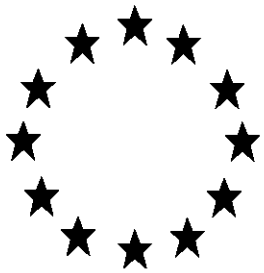
Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report[i]



Cypermethrin cis:trans/40:60

Product-type 8
(Wood Preservative)

12 July 2013

Belgium

Cypermethrin (PT8)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 12 July 2013

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Principle of evaluation

This assessment report has been established as a result of the evaluation of cypermethrin cis: trans/40:60 product-type 8 (Wood Preservative), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with the original view to the possible inclusion of this substance into Annex I or IA to that Directive. The evaluation has therefore been conducted in the view to determine whether it may be expected, in light of the common principles laid down in Annex VI to Directive 98/8/EC, that there are products in product-type 8 containing cypermethrin that will fulfil the requirements laid down in Article 5(1) b), c) and d) of that Directive.

1.2. Purpose of the assessment

The aim of the assessment report is to support a decision on the approval of cypermethrin for product-type 8, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 8 that contain cypermethrin. 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 conclusions of this report were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Regulation (EU) No 528/2012.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report shall be taken into account.

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

1.3. Procedure followed

This assessment report has been established as a result of the evaluation of cypermethrin cis: trans/40:60 product-type 8 (Wood Preservative), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[2].

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1 Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

2 Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

Cypermethrin (CAS no. 52315-07-8) was notified as an existing active substance, and has been supported by Agriphar S.A., hereafter referred to as the applicant, in product-type 8.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[3] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 7(1) of that Regulation, Belgium was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for cypermethrin as an active substance in Product Type 8 was 24 Marsh 2004, in accordance with Annex V of Regulation (EC) No 2032/2003[4]. No dossier has been received within the deadline specified and pursuant to Article 8(3) and (4) and Article 9(5) of Regulation (EC) No 2032/2003, the Commission informed the Member States thereof. That information was also made public by electronic means on 30 April 2004. Within three months of the electronic publication of that information, a company indicated an interest in taking over the role of participant in accordance with Article 8(4) of Regulation No 2032/2003. The new deadline of 31 March 2006 has therefore been established for the submission of a complete dossier.

On 30/03/2006, Belgium competent authorities received a dossier from the applicant Agriphar S.A.. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 30/06/2006.

On 05/03/2010, the Rapporteur Member State submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 18/03/2010. The competent authority report included a recommendation for the inclusion of cypermethrin in Annex I to the Directive for product-type 8.

In accordance with Article 16 of Regulation (EC) No 1451/2007, the Commission made the competent authority report publicly available by electronic means on 06/06/2012. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Commission.

3 Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

4 Commission Regulation (EC) No 2032/2003 of 4 November 2003 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/ 8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market, and amending Regulation (EC) No 1896/2000. OJ L307, 24.11.2003, p1

Revisions agreed upon were presented at technical and competent authority meetings and the competent authority report was amended accordingly.

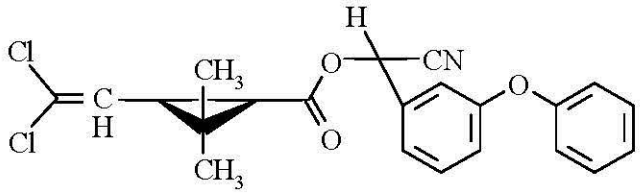
In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on 12 July 2013.

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

2.1.1. Identity, Physico-Chemical Properties & Methods of Analysis

2.1.1.1. Identity

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%

2.1.1.2. 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			

Additionnal information regarding cypemethrin identification is available in the confidential annex folder.

2.1.1.3. 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 °C). 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)

Cypermethrin cis:trans/40:60 is used as an insecticide active substance in wood preservatives for the preventative and remedial treatment of wood and constructional timber against wood destroying insects.

2.1.2. Intended Uses and Efficacy

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) avoiding unnecessary suffering of target organisms and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

In addition, in order to facilitate the work of granting or reviewing authorisations, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.2.1. Field of use envisaged / Function

Product Type 08: Wood Preservatives

Cypermethrin cis:trans/40:60 is an insecticide for use in wood preservation (Product type 8 of the EU Biocidal Products Directive) in indoor and outdoor use (Use classes 1-3).

Cypermethrin is used in preventive and remedial treatment of wood and constructional timber in areas with moderate or subtropical climate against wood destroying insects. Application methods are industrial application by vacuum pressure, double vacuum pressure, dipping and spraying or non-industrial for amateur or professional, by brushing or spraying methods.

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

Cypermethrin cis:trans/40:60 is used to control wood destroying insects, including:

Hylotrypes bajulus (house longhorn beetle)

Anobium punctatum (furniture beetle)

Reticulitermes santonesis (termites)

Lyctus brunneus (beetle)

2.1.2.3. 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.

2.1.2.4. Efficacy studies

A number of laboratory efficacy studies have been undertaken with the formulated product Cypermethrin 10 g/L ME. The test designs have been described in separate summary documents under Point IIIB.5.
The formulated product cypermethrin 10 g/L ME was only tested against *Reticulitermes santonensis* (termites) and against recently hatched larvae of *Hylotrupes balujus* (house longhorn beetles).
According to the results, cypermethrin 10 g/L ME at an application rate higher than 0,02 g A.S./m^2 by brushing is 100% effective against recently hatched larvae of *Hylotrupes balujus.* Cypermethrin 10 g/L ME at an application rate higher than 0,2 g A.S./m^2 by brushing is 100% effective against *Reticulitermes santonensis* (termites).
For vaccum pressure treatments, retention rates equal or greater than 0.1 kg/m^3 cypermethrin are applicable and effective against *Hylotrupes balujus* and *Reticulitermes santonensis*

However, effective retention rates against *Anobium punctatum* (furniture beetles) and *Lyctus brunneus* were not clearly established. At the product authorisation step, additional studies will have to be performed to evaluate which application method and retention rate is effective for the target organism considered.

According to the results of tests performed with the active substance with ageing procedures and surface treatments, a very good level of efficacy was achieved against *Lyctus brunneus*, *Hylotrupes balujus* and *Reticulitermes santonensis* with at least an application rate of 0,2 g A.S./m^2.
For vacuum-pressure procedures, the effective applications rates are near the same as those established with the formulated product.
Furthermore, according to others efficacy tests performed with the active substance without ageing procedures, the effective application rate depends on the development stage of the insect.

Considering the curative insecticidal activity of the active substance cypermethrin, test results performed according to EN standards suggest an application rate of 0,3 g A.S./m^2 as effective against
Anobium punctatum and *Hylotrupes balujus.* However, BE CA is of the opinion that additional tests should be performed at the product authorisation level to conclude on the curative activity of cypermethrin.

Experimental data on the effectiveness of the active substance against target organisms

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results (effects, mode of action, resistance)
Cypermethrin CYP/E28	*Anobium punctatum* (3-5 mg larvae)	EN 21 - Impregnation (vacuum-pressure) w/o ageing procedure - 12 months test 0.0097; 0.0203 and 0.0393 kg/m^3	100% efficacy with 0.0393 kg/m^3 Toxic values : 0.0203 and 0.0393 kg/m^3
	Hylotrupes bajulus (recently hatched larvae)	EN 47 – Impregnation (vacuum-pressure) w/o ageing procedure - 12 weeks test 0.00022; 0.00111 and 0.0057 kg/m^3	100% efficacy with 0.0057 kg/m^3 Toxic values : 0.00111 and 0.0057 kg/m^3
	Hylotrupes bajulus (50 -150 mg larvae)	EN 47 – Impregnation (vacuum-pressure) w/o ageing procedure - 12 weeks test 0.0033; 0.0067 and 0.01335 kg/m^3	100% efficacy with 0.01335 kg/m^3 Toxic values : 0.0067 and 0.01335 kg/m^3
Cypermethrin CYP/E144 * With ageing procedures according to BS 5761 (equivalent to EN73 and EN84)	*Anobium punctatum* (freshly laid eggs)	EN 49.2 – Impregnation (vacuum-pressure) 12 weeks test - 0.00035 to 0.0056 kg/m^3	Toxic values : 0.00067 and 0.00154 kg/m^3
	Reticulitermes santonensis (termites)	EN 117 – Impregnation (vacuum-pressure) (w/o ageing procedure) 0.0246 to 0.4144 kg/m^3	Toxic values : 0.0497 and 0.1 kg/m^3
	Hylotrupes bajulus (recently hatched larvae)	EN 46 – Surface treatment (brushing) 12 weeks test* - 0.000125 to 0.001%	Toxic values : 0.00025 to 0.0005%
	Lyctus brunneus	EN 20.1 – Surface treatment (brushing) 12 weeks test* - 0.1 g a.i./m^2	No infestation (with an emulsion formulation)
	Reticulitermes santonensis (termites)	EN 118 – Surface treatment (brushing) 12 weeks test* - 0.3 g a.i./m^2	Damage grade 0 (with an emulsion formulation)
	Anobium punctatum (adults)	Emergence tests 0.3 g a.i./m^2	100% efficacy (12 weeks) with emulsion formulations
	Anobium punctatum (larvae)	EN 48 - Eradicant tests 0.3 g a.i./m^2	> 90% mortality in kerosene-based solvent - OK (Mortality > 80% according to EN 14128)
	Hylotrupes bajulus (larvae)	EN 22 - Eradicant tests 0.3 g a.i./m^2	> 90% mortality in organic solvent (such as kerosene) - OK (Mortality > 80% according to EN 14128)

Experimental data on the effectiveness of the active substance against target organisms

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance
Cypermethrin 10 /L ME	*Hylotrupes bajulus L.* (recently hatched larvae)	EN 46.1 after EN 73 0.02 - 0.1 - 0.2 g a.s./m^2 (2 coatings - 4 weeks test)	Surface (brush) treatment - preventive	100% efficacy at all three dose levels (all larvae had died after 4 weeks without leaving traces of gnawing)
	Hylotrupes bajulus L. (recently hatched larvae)	EN 46.1 after EN 84 0.02 - 0.1 - 0.2 g a.s./m^2 (2 coatings - 4 weeks test)	Surface (brush) treatment - preventive	100% efficacy at all three dose levels (all larvae had died after 4 weeks without leaving traces of gnawing)
	Hylotrupes bajulus L. (recently hatched larvae)	EN 47 after EN 73 0.0001 – 0.00511 kg a.s./m^3 12 weeks test	Vacuum pressure treatment - preventive	Toxic values > 0.00511 kg a.s./m^3 because after 12 weeks, insects stay alive with all tested concentrations ! => New tests with concentrations higher than 0.00511 kg a.s./m^3 should be performed.
	Hylotrupes bajulus L. (recently hatched larvae)	EN 47 after EN 84 0.0001 – 0.00195 kg a.s./m^3 12 weeks test	Vacuum pressure treatment - preventive	Toxic values > 0.00195 kg a.s./m^3 because after 12 weeks, insects stay alive with all tested concentrations => New tests with concentrations higher than 0.00195 kg a.s./m^3 should be performed.
	Reticulitermes santonensis	EN 118 after EN 73 0.2 – 2 g a.s./m^2 (2 coatings - 8 weeks test)	Surface (brush) treatment - preventive	100% efficacy at all dose levels (no signs of attack or only traces of gnawing of the wood)
	Reticulitermes santonensis	EN 118 after EN 84 0.2 – 2 g a.s./m^2 (2 coatings - 8 weeks test)	Surface (brush) treatment - preventive	100% efficacy at all dose levels (no signs of attack or only traces of gnawing of the wood)
	Reticulitermes santonensis	EN 117 after EN 73 0.0049 – 0.0985 kg a.s./m^3 (8 weeks test)	Vacuum pressure treatment - preventive	Toxic threshold value was found to be 0.024 - 0.0985 kg a.s./m^3 (according to EN 599, no survival insects with no sign of attack or attack < 2)
	Reticulitermes santonensis	EN 117 after EN 84 0.005 – 0.1095 kg a.s./m^3 (8 weeks test)	Vacuum pressure treatment - preventive	Termites (especially workers) still alive with all the tested concentrations => New tests with concentrations higher than 0.1095 kg a.s./m^3 should be performed.

2.1.2.5. 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 biocide uses of cypermethrin cis:trans/40:60. It is recommended to watch out for the apparition of any resistance pyrethroids as cypermethrin. In case of apparition of resistance phenomena in wood preservative context, actives substances with other mode of action should be used

2.1.3. Classification and Labelling

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

Current Classification	*as in Directive 67/548/EEC (29th ATP)*
Class of danger	*Xn: Harmful* *N: Dangerous for the environment*
R phrases	*R20: Harmful by inhalation* *R22: Harmful if swallowed* *R37: Irritating to respiratory system* *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 36/37/39:Wear suitable protective clothing, gloves and eye/face protection* *S60: This material and its container must be disposed of as hazardous waste* *S61: Avoid release to the environment*

Current Classification	**as in EU Regulation CLP 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
New 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 Aquatic chronic 1
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
Precautionary Statement Codes	P260 Do not breath vapours/spray 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

2.1.3.2. Justification for the proposal

The classification of cypermethrin cis:trans/40:60 was agreed at the 29th ATP and appears in Annex I of Directive 67/548/EEC containing the list of harmonised classifications and labelling for substances which are legally binding within the EU.

In addition, cypermethrin *cis:trans/40:60* has a harmonised classification as listed in Annex VI table 3.1. to Regulation (EC) No 1272/2008, which is also understood to be a legally binding inclusion.

No new scientific information/data is available that may affect the classification of the active substance. Nevertheless, in the second ATP of CLP-Regulation (EC) No 1272/2008 the guidance values have been modified for 'specific target organ toxicity following repeated exposure'. As a result of this, 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 should be adapted and include also: **GHS08; STOT RE2; H373. May cause damage to organs through prolonged or repeated exposure.**

The proposal for the new classification and labelling has to be submitted to and validated by ECHA.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. 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 most 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.

Nonetheless, it has been shown that trans-isomer are metabolised more rapidly than the cis isomer which may be the cause of the higher toxicity of the cis isomer in mammal compared to the trans isomer.

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

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. This value of absorption might be different for other formulations/dillutions.

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.

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 reliability because of procedural flaws such as deviating route of administration, single versus repeated exposure, other sampling times, no use of positive controls, no 2^{nd} or 3^{rd} 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 classification as a Category 3 mutagen is warranted. 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/40:60induced functional impairments at the neurotransmitter receptor levels in neonatal rats. However, since the multi-generation 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 predictive 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, it can be concluded that there is no evidence giving rise to concern for an additional risk for the newborn or young humans that should trigger further investigations.

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/40:60 on 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.

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 oestrogen-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.

2.2.1.3. Effects assessment

The relevant critical endpoints of cypermethrin cis:trans/40:60 in the toxicological studies are identified as the effect on the central nervous system, characterised by clinical signs (CS syndrome) and peripheral nerve damage; a decrease in delayed type hypersensitivity; and the effect on the liver, characterised by increase in organ weight associated with increased microsomal enzyme activity. The NOAELs have been derived from the studies in the most sensitive species showing these effects. It is suggested to consider these effects in the risk assessment.

Acute $NOAEL_{oral}$ = 20 mg/Kg bw/day (rat, acute delayed neurotoxicity)

Medium-term $NOAEL_{oral}$ = 12.5 mg/Kg bw/day (dog, 90-days)

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

2.2.1.4. Exposure assessment

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 based on studies using the oral route of administration, i.e. setting the level of internal exposure that is toxicologically acceptable.

Assessment factors: default 100-fold.

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 = 0.088 mg/Kg bw/d

Medium-term AEL = 0.055 mg/Kg bw/d

Long-term AEL = 0.022 mg/Kg bw/d

2.2.1.5. Risk characterisation

The risk charaterisation 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 RPE will always be worn by professional users.

2.2.1.5.1. Human health risk for professionals (Primary exposure)

Cypermethrin 10 g/l ME is intended for use in industrial wood preservation facilities as an insecticide for the preventive treatment of wood and constructional timber (PT8.01). The biocidal product can also be used by professionals for remedial and preventative treatment of wood (PT8.02).

Table 2.2.1.5.1a Industrial workers in production/formulation

Exposure Scenario		Estimated Internal Exposure			Relevant NOAEL/LOAEL [mg/Kg.bw day] - Reference Value	AF	MOE	Exposure
		estimated inhalation uptake [mg/Kg bw day]	estimated dermal uptake [mg/Kg bw]	estimated total uptake [mg/Kg.bw day]	e.g: AEL (acute or medium or chronic)	MOE_{ref}		/AEL
Tier 1 (risk reduction already included)	Formulation: dilution step	1.67×10^{-7}	0.0084 †	0.0084	$NOAEL_{systemic}$: 2.2 mg/Kg bw/d long-term AEL: 0.022 mg/Kg bw/d	100	262	0.382
Tier 2								

† Dipping model 1 indicative values for dermal exposure: **hand exposure inside 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, in the tier 1, the use of appropriate PPE including chemical resistant gloves is already taken into account for this industrial scenario.

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

Table 2.2.1.5.1b. Professional industrial users PT8.01

Exposure Scenario		Estimated Internal Exposure			Relevant NOAEL/LOAEL [mg/Kg.bw day] - Reference Value	AF	MOE	Exposure
		estimated inhalation uptake [mg/Kg bw day]	estimated dermal uptake [mg/Kg bw]	estimated total uptake [mg/Kg.bw day]	e.g: AEL (acute or medium or chronic)	MOE_{ref}		/AEL
Tier 1 (risk reduction included: local exhaust and PPE)	**Vacuum pressure impregnation, water-based**	0.0002	0.0063 †	0.0065 †	$NOAEL_{systemic}$: 2.2 mg/Kg bw/d	100	338	0.295
	Dipping, water-based	0.0001	0.0028 †	0.0029 †	long-term AEL:	100	759	0.132
	Spraying, spray cabinet	0.0009	-	0.0009	0.022 mg/Kg bw/d	100	2444	0.041
Tier 2	/							

† Handling model 1 indicative values for dermal exposure: **hand exposure inside gloves**

As cypermethrin cis:trans/40:60 has a slight skin and eye (but no classification required) and respiratory irritating potential, professional industrial operators must use proper PPE to prevent exposure. It is assumed that engineering controls such as local exhaust ventilation, RPE, and PPE (proper work clothing, chemical resistant footwear, goggles and gloves) are available and used in an industrial treatment plant.

In practice, primary dermal exposure of the professional operator will be reduced by the effects of exposure reduction measures and the use of proper PPE. Thus, with the exposure reduction measures already taken, and with the assumption that the obligatory local exhaust, RPE and PPE is used, a sufficient margin of exposure is maintained and the total internal dose is below the long-term AEL. It can be concluded that the actual risks at the workplace will be probably low.

Conclusion: There is no concern for the professional industrial operators (PT8.01), using the biocidal product during the vacuum and dipping process, and the spraying in a spray cabinet, provided there is a local exhaust and appropriate RPE and PPE is worn.

Table 2.2.1.5.1c. Professional users PT8.02

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	**Manual spraying (indoor, hand-held sprayer)**	0.0043	0.0050 †	0.0093†	$NOAEL_{systemic}$: 2.2 mg/Kg bw/d	100	237	0.422
	Brush-painting (indoor)	**0.0004**	**0.120**	**0.120**	long-term AEL:	**100**	**18**	**5.455**
	Brush-painting (oudoor)	0.0005	0.0060	0.0064	0.022 mg/Kg bw/d	100	344	0.291
Tier 2 (use of PPE: chemical resistant gloves; RPE)	**Brush-painting (indoor)**	0.00002	0.0145	0.0145	$NOAEL_{systemic}$: 2.2 mg/Kg bw/d long-term AEL: 0.022 mg/Kg bw/d	100	152	0.659

† Spraying model 1 indicative values for dermal exposure: **hand exposure inside gloves**

Although the biocidal formulation cypermethrin 10 g/l ME did not show irritant properties to the skin and eye, 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 and RPE to prevent exposure.

In practice, primary dermal and inhalation exposure of the professional operator will be reduced by the use of PPE (proper work clothing, chemical resistant footwear, goggles and gloves) and RPE. Thus, with the assumption that the obligatory PPE and RPE are used, a sufficient margin of exposure is maintained and the total internal dose is below the long-term AEL.

Conclusion: There is no concern for the professional operators (PT8.02), using the biocidal product during spraying indoor, brush-painting indoor and outdoor, provided appropriate PPE and RPE is worn.

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

The biocidal product is available for the consumer for preventative and remedial treatment of wood.

Table 2.4.2.1. Non-professional users PT8.02

Exposure Scenario		Estimated Internal Exposure			Relevant NOAEL/LOAEL [mg/Kg.bw day] - Reference Value	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]	e.g: AEL (acute or medium or chronic)			
Tier 1 (no PPE)	**Brush painting indoor**	0.00017	0.06835	0.06852	$NOAEL_{systemic}$: 8.8 mg/Kg bw/d	100	128	0.779
	Brush painting outdoor	0.00022	0.00766	0.00788		100	1117	0.090
	Spraying indoor	0.00241	0.03848	0.04089	acute AEL: 0.088 mg/Kg bw/d	100	215	0.465
	Spraying outdoor	0.00014	0.02964	0.02977		100	296	0.338
Tier 2	/							

As the active substance, cypermethrin cis:trans/40:60, has a slight skin and eye (but no classification required) and respiratory irritating potential, prolonged skin contact must be avoided under practical conditions. However, the biocidal formulation, cypermethrin 10 g/l ME, did not show irritant properties to the skin and eye.

For the non-professional user, the biocidal product for preventive and remedial treatment of wood must only made available as a ready-to-use product.

Conclusion: There is no concern for the non-professional, using the biocidal product during spraying indoor and outdoor, and brush-painting indoor and outdoor, provided the biocidal product is only made available as a ready-to-use product.

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

Indirect exposure to the general public and professionals will be through the use of the treated timber. Professionals and amateurs get exposed through cutting and shaping the timber. The general public gets exposed through living and working in buildings containing treated wood.

Table 2.2.1.5.3. 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 (Worst Case) Acute Scenario	Intended use	Adult (non-prof) sanding treated wood	2.604×10^{-5}	-	-	2.604×10^{-5}	$NOAEL_{systemic}$: 8.8 mg/Kg bw/d Acute AEL: 0.088 mg/Kg bw/d	100	3.4×10^{5}	2.96×10^{-4}
	Unintended use	Infant chewing treated wood	-	-	0.009	0.009	$NOAEL_{systemic}$: 8.8 mg/Kg bw/d Acute AEL: 0.088 mg/Kg bw/d	100	978	0.102
		Adult hand exposition to wet surface	-	0.0018	-	0.0018		100	4889	0.020
		Infant hand exposition to wet surface	-	0.0026	-	0.0026		100	3385	0.030
Tier 1 (Worst Case) Chronic Scenario	Intended use	Adult (professional) sanding treated wood	15.62×10^{-5}	2.17×10^{-5}	-	17.79×10^{-5}	$NOAEL_{systemic}$: 2.2 mg/Kg bw/d Chronic AEL: 0.022 mg/Kg bw/d	100	1.2×10^{4}	8.1×10^{-3}
	Unintended use	Adult inhaling volatilised residues indoor	3.12×10^{-13}	-	-	3.12×10^{-13}	$NOAEL_{systemic}$: 2.2 mg/Kg bw/d Chronic AEL: 0.022 mg/Kg bw/d	100	7.1×10^{12} 5.5 x 10^{122}	1.4×10^{-11}
		Infant inhaling volatilised residues indoor	4.036×10^{-13}	-	-	4.036×10^{-13} 3.39 x 10^{-3}		100	649	1.8×10^{-11}
		Infant playing on treated wood structure and mouthing hands	-	3.09×10^{-6}	3.39×10^{-3}			100		0.154
		Adult-cleaning work clothes at home	-	0.0152	-	0.0152		100	145	0.691

Conclusion: There is no concern for indirect secondary exposure for adults, children and infants from the use of cypermethrin cis:trans/40:60 in the biocidal product, cypermethrin 10 g/l ME, as a wood preservative either for PT8.01 or PT8.02.

2.2.2. Environmental Risk Assessment

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 invertabrates (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 persistant compared with the other stereoisomers, whereas 1R *trans* α S was likely the least persistant 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.

2.2.2.1. Fate and distribution in the environment

2.2.2.1.1. 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 direved DT50 of 1.65 day. The respective values at 12°C for pH7 and pH 4 are 98.8 days and > 7630 days.

2.2.2.1.2. 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, cypermthrin 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.

2.2.2.1.3. 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**

2.2.2.1.4. 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.

2.2.2.1.5. Distribution

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.

2.2.2.2. Effects assessment

2.2.2.2.1. Aquatic compartment

Acute toxicity

Cypermetrin 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

Cypermethrin cis:trans/40:60 shows effects on the reproduction of fish at concentration as low as 0.01µg/l. Hatching success evaluation indicates that effect might appear at concentration close to 0.032µg/L. However, no real NOEC was determined due to a non-monotonic response for this parameter. Fry survival is impaired at 0.30µg/L and significant effects on the growth rate (weight) appear at the same concentration. Nevertheless the interpretation of the results is

difficult and impairs the reliability of the study. A new study has been commissioned by the applicant to further address the chronic toxicity to fish. The result of the new study will be availlabble for the PT 18anex I inclusion. A conservative approach decided at TM level sets the overall NOEC for the chronic toxicity to fish to 0.01µg/L. The chronic effects on aquatic invertebrates, indicates that cypermethrin cis:trans/40:60 has a similar effect on invertebrates compared to fish. The derived NOEC is 0.04µg/L and the EC50 is 0.35µg/L.

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.

2.2.2.2.2. 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).

2.2.2.2.3. Terrestrial compartment

Plant

A vegetative vigour 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.

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.

2.2.2.2.4. 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}

2.2.2.3. 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.

2.2.2.3.1. 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 0.01 µg/l (agree at TM II 2012) for Fishes (Chronic test). Therefore, using the AF of 10, the PNEC water is 0.001µg/l

PNECwater = 0.001 µg/l

2.2.2.3.2. 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= 0.125 mg/Kg

2.2.2.3.3. 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

2.2.2.3.4. PNEC soil

Two acute tests on earthworms was provided, which both presented small deficiences. 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 5.2 mg/Kg $_{dry\ soil}$

The field trial on miniralization 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 to the Chronic NOEC (biomass) of 5.2 mg/Kg

PNECsoil = 0.1mg/Kg$_{soil}$

2.2.2.4. 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 cypemethrin.TDCVC and CDCVC metabolites does not fulfil the T criteria

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

2.2.2.5. Endocryne disruption, POP

Cypermethrine 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

2.2.2.6. Exposure assessment

2.2.2.6.1. Exposure assessment according to ESD

The summary of the PECs for the different scenario's envisaged is presented in section 2.2.2.7 below.

In a first tier (TIER I) emission to the environment has been calculated without taking into account any degradation process. When the result of the risk characterisation reveal a risk for a dedicated scenario/compartment combination, a tier II assessment have been performed which take into account the biodegradation rates in the considered compartment.

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

Cypemethrin cis:trans/40:60 is characterized by Log Kow values ranged from 5.3-5.6 which indicates a high potential for bioaccumulation. The results of an experimental BCF test tends to impaired the theoretical results. However, deviation in the test protocol lowers the relevance of the last result. A QSAR (BCFwin; EPISUIT) confirms the low potential for bioaccumulation providing a BCF of 417 L/Kgwwt. Both results suffer of uncertainty. As a consequence, bioaccumulation of the active substance should not be completely excluded.

Regarding the terrestrial compartment, cypermethrin cis:trans/40:60 is characterised by a koc value ranged from 80653 to 574360, indicating a high potential to adsorb to the soil particles, reducing the bioavailability. Conversely, the active may also adsorb to biological surfaces such as skin which may lead to toxic effect in higher organisms after biomagnification. A risk for secondary poisoning will have to be performed at product authorisation based on the formulation and the envisaged used.

2.2.2.7. Risk characterisation

2.2.2.7.1. Environmental risk for the water compartment

Industrial application and storage

Table 2.2.2.7.1.1 Pec/pnec aqua from industrial application and storage

Industrial treatment of wood ; water and sediment risk **$PNEC_{aquatic}$ = 1.0E-06 mg/l** **$PNEC_{sediment}$ =1.25E-02mg/Kg_{wwt}** **PNECstp = 1.63 mg/l**	**Local PECs***	**PEC/PNEC**
Vacuum pressure and pressure processes		
Surface water during emission episode (dissolved)	4.43E-05 mg/l	**4.43E+01**
Sediment during emission episode	0.509 mg/kgwwt	**4,07E+03**
STP	4.16E-04 mg/l	2.555E-04
Drenching and dipping		
Surface water during emission episode (dissolved)	1.9E-03 mg/l	**1.90E+03**
Sediment during emission episode	21.8mg/kgwwt	**1.72E+04****

STP	2.77E-04 mg/l	1.6E-04
Automated Spraying		
Surface water during emission episode (dissolved)	3.1E-05 mg/l	**3.1**
Sediment during emission episode	0.355 mg/kgwwt	**2.84E+03****
STP	5.55E-04 mg/l	3.4E-04

Given the very low PECs in STP from both industrial application methods, it is considered that the risk of adverse environmental effects to STP micro-organisms from combined exposure resulting from wood preservative application procedures is negligible.

The data from the EUSES 2.1.1 model of vacuum pressure, Drenching and dipping or automated spraying wood preservation treatment facilities lead to a conclusion that emission to surface water is of concern for each application method.

The sediment PEC/PNEC figures indicate concern for this compartment. Therefore the RCR values picture the fact that application of cypermethrin should only be done in facility where all emissions are collected and treated as waste. As a matter of fact, if no emission to water is possible, the risk for surface water and the sediment is also excluded for the application phase.

Use phase

Noise barrier scenario

Industrial applicication

Table 2.2.2.7.1.2 Pec/pnec aqua, industrial, leaching, noise barrier

Noise-barrier: STP; PT8.01 **$PNEC_{aquatic}$ = 1.0E-06 mg/l** **$PNEC_{sediment}$=1.25E-02mg/Kg_{wwt}** **PNECstp = 1.63 mg/l**	**Local PECs (annual)**	**PEC/PNEC**
Vacuum pressure and pressure processes		
Surface water during emission episode (dissolved)	6.26E-07 mg/l	6.26E-01
Sediment during emission episode	7.18E-03mg/Kg_{wwt}	**5.74***
Agricultural soil (total) averaged over 30 days	2.24E-05mg/Kg_{wwt}	2.24E-04
STP	6.28E-07 mg/l	3.8528E-07
Drenching and dipping (covers automated spraying)		
Surface water during emission episode (dissolved)	1.54E-05 mg/l	**1.51E+01**
Sediment during emission episode	1.76E-01 mg/Kg_{wwt}	**8.536 E+02***
Agricultural soil (total) averaged over 30 days	6.74E-03 mg/Kg_{wwt}	6.730E-02

STP	2.73E-04 mg/l	1.675E-04
TIER II assessment (dipping)		
Surface water during emission episode (dissolved)	1.31E-06 mg/l	**1.31E+00**

*Log Pow>5 so ratio increased by factor 10

Following vacuum and pressure application, no risk has been identified for the water compartment or the STP. However the surface treatment (dipping and spraying) result in a clear risk for the surface water and the sediment and should not be authorised for a noise barrier or a similar use.

Bridge over pond scenario

Industrial application

Table 2.2.2.7.1.3 Pec/pnec aqua, industrial, leaching, bridge over pond

Bridge over pond: PT8.01 **$PNEC_{aquatic}$ = 1.0E-06 mg/l** **$PNEC_{sediment}$=1.25E-02mg/Kg_{wwt}**	**Local PECs**	**PEC/PNEC**
Vacuum pressure and pressure processes		
Concentration in surface water after initial period (30days)	**2.97E-06 mg/l**	2.97
Concentration in surface water after longer period (7300days)	**6.93E-07 mg/l**	0.693
Concentration in sediment at the end of initial assessment period (30 days)	**3.71E-05 mg/Kg_{wwt}**	29.7*
Concentration in sediment at the end of longer assessment period (7300 days)	**8.66E-06 mg/Kg_{wwt}**	6.93*
Drenching and dipping (covers automated spraying)		
Concentration in surface water after initial period (30days)	**1.39E-03 mg/l**	1390
Concentration in surface water after longer period (5475days)	**1.52E-05 mg/l**	15.2
Concentration in sediment at the end of initial assessment period (30 days)	**17.4 mg/Kg_{wwt}**	**13920**
Concentration in sediment at the end of longer assessment period (5475 days)	**1.9E-01 mg/Kg_{wwt}**	152

*Log Pow>5 so ratio increased by factor 10

The result of the assessment indicated that the use of cypermethrin causes unacceptable risk for the aquatic environment, when the active is applied either by vacuum and pressure treatment or by surface treatment (dipping or spraying).

Non-industrial application

Table 2.2.2.7.1.4 Pec/pnec aqua, non-industrial, leaching, bridge-over-pond

Application and emission due to leaching **$PNEC_{aquatic}$ = 1.0E-06 mg/l** **$PNEC_{sediment}$=125E-04mg/Kg_{wwt}** **$PNEC_{soil}$ = 0.1 mg/Kgwwt**	**Local PECs (from application and emission)**	**PEC/PNEC**
Professional		
Tier I		
PEC in water after initial assessment period	4.73E-03 mg/l	**4.73E+03**
PEC after longer assessment period	4.77E-03 mg/l	**4.77E+03**
PEC in sediment after initial assessment period (1825d)	5.75E-01 mg/Kg	**4.6E+02**
PEC in sediment after longer assessment period (1825d)	9.75E-01 mg/Kg	**7.8E+02**
Tier II		
PEC in water after initial assessment period	1.816E-05 mg/l	**1.816E+01**
PEC after longer assessment period	5.68E-06 mg/l	**5.68E00**
PEC in sediment after initial assessment period (1825d)	5.92E-02 mg/Kgwwt	**4.36E01**
PEC in sediment after longer assessment period (1825d)	5.97E-02 mg/Kgwwt	**4.77E01**
Amateur		
Tier I		
PEC in water after initial assessment period	4.86E-03 mg/l	**4.8E+03**
PEC after longer assessment period	7.9E-03 mg/l	**7.9E+03**
PEC in sediment after initial assessment period (1825d)	9.75E-01 mg/Kg	**7.8E+02**
PEC in sediment after longer assessment period (1825d)	9.75E-01 mg/Kg	**7.8E+02**
Tier II		
PEC in water after initial assessment period	2.138E-05 mg/l	**2.13E+01**
PEC after longer assessment period	8.9E-06 mg/l	**8.9E00**
PEC in sediment after initial assessment period (1825d)	9.83E-02 mg/Kgwwt	**7.86E01**
PEC in sediment after longer assessment period (1825d)	9.88E-02 mg/Kgwwt	**7.9E01**

The result indicates that a clear risk exists for both the water and the sediment. No appropriate risk mitigation measure has been identified. Therefore, wooden structure above or close to water ecosystem should not be treated with cypermethrin containing products.

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

Table 2.2.2.7.2.1 Pec air, industrial.

	Local PEC's mg/m^3
Vacuum pressure and pressure processes (HC3)	
Annual average in air	5.71E-07
Drenching and dipping	
Annual average in air	7.62E-08
Automated Spraying	
Annual average in air	4.57E-07

The vapour pressure of cypermethine cis:trans/40:60 is such that emissions to air are very limited. The result of EPIWIN model indicates that cypermethrin cis:trans/40:60 is photolysed in air and should not tends to accumulate.

Atmospheric risk: Cypermethrin has a low volatility and emissions to the air compartment are expected to be low.

Global warming: Data not available on absorbance in so-called atmospheric window (800-1200nm). However, the vapour-pressure is so low, together with an atmospheric half-life less than one year that this is not considered to be an issue.

Stratospheric ozone: AOP v1.91 gives an overall ozone rate constant = 0.02326 cm3/molecule-sec; half-life 49.27 days and according to the TGD on risk assessment (Part II, Section 3.7.2) ozone depletion values approach zero for molecules with atmospheric half-lives less than one year.

Tropospheric ozone: According to the TGD on risk assessment (Part II, section 3.7.2) there is at present no procedure available to estimate the effect on tropospheric ozone if only the basic characteristics of a substance are known

Acidification: It is possible that oxidation of cypermethrin will lead to formation of Nitrogen-containing oxides. However, due to the low expected emissions to the air compartment, it is not expected that this will have an effect on acidification of the receiving soil or surface water.

Therefore, no risk for the air compartment is expected for cypermethrin cis:trans/40:60.

2.2.2.7.3. Environmental risk in the terrestrial compartment

Industrial application and storage

Table 2.2.2.7.3.1: Pec/Pnec in soil from industrial application and storage

Industrial treatment of wood ; soil risk **$PNEC_{soil}$ = 0.1 mg/Kgwwt**	**Local PEC's**	**PEC/PNEC**
Vacuum pressure and pressure processes (HC3)		
Concentration in soil at the storage place at the end of the initial assessment period TIME1 (30 days)	5.9E-03 mg/kgwwt	5.90E-02
Concentration in soil at storage place at the end of a longer assessment period TIME2 (7300days)	1.45 E-03mg/kgwwt	1.45E-02
Agricultural soil (total) averaged over 30 days	9.34E-03 mg/kgwwt	9.34E-02
Tier II assessment		
Steady state concentration at storage place	4.92 E-03mg/Kgwwt	4.92E-02
Drenching and dipping		
Concentration in soil at the storage place at the end of the initial assessment period TIME1 (30 days)	2.79 mg/Kgwwt	**2.79E+01**
Concentration in soil at storage place at the end of a longer assessment period TIME2 (7300days)	680mg/Kgwwt	**6800**
Agricultural soil (total) averaged over 30 days	5.89E-03 mg/Kgwwt	5.89E-02
Tier II assessment		
Steady state concentration in soil a storage place	2.31mg/Kgwwt	**23.1**
Automated Spraying		
Concentration in soil at the storage place at the end of the initial assessment period TIME1 (30 days)	2.80mg/Kgwwt	**28**
Concentration in soil at storage place at the end of a longer assessment period TIME2 (7300days)	682mg/Kg_{wwt}	**6820**
Agricultural soil (total) averaged over 30 days	1.98E-02mg/Kgwwt	1.98E-01
Tier II assessment		
Steady state concentration in soil a storage place	2.32 mg/Kg_{wwt}	**23.2**

According to the assessment, there is no risk expected soil compartment following industrial application by vacuum and pressure process. However a clear risk exists for the soil organism for surface treatment application which requires risk mitigation measures.

Use phase

Fence scenario

From industrial application

Table 2.2.2.7.3.2 : Pec/Pnec in soil, industrial , fence

Outdoor use fence PT 8.01 $PNEC_{soil}$ = 0.1 mg/Kg_{wwt}	**Local PECs** (mg/Kg_{wwt})	**PEC/PNEC**
Vacuum/pressure impregnation (HC3)		
PEC in soil after initial assessment period (30 d)	9.13E-04	9.13E-03
PEC in soil after longer assessment period (7300days)	9.13E-04	9.13E-03
Dipping(covers spraying)		
PEC in soil after initial assessment period (30 d)	4E-01	**4.00E+00**
PEC in soil after longer assessment period (7300days)	1.88	**14.1**
Tier II assessment (dipping)		
PEC in soil after initial assessment period (30 d)	1.57E-03	1.57E-02
PEC in soil after longer assessment period (7300days)	6.84E-04	6.84E-03

The result shows that for the fence scenario, the use of cypermethrin cis:trans/40:60 does not causes unacceptable risk for the soil compartment.

From non-industrial application

Table 2.2.2.7.3.2 : Pec/Pnec in soil, non-industrial , fence

Application and emission due to leaching $PNEC_{aquatic}$ = 1.0E-06 mg/l $PNEC_{sediment}$=125E-04mg/Kg_{wwt} $PNEC_{soil}$ = 0.1 mg/Kgwwt	**Local PECs (from application and emission)**	**PEC/PNEC**
BRUSHING FENCE		
Professional		
Tier I		
PEC in soil after initial assessment period (30 d)	4.36E-01 mg/Kg_{wwt}	**4.36E00**
PEC in soil after longer assessment period (1825d)	8.24E-01 mg/Kg_{wwt}	**8.24E00**
Tier II		
PEC in soil after initial assessment period (30 d)	1.06E-01 mg/Kg_{wwt}	**1.06E00**
PEC in soil after longer assessment period (1825d)	1.9E-02 mg/Kg_{wwt}	1.9E-01
Amateur		
Tier I		
PEC in soil after initial assessment period (30 d)	4.46E-01 mg/Kg_{wwt}	**4.46E00**
PEC in soil after longer assessment period (1825d)	8.54E-01mg/Kg_{wwt}	**8.54E00**

Application and emission due to leaching **$PNEC_{aquatic}$ = 1.0E-06 mg/l** **$PNEC_{sediment}$=125E-04mg/Kg_{wwt}** **$PNEC_{soil}$ = 0.1 mg/Kgwwt**	**Local PECs (from application and emission)**	**PEC/PNEC**
Tier II		
PEC in soil after initial assessment period (30 d)	1.3E-01 mg/Kg_{wwt}	**1.3E00**
PEC in soil after longer assessment period (1825d)	2.3E-02 mg/Kg_{wwt}	2.3E-01

According to the scenario, a risk is identified if an assessment factor of 5 is applied to the leaching rate in accordance with the decision of the leaching workshop (2005) for both professional and non-professional application (Table 2.2.2.7.3.2). When the additional AF is not applied, no risk is identified.

Noise barrier scenario

Industrial application

Table 2.2.2.7.3.4 : Pec/Pnec in soil, industrial , noise barrier

Noise-barrier PEC in soil close to wood. PT8.01. **$PNEC_{soil}$ = 0.1 mg/Kgwwt**	**Local PECs**	**PEC/PNEC**
Vacuum/pressure impregnation (HC3)		
PEC after initial assessment period (30 d)	3.77E-04 mg/Kg_{wwt}	3.77E-03
PEC after longer assessment period (7300days)	1.60E-02mg/Kg_{wwt}	1.60E-01
Dipping(covers spraying)		
PEC after initial assessment period (30 d)	1.76E-01 mg/Kg_{wwt}	**1.76E+00**
PEC after longer assessment period (7300days)	3.51E-01 mg/Kg_{wwt}	**3.51E+00**
TierII assessment(dipped/spray treated)		
PEC after initial assessment period (30 d)	6.14E-02 mg/Kg_{wwt}	6.14E-01
PEC after longer assessment period (7300days)	2.21E-03 mg/Kg_{wwt}	2.21E-02

According to the scenario, no risk is identified for the soil compartment following use of cypermethrin-treated wood in a noise barrier.

House scenario

Industrial application

Table 2.2.2.7.3.5 : Pec/Pnec in soil, industrial , house

House- soil ; PT8.01 **PNECsoil = 0.1 mg/Kgwwt**	**Local PECs**	**PEC/PNEC**
Vacuum/pressure impregnation (HC3)		

House- soil ; PT8.01 PNECsoil = 0.1 mg/Kgwwt	Local PECs	PEC/PNEC
PEC in soil after initial assessment period (30 d)	1. E-03mg/Kg_{wwt}	1.0E-02
PEC after longer assessment period (7300days)	4.29E-02 mg/Kg_{wwt}	4.29E-01
Dipping(spraying)		
PEC after initial assessment period (30 d)	4.72E-01 mg/Kg_{wwt}	**4.72E+00**
PEC after longer assessment period (7300days)	9.41E-01 mg/Kg_{wwt}	**9.41E+01**
Tier II assessment (dipping and spraying)		
PEC after initial assessment period (30 d)	1.64E-02 mg/Kg_{wwt}	1.64E-01
PEC after longer assessment period (7300days)	4.21E-03 mg/Kg_{wwt}	4.21E-02

According to the risk assessment, no unacceptable risk is predicted following use of cypermethrin as wood preservative in house scenario for the soil compartment.

Non-industrial application

Table 2.2.2.7.3.6: Pec/Pnec in soil, non-industrial, house

House- soil ; PT8.02 $PNEC_{soil}$ = 0.1 mg/Kgwwt	Local PECs (from application and emission)	PEC/PNEC
Professional		
Tier I		
PEC in soil after initial assessment period (30 d)	**5.27-01 mg/Kg_{wwt}**	**5.27E00**
PEC in soil after longer assessment period (1825d)	9.93E-01 mg/Kg_{wwt}	**9.93E00**
Tier II		
PEC in soil after initial assessment period (30 d)	2.17E-01 mg/Kg_{wwt}	**2.17E00**
PEC in soil after longer assessment period (1825d)	3.22E-02 mg/Kg_{wwt}	3.2E-01
Amateur		
Tier I		
PEC in soil after initial assessment period (30 d)	**5.64E-01 mg/Kg_{wwt}**	**5.64E00**
PEC in soil after longer assessment period (1825d)	1.03E00 mg/Kg_{wwt}	**1.03E+1**
Tier II:		
PEC in soil after initial assessment period (30 d)	2.48E-01 mg/Kgwwt	**2.48E00**
PEC in soil after longer assessment period (1825d)	3.27E-02 mg/Kgwwt	3.27E-01

For both professional and amateur use, a tier 2 assessment showed a PEC/PNEC greater than 1 for the initial assessment period (30 days). The tier II for long term assessment show no risk for the soil compartment.

2.2.3. Summary of acceptable use

Scenario			Human primary exposure		Human secondary exposure		Aquatic compartment	STP	Terrestrial compartment	Efficacy
			Professional with RPE and PPE	**Non professional**	**Worker**	**Consumer**				
PRODUCTION/FORMULATION										
Formulation : dilution step			Acceptable	NR	Acceptable	Acceptable	NR	NR	NR	NR
Overall conclusion										
INDUSTRIAL APPLICATION: VACUUM PRESSURE (PT 8.01)										
Application and storage (Without RMM)			**Acceptable**	NR	NE	NR	**Not Acceptable**	Acceptable	Acceptable	NR
Wood in-service	Classes 1-2		NR	NR	Acceptable	Acceptable	NR	NR	NR	Not fully demonstrated*
	Class 3	Noise barrier					Acceptable	Acceptable	Acceptable	
		Bridge over pond					**Not Acceptable**	NR	NR	
		Fence					NR	NR	Acceptable	
		House					NR	NR	Acceptable	
INDUSTRIAL APPLICATION: SURFACE TREATMENT (DIPPING /SPRAYING) (PT8.01)										
Application and storage (Without RMM)			**Acceptable**	NR	NE	NR	**Not Acceptable**	Acceptable	**Not Acceptable**	NR
Wood in-service	Classes 1-2		NR	NR	Acceptable	Acceptable	NR	NR	NR	Fully demonstrated
	Class 3	Noise barrier					**Not Acceptable**	Acceptable	Acceptable	
		Bridge over pond					**Not Acceptable**	NR	NR	
		Fence					NR	NR	Acceptable	
		House					NR	NR	Acceptable	

Scenario	Human primary exposure		Human secondary exposure		Aquatic compartment	STP	Terrestrial compartment	Efficacy
	Professional with RPE and PPE	**Non professional**	**Worker**	**Consumer**				
Overall conclusion: • During industrial treatments, collective protective equipment shall be ensured when appropriate, and the operators must wear the appropriate personal protective equipments. • During industrial application the emissions to surface water have to be forbidden. Appropriate mitigation measures such as waste recycling or incineration have to be performed. • All timbers treated by industrial process will have to be stored on impermeable hard standing or under a protective roof to prevent direct losses to soil and surface water and to allow losses to be collected and treated appropriately (e.g. incineration) • Use of pre-treated timber by surface application method should not be allowed when direct emission to water is conceivable. □Pre-treated timber must not be in contact with or above surface water.								
NON-INDUSTRIAL APPLICATION: SURFACE TREATMENT (Brushing/Spraying) (PT8.02)								
Application			**Acceptable** with RPE and PPE	**Acceptable** Ready to use only	NE	NR				
Wood in-service	Classes 1-2		NR	NR	Acceptable	Acceptable	NR	NR	NR	Fully demonstrated
	Class 3	Noise barrier					NR	NR	NR	
		Bridge over pond					**Not Acceptable**	NR	NR	
		Fence					NR	NR	**Acceptable**	
		House					NR	NR	**Acceptable**	
Overall conclusion: ➢ Non industrial treatment of timber should not be authorised for structures close or above fresh water. When treating wooden structures outside, a protection should be place to cover the ground										

NR= Non Relevant
NE= Not Evaluated
*See table *"Experimental data on the effectiveness of the active substance against target organisms" page 13for further detail*

2.2.4. List of endpoints

In order to facilitate the work of Member States in granting or reviewing authorisations, the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

3. PROPOSED DECISION

3.1. Background to the proposed Decision

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 wood destroying insects may be sufficient effective for these uses and without unacceptable risk to human health nor to the environment, excepted the use of impregnated wood close or above fresh water, or any application leading to direct release of the product to surface water (ex. Fence application or bridge over pond).

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 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 in industrial pre-treatment of timber (PT8.01) in hazard class 1, 2, 3;

The professional use (PT8.02), both preventive and remedial treatment of wood;

The non-professional use (PT8.02), both preventive and remedial treatment of wood;

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. However, the impregnation plans should collect any losses of product and treat them as chemical waste. Cypermethrin *cis:trans*/40:60 is characterised by Koc value in soil ranging from 80653to 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.

Cypermethrin does not meet neither POP / vPvP-criteria nor P- and B- criteria and is therefore not a potential PBT substance. Regarding Endocrine disruption, no further data than those used for Human Toxicology are available. No known Endocrire Disruption effect is however reported in literature.

The classification of the active substance is currently under review and a Stot RE 2 classification is proposed (see proposal page 6; this document).

3.2. Proposed decision

The overall conclusion from the evaluation of cypermethrin *cis:trans*/40:60 for use in Product Type 8 (Wood Preservatives), is that it may be possible 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.

It is therefore proposed to approve cypermethrin cis:trans/40:60 as an active substance for use in product-type 8 (Wood Preservative), subject to the following specific conditions:

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 conclusions of this assessment.
3. The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not adressed in the Union level risk assessment of the active substance.
4. The following particular conditions also apply:
    1) For industrial or professional users, safe operational procedures and appropriate organizational measures shall be established. Where exposure cannot be reduced to an acceptable level by other means, products shall be used with appropriate personal protective equipment.

    2) Appropriate risk mitigation measures shall be taken to protect the soil and aquatic compartments. In particular :

        a. Labels and, where provided, safety data sheets of products authorised shall indicate that industrial application shall be conducted within a contained area or on impermeable hard standing with bunding, that freshly treated timber shall be stored after treatment under shelter or on impermeable hard standing, or both, to prevent direct losses to soil or water, and that any losses from the application of the product shall be collected for reuse or disposal.

        b. Products shall not be authorised for industrial treatment by dipping or spraying of wood that will be exposed to weathering, unless data is submitted to demonstrate that the product will not present unacceptable risks, if necessary by the application of appropriate mitigation measures.

        c. Products shall not be authorised for treatment of outdoor constructions near or above water, or for treatment of wood that will be used for outdoor constructions near or above water, unless data is submitted to demonstrate that the product will not present unacceptable risks, if necessary by the application of appropriate mitigation measures.

3.3. Elements to be taken into account when authorising products

- Cypermethrin *cis:trans*/40:60 should not be authorised for other purposes without performing a risk assessment for any non-investigated use.
- Professional users must wear appropriate RPE and PPE (coverall, chemical resistant footwear, goggles, gloves) to prevent exposure under all conditions
- Only the ready-to-use biocidal product, containing cypermethrin *cis:trans*/40:60 must be made available to non-professional users to reduce the exposure to a minimum.
- Products must be labelled appropriately to ensure their safe storage, handling, use, disposal, and transport in accordance with national arrangements.
- Products containing cypermethrin *cis:trans*/40:60, are recommended for 1° the professional use in industrial pre-treatment of timber (PT8.01) in hazard class 1, 2, 3 (vacuum pressure impregnation, dipping, spraying in spray cabinet) and 2° the professional use (PT8.02) both preventive and remedial (spraying indoor, brush painting indoor and outdoor), provided engineering controls such as local exhaust ventilation (industrial setting) and appropriate RPE and PPE are made available and used.
- No combined exposure assessment has been performed for industrial or professional users (primary + secondary exposure) . Before authorising a product for industrial or professional users, Member states should evaluate the combined exposure to the product.
- Cypermethrin *cis:trans*/40:60 should only be applied in facilities were all emission to the environment are collected and treated as chemical waste. Non industrial and amateur application of the product should not be performed on wood or wooden structure in direct contact or above fresh water or were direct emission to fresh water is foreseeable.
- The submission of new leaching test might solve uncertainties regarding the use of an additional assessment factor in the evaluation of the environmental exposure.
- At the product authorization stage, additional efficacy data should be submitted in order to demonstrate the efficacy of the formulated product particularly for the following aspect:
  - For remedial applications, additional efficacy data will be required on formulated product, and for termites and other organisms, field tests are highly recommended.
  - As the product formulation has been modified since the achievement of the test, tests efficacy against Anobium punctatum should be performed in compliance with EN 49-1 and 49-2 standards in view of product authorisation.

- Efficacy on termites was demonstrated only on Reticulitermes santonensis. Further efficacy tests shall be performed on other representative species of termite in view of product authorisation, if efficacy against termites is claimed.
- Resistance to pyrethroid insecticides has been reported for a number of pests both in agriculture and public health; it is recommended to watch out for the apparition of any resistance to pyrethroid such as cypermethrin. In case of apparition of resistance phenomena in wood preservative context, actives substances with other mode of action should be used.

- Cypermethrin *cis:trans*/40:60 should be further assessed with regards to its potential endocrine disruptor properties once further guidance is available and preferably before the product authorisation stage. The conclusion of that assessment might lead to review the active substance approval

- Dermal absorption values used in the applications for product authorisation should be justified, if available by the submission of specific dermal absorption data on the product, or by read-across to existing data if scientifically justified, or by using default values.

3.4. Requirement for further information

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the approval of cypermethrin cis:trans/40:60 in accordance with Article 9 of Regulation (EU) No 528/2012.

3.5. Updating this Assessment Report

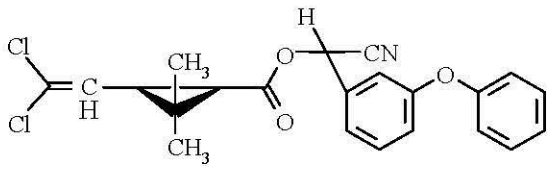
This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information submitted in relation with Regulation (EU) No 528/2012. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the approval of Cypermethrine cis :trans/ 40:60.

Appendix I: List 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 °C*
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 °C)* *Heptane: 57 g/L (20 °C)*
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 °C: 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 water at Σ > 290 nm (point VII.7.6.2.2)	0.0308
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 (%)	g a.s./m^2 wood (1)	Kg a.s./m^3 wood (2)	
PT8.01	Wood destroying insects	Dipping	Single application only	ME	1%	0.2	0.4	0.02	Preventative and remedial treatment, professional users
PT8.01	Wood destroying insects	Vacuum-pressure	Single application only	ME	1%	0.05	-	0.1	Preventative and remedial treatment, professional users
PT8.01	Wood destroying insects	Spraying cabinets	Single application only	ME	1%	0.3	0.6	0.03	Preventative and remedial treatment, professional users
PT8.02	Wood destroying insects	Brushing	Single application only	ME	1%	0.1	0.3	0.015	Preventative and remedial treatment, professional and non-professional users

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 (%)	g a.s./m^2 wood (1)	Kg a.s./m^3 wood (2)	
PT8.02	Wood destroying insects	Spraying	Single application only	ME	1%	0.1	0.3	0.015	Preventative and remedial treatment, professional and non-professional users

(1) Assuming total solution uptake of 200g/m^2 for industrial application (8.01) and 300ml/m^2 for non-industrial application (8.02)

(2) Assuming 1m^3 wood has an area of 50m^2

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.
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	0.088 mg/Kg bw/d	Rat, acute delayed neurotoxicity, oral behavioural effects	100 44%
Medium-term AEL	0.055 mg/Kg bw/d	Dog, 90-days, oral	100 44%
Long-term AEL	0.022 mg/Kg bw/d	Rat; 2-years, oral	100 44%

Acceptable exposure scenarios (including method of calculation)

Industrial Production/Formulation of active substance	Industrial production and formulation. Described in detail in Document II-B and II-C.

	No concern.
Professional users PT8.01	Industrial application by vacuum-pressure, dipping and enclosed spraying cabinets. Described in detail in Document II-B and II-C. No concern, provided there is a local exhaust, and appropriate RPE and PPE is worn.
Professional users PT8.02	Remedial and preventative treatment by spraying (indoor) and brush painting (indoor, outdoor). Described in detail in Document II-C. No concern, provided appropriate RPE and PPE is worn.
Non-professional users	Remedial and preventative treatment by spraying (indoor, outdoor) and brush painting (indoor, outdoor). Described in detail in Document II-B and II-C. No concern, provided the biocidal product is only made available as a ready-to-use product for the consumer.
Indirect exposure as a result of use	Acute exposure scenarios: 1° Adult (non-prof) sanding treated wood, 2° Infant chewing treated wood, 3° Adult hand exposition to wet surface, 4° Infant hand exposition to wet surface. Chronic exposure scenarios: 1° Adult (professional) sanding treated wood, 2° Adult inhaling volatilised residues indoor, 3° Infant inhaling volatilised residues indoor, 4° Child playing on treated structures and mounting hands, 5° Adult cleaning work clothes at home. Described in detail in Document II-C. No concern

Chapter 4: Fate and Behaviour in the Environment

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	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) ⇒ 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°±2C) 0.948 (12°C)
DT90 water	1.5 days (20°±2C)
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	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.

dependence)	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/cm³ 0.02326*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 = 0.00001 mg/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 $_{dry\ soil}$ Biomass 30.8 mg.a.s./Kg $_{dry\ soil}$ Reprod. 5.2 mg a.s./Kg $_{dry\ soil}$

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 II: List of Intended Uses

Product Type 08: Wood Preservatives

Cypermethrin cis:trans/40:60 is an insecticide for use in wood preservation (Product type 8 of the EU Biocidal Products Directive) in indoor and outdoor use (Use classes 1-3).

Cypermethrin is used in preventive and remedial treatment of wood and constructional timber in areas with moderate or subtropical climate against wood destroying insects. Application methods are industrial application by vacuum pressure, double vacuum pressure, dipping and spraying or non industrial for amateur or professional, by brushing or spraying methods.

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 (%)**	**g a.s./m^2 wood (1)**	**Kg a.s./m^3 wood (2)**	
PT8.01	Wood destroying insects	Dipping	Single application only	ME	1%	0.2	0.4	0.02	Preventative and remedial treatment, professional users
PT8.01	Wood destroying insects	Vacuum-pressure	Single application only	ME	1%	0.05	-	0.1	Preventative and remedial treatment, professional users
PT8.01	Wood destroying insects	Spraying cabinets	Single application only	ME	1%	0.3	0.6	0.03	Preventative and remedial treatment, professional users
PT8.02	Wood destroying	Brushing	Single application	ME	1%	0.1	0.3	0.015	Preventative and remedial treatment,

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 (%)	g a.s./m^2 wood (1)	Kg a.s./m^3 wood (2)	
	insects		only						professional and non-professional users
PT8.02	Wood destroying insects	Spraying	Single application only	ME	1%	0.1	0.3	0.015	Preventative and remedial treatment, professional and non-professional users

(1) Assuming total solution uptake of 200g/m^2 for industrial application (8.01) and 300ml/m^2 for non-industrial application (8.02)

(2) Assuming 1m^3 wood has an area of 50m^2

Appendix III: 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. Toxicoligy 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.		

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
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	-
[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)	AG
[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 Huntigdon Life Sciences Ltd., report no. HZL 010/053287 GLP, unpublished	Yes (Exist./First)	AG

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, 1.3 (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)	AG
[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)	AG
[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)	AG

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(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)	AG
[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)	AG
[redacted]	IIA, 3.2.	1980	Acute oral LD5 in the rat of CGA 55186 technical. Ciba-Geigy Ltd., project no. 800665 (CYP/T82a). Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	AG
Batiste-Alentorn M., Xamena N., Velázquez A., Creus A., Marcos R	IIA, 3.6.2	1986	Mutagenicity testing of the pyrethroid insecticde cypermethrin in Drosophila. Mutagenesis 1: 343-346.	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,7.4.1.4)	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)	AG
Bhunya S.P., Pati P.C.	IIA, 3.6.2	1988	Genotoxic effects of a synthetic pyrethroid insecticde, cypermethrin, in mice in vivo. Toxicology letters 41: 223-230.	No	
Bradberry S.M., AGe S.A., Proudfoot A.T., Vale J.A	IIA, 3.11	2005	Poisoing 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). Ciba-Geigy Ltd, report No.:840047 (CYP/T82g) Chimac-Agriphar S.A., document no. KII A, 5.2/01 Non-GLP, unpublished	Yes (Exist./First)	AG
[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)	AG

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)	AG
[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)	AG
[redacted]	IIA, 3.5.2 IIC, 1.2.1	1977	A 13 week feeding study of WL 43467 (cypermethrin) in dogs. Shell UK Ltd., report no. TLGR.77.127 (CYP/T9). Chimac-Agriphar S.A. , doc. No. KII A, 5.3.2.2/01.	Yes (Exist./First)	AG
[redacted]	IIA, 3.4 (IIIA,6.4.1 (02))	1977	A 13 week feeding study of WL 43467 (cypermethrin) in dogs Shell UK Ltd., report no. TLGR.77.127 (CYP/T9) Chimac-Agriphar S.A., document no. KII A, 5..3.2.2/01 Not GLP, unpublished	Yes (Exist./First)	AG
[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)	AG
[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)	AG

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]	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)	AG
[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)	AG
Cantalamessa F.	IIA, 3.2. IIC, 1.2.1	1993	Acute toxicity of two pyrethroids, permethrin, and cypermethrin in neonatal and adult rats. Short communication. Arch Toxicol. 67: 510-513.	No	
Cantalamessa F., Barili P., Vavagna R., Sabbatini M., Tenore G., Amenta F.	IIA, 3.8.1	1998	Influence of neonatal treatment with the pyrethroid insecticde cypermethrin on the development of dopamine receptors in the rat kidney. Mechanisms of Aging and Development 103: 165-178.	No	
Chauhan L.K., Agarwal D.K., Sundararaman V	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. Toxicology Letters 93: 153-157.	No	
Chauhan L.K., Chandra S., Saxena P.N., Gupta S.K.	IIA, 3.6.2	2005	*In vivo* cytogenic effects of a commercially formulated mixture of cypermethrin and quinalphos in mice. Mutat. Res. 587: 120-125.	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
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	
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	

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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	
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[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)	AG
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	
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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.		

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El-Toukhy M.A., Girgis R.S.	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. J. Environ. Sci. Health B 28: 599-619.	No	
Farag A.T., Goda N.F., Shaaban N.A., Mansee A.H.	IIA, 3.8.2	2007	Effects of oral exposure of synthetic pyrethroid, cypermethrin on the behavior of F1-progeny in mice. Reproductive Toxicology 23: 560-567.	No	
[redacted]	5.10.2/01	2006	Determination of the preventative action against recently hatched larvae of Hylotrupes bajulus (L.) according to EN 46 (06/2005) after evaporative ageing procedure according to EN 73 (-04/90). MPA Eberswalde, Materialprüfanstalt Brandenburg GmbH, Germany; report no. 32/05/8724/01, 32/05/8724/02, 32/05/8724/03. GLP not applicable, unpublished.	Yes (New/First)	AG

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[redacted]	5.10.2/02	2006	Determination of the preventative action against recently hatched larvae of Hylotrupes bajulus (L.) according to EN 46 (06/2005) after leaching procedure according to EN 84 (-05/97). MPA Eberswalde, Materialprüfanstalt Brandenburg GmbH, Germany; report no. 32/05/8724/04, 32/05/8724/05, 32/05/8724/06. GLP not applicable, unpublished.	Yes (New/First)	AG
[redacted]	5.10.2/03	2006	Determination of the toxic values against recently hatched larvae of Hylotrupes bajulus (L.) according to EN 47 (06/2005) after evaporative ageing procedure according to EN 73 (04/90). MPA Eberswalde, Materialprüfanstalt Brandenburg GmbH, Germany; report no. 32/05/8724/07 GLP not applicable, unpublished.	Yes (New/First)	AG
[redacted]	5.10.2/04	2006	Determination of the toxic values against recently hatched larvae of Hylotrupes bajulus (L.) according to EN 47 (06/2005) after leaching procedure according to EN 84 (05/97). MPA Eberswalde, Materialprüfanstalt Brandenburg GmbH, Germany; report no. 32/05/8724/08. GLP not applicable, unpublished.	Yes (New/First)	AG

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[redacted]	5.10.2/06	2006	Determination of the preventative action against Reticulitermes santonesis de Feytaud according to EN 118 (06/2005) after leaching procedure according to EN 84 (05/97). MPA Eberswalde, Materialprüfanstalt Brandenburg GmbH, Germany; report no. 32/05/8724/14, 32/05/8724/15, 32/05/8724/16; GLP not applicable, unpublished.	Yes (New/First)	AG
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[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)	AG
[redacted]	IIA, 4.2.3 (IIIA,7.5.3.1 .3)	2003	Cypermethrin: Reproduction study with the northern bobwhite quail Wildlife International Ltd., project no. 547-103 (CYP/T329) Chimac-Agriphar S.A., document no. KII A, 8.1.3/02 GLP, unpublished	Yes (Exist./First)	AG
Gabbianelli R., Nasuti C., Falcioni G., Cantalamessa F.	IIA, 3.6.2	2004	Lymphocyte DNA damage in rats exposed to pyrethroids: effect of supplementation with Vitamins E and C. Toxicology 203: 17-26.	No	
[redacted]	IIA, 4.2.3 (IIIA,7.5.3.1 .1)	2002	Cypermethrin: A dietary LC50 study with the Northern bobwhite quail Wildlife International Ltd., report No. 547-101 (CYP/T324) Chimac-Agriphar S.A., document no. KII A, 8.2.1/01 GLP, unpublished	Yes (Exist./First)	AG

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[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)	AG
[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. Safepharm Laboratories Ltd, report no. 722/031. Chimac-Agriphar SA, document no. KIII A, 7.1.3/01.GLP, unpublished.	Yes (New/First)	AG

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[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)	AG
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	
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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 Shell UK Ltd., report no. TLGR.0027.76 (CYP/T3) Chimac-Agriphar S.A., document no. KII A, 5..3.2.1/01 Not-GLP, unpublished	Yes (Exist./First)	AG
[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 Shell Toxicology Laboratory, Tunstall, report no. TLGR.0188.78 (CYP/T13) Chimac-Agriphar S.A., document no. KII A, 5.6.1/01 Not GLP, unpublished	Yes (Exist./First)	AG
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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	-

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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	
[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)	AG
[redacted]	IIA, 4.2.1 (IIIA,7.4.3.2)	2005	Cypermethrin cis:trans/40:60 Fathead Minnow, early Life Stage test Charles River Laboratories, report no. 805972 GLP, unpublished	Yes (Exist./First)	AG

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[redacted]	IIA, 3.2 (IIIA, 6.1.2) IIC, 1.2.1	1984b	Acute Dermal LD50 in the Rat of CGA 55186 Tech. (cypermethrin); Ciba-Geigy Ltd, report No.:840045 (CYP/T 82f). Chimac-Agriphar S.A., document no. KII A, 5.2/01 Non-GLP, unpublished	Yes (Exist./First)	AG
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[redacted]	IIA, 3.9 (IIIA,6.12.1)	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., 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	
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Lisi P.	IIA, 3.4.2, 3.11	1992	Sensitization risk of pyrethroid nsecticdes. 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*; Covance Laboratories Ltd; study no. 1669/018 GLP, unpublished	Yes (Exist./First)	AG

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[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)	AG
[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)	AG
[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 Shell International Chemical Company, report no. TLGR.78.189 (CYP/T10) Chimac-Agriphar S.A., document no. KII A, 5.5.1/01 Not GLP, unpublished	Yes (Exist./First)	AG
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 – International Institute of Biotechnology and Toxicology, Tamil Nadu, India. **Report number 0805303 (unpublished)**	Yes (Exist/first)	AG

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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 Covance Laboratories Limited, report no. 1669/029 GLP, unpublished	Yes (Exist./First)	AG
Nehéz M., Lorencz R., Dési I	IIA, 3.6.2	2000	Simultateous 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	
[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)	AG

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[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 Shell Toxicology Laboratory, Tunstall, report no. TLGR.0134.77 (CYP/T8) Chimac-Agriphar S.A., document no. KII A, 5.7/01 Not GLP, unpublished	Yes (Exist./First)	AG
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Pore M.P.	IIA, 3.4.1	1993	Sin sensitisation test in guinea-pigs with cypermethrin; Gharda Chemicals Ltd. Prject no. 2433. In 91/414 DAR for Cypermethrin, Annex B, prepared by the BE CA.	No	
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; Rallis Research Centre, India, report no. 4242/05, 15 July 2005 (unpublished).	Yes (Exist./First)	AG
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	-
Rhodes C. et al.	IIA, 3.1.1	1984	The bioaccumulation and biotransformation of *cis, trans*-cypermethrin in the rat. Pest. Sci. 25: 471-480.	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) Covance Laboratories Ltd., report no. 1669/032 GLP, unpublished	Yes (Exist./First)	AG

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[redacted]	IIA, 3.2 IIC, 1.2.1	1983	Acute oral toxicity of WL85871 in comparison with WL43467. Shell International Chemical Company, report no. SBGR.83.101.	No	
Rose G.P. and Dewar A.J	IIA, 3.9.2	1983	Intoxication with four synthetic pyrethroids fails to show any correlation between neuromuscular dysfunction and neurobiochemical abnormalities in rats. Arch. Toxicol. 53: 297-316.	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	
Santoni G., Cantalamessa F., Mazzucca L., Romagnoli S., Piccoli M	IIA, 3.8.1	1997	Prenatal exposure to cypermethrin modulates rat NK cell cytotoxic functions. Toxicology 120: 231-242.	No	
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Santoni G., Cantalamessa F., Spreghini E., Sagretti O., Staffolani M., Piccoli M	IIA, 3.8.1	1998	Alterations of T cell distribution and functions in prenatally cypermethrin-exposed rats: possible involvement of catacholamines. Toxicology 138: 175-187.	No	

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[redacted]	IIA, 3.2	1980	Acute oral LD50 in the mouse of technical CGA 55186. Ciba-Geigy Ltd., project no. 800664 (CYP/T82d). Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	AG
[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)	AG
[redacted]	IIA, 3.3.3	1984a	Acute dermal irritation/corrosion study in the rabbit of CGA 55186 technical. Ciba-Geigy Ltd., project no. 840044 (CYP/T82h). Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	AG
[redacted]	IIA, 3.3.2, 3.3.3	1984b	Acute eye irritation/corrosion study in the rabbit of CGA 55186 technical. Ciba-Geigy Ltd., project no. 840043 (CYP/T82i). Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	AG
[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)	AG
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	
Shukla Y., Taneja P.	IIA, 3.6.2	2002	Mutagenic potential of cypermethrin in mouse dominant lethal assay. J. Environ. Patol. Toxicol. Oncol. 21: 259-265	No	

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Shukla Y., Yadav A., Arora A	IIA, 3.7	2002	Carcinogenic and cocarcinogenic potential of cypermethrin on mouse skin. Cancer Letters 182: 33-41.	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) Ciba-Geigy Ltd, report No.:840044 (CYP/T82h) Chimac-Agriphar S.A., document no. KII A, 5.2/01 Non-GLP, unpublished	Yes (Exist./First)	AG
[redacted]	IIA, 3.2.2 (IIIA,6.1.4 (01))	1984a	Acute Eye Irritation / Corrosion Study in the Rabbit of CGA 55186 Tech. (cypermethrin) Ciba-Geigy Ltd, report No.:840043 (CYP/T82i), Chimac-Agriphar S.A., document no. KII A, 5.2/01 Non-GLP, unpublished	Yes (Exist./First)	AG
[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)	AG
Sonawane, K.K.		2007	Analysis and certification of limits for cypermethrin technical. [redacted] report NO. SP 0701 FB 059, GLP, Unpublished	Yes (Exist./First)	AG
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 vitro* 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	
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Surrallés J., Xamena N., Creus A., Catalùan J., Norppa H., Marcos R.	IIA, 3.6.1	1995	Indusction 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)	AG
[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)	AG

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[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)	AG
[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)	AG
[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 Toxicological Research Centre, Report no. 90-016 (CYP/T133) Chimac-Agriphar S.A., document no. KII A, 8.2.3/01 Not GLP, unpublished	Yes (Exist./First)	AG
Tamang R.K., Jha G.J., Gupta M.K., Chauhan H.V.S., Tiwary B.K.	IIA, 3.10.1	1988	*In vivo* immunosuppression by synthetic pyrethroid (cypermethrin) pesticide in mice and goats. Veterinary Immunology and Immunopathology 19: 299-305.	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 Life Science Research, Laboratory report no. 78/SHL2/364 (CYP/T11) Chimac-Agriphar S.A., document no. KII A, 5.6.2.1/01 Not GLP, unpublished	Yes (Exist./First)	AG

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[redacted]		1980	Acute oral LD50 in the rabbit of technical CGA 55186. Ciba-Geigy Ltd., project no. 800666 (CYP/T82e). Chimac-Agriphar S.A. , doc. No. KII A, 5.2/01.	Yes (Exist./First)	AG
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). Notox B.V., report no. 430313. Chimac-Agriphar SA, document no. KIII A, 7.1.1/01. GLP, unpublished.	Yes (New/First)	AG
[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). Notox B.V., study ref. 417871. Chimac-Agriphar SA, document no. KIII A, 7.1.4/01. GLP, unpublished	Yes (New/First)	AG

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[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. Notox B.V.; study ref. 417882. Chimac-Agriphar SA, document no. KIII A, 7.1.5/01. GLP, unpublished.	Yes (New/First)	AG
[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). Notox B.V.; study ref. 417893. Chimac-Agriphar SA, document no. KIII A, 7.1.6/01. GLP, unpublished.	Yes (New/First)	AG
Varshneya C., Singh T., Sharma L.D., Bahba H.S., Garg S.K.	IIA, 3.5.2, 3.10.1	1992	Immunotoxic responses of cypermethrin, a synthetic pyrethroid insecticide in rats. Short communication. Indian J. Physiol. Pharmacol. 36: 123*126.	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 abd 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	CAG

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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	CAG
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)	AG

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[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)	AG
[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)	AG
[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)	AG
[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)	AG

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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	
Yousef M.I., El-Deerdash F.M., Kamel K.I., Al-Salhen K.S	IIA, 3.5.2	2003a	Changes in some hematological and biochemical indices of rabbits induced by isoflavones and cypermethrin. Toxicology 189: 223-234	No	
Yousef M.I., El-Demerdash F.M., Al-Salhen K.S.	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. Journal of Environmental Scinece and Health Part B – Pesticides, Food Contaminants, and Agricultural Wastes B38: 463-478.	No	

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