Document II-C

Risk Characterisation for the Use of the Active Substance in Biocidal Product(s)

CYPERMETHRIN

CAS No. 52315-07-8

from Arysta LifeScience Benelux sprl, Belgium

for use in Insecticides (Product Type 18)

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1 RISK CHARACTERISATION FOR HUMAN HEALTH

1.1 GENERAL ASPECTS

The biocidal product Cypermethrin 100 g/L EW, containing 10% cypermethrin cis:trans/40:60, is an opaque white liquid which will be used for the control of crawling and flying insect pests in and around domestic and public buildings, including farm buildings and animal housing and food processing factories, by professional operators only. Therefore, risk characterisation is focused on industrial workers and professional pest controllers (PT18.01) and indirect exposure of the residents/general public post-application.

1.2 HAZARD CHARACTERIZATION (CRITICAL ENDPOINTS AND ACCEPTABLE EXPOSURE LEVELS)

1.2.1 Critical Endpoints

The risk assessment has been based on the hazardous properties of the active substance cypermethrin. The most relevant data for each endpoint is brought forward for the risk characterisation.

Main target organs identified:

Central nervous system: Neurotoxicity was characterised, in the rat and the dog, by clinical signs including piloerection, nervousness and uncoordinated movement, ataxia, splayed gait and hyperesthesia. In the rat, peripheral nerve damage was shown by histopathology. In light of the neurotoxicity of cypermethrin and findings in a developmental neurotoxicity study with beta-cypermethrin (**submitted in the PPP framework but not under BPR**), the BPC-WG concluded that a DNT study with cypermethrin **should be submitted six months before substance inclusion**

Liver: the effects observed in the liver consisted of increased organ weight associated with increased microsomal enzyme activity but not associated with histological lesions in the rat.

Table 1.2.1.1. Results of key studies relevant for setting the reference doses

Endpoints	Study design	Effects	Results	Reference
Acute toxicity	Oral Rat	Action on central nervous sytem: sedation, ataxia, splayed gait, tip-toe walk, tremors, convulsions.	Cis:trans/40:60 LD50 = 500 mg/kg bw (groundnut oil) LD50 = 1732 mg/kg bw (arachis oil) Cis:trans/50:50 LD50 = 287 mg/kg bw (10% in corn oil) Cis:trans/37:63 LD50 = 250 mg/kg bw (corn oil)	[redacted]
	Dermal Rat	No systemic effects/mortalities, no local reaction. Clinical signs: dyspnea, ruffled fur, curved and ventral body position.	Cis:trans/40:60 LD50 > 2000 mg/kg bw	[redacted]
	Inhalation Rat	Clinical signs: dyspnea, ruffled fur, curved body position, convulsions. Irritability and hyperkinetic behavior	Cis:trans/40:60 LC50 = 3281 mg/m³	[redacted]
	Acute delayed neurotoxicity Rat	Behavioral effects	LOAEL = 60 mg/kg bw/d **NOAEL = 20 mg/kg bw/d (corn oil)**	[redacted]
Medium-term toxicity	Oral/diet 90 days Rat	Neurotoxicity: ataxia, hypersensitivity and abnormal gait during first 5 weeks. Histopathology: peripheral nerve damage Decrease in bw gain, increase in relative liver and kidney weight, increase in plasma AP and urea, decrease in HB and RBC.	LOAEL = 80 mg/kg bw/d NOAEL = 20 mg/kg bw/d	[redacted]
	Oral/diet 90 days Dog	Neurotoxicity: diarrhea, licking and chewing of the paws, whole body tremors, stiff exaggerated hind leg gait, ataxia, incoordination and hyperaesthesia. Decrease in food intake and bw, decrease in RBC, KCCT (f), focal bronchopneumonia.	LOAEL = 37.5 mg/kg bw/d **NOAEL = 12.5 mg/kg bw/d**	[redacted]
Long-term toxicity	Oral/diet 2 years Rat	Decreased bw and food consumption. Liver and kidney toxicity	LOAEL = 50 mg/kg bw/d **NOAEL = 5 mg/kg bw/d**	[redacted]

	Oral/diet 3-generation Rat	Paternal: Decreased bw gain and food intake. No evidence of any neurotoxic responses. Offspring: Reduced litter size and pup weight at parental toxic doses. Fertility: not affected.	$LOAEL_{parental}$ = 50 mg/kg bw/d $NOAEL_{parental}$ = 10 mg/kg bw/d $LOAEL_{developmental}$ = 50 mg/kg bw/d $NOAEL_{developmental}$ = 10 mg/kg bw/d $NOAEL_{reproductive}$ = 50 mg/kg bw/d	[redacted]

1.2.1.1 Hazard identification of the Active Substance

ADME

Absorption of cypermethrin 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 [redacted] 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, 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 is stereoselective with a preference for the *trans*-isomers (human and animal data).

Dermal absorption. The *in vivo* dermal absorption study in rats provided the most reliable dermal absorption data. The dermal absorption of cypermethrin determined in rats *in vi*vo resulted in an absorption of 7.6% and 12.7% of the applied dose for the concentrate (500 g/L) and spray dilution (25 mg/L). For the assessment of the human internal dermal exposure, a value of **13%** is used.

Absorption by inhalation. Pyrethroids 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, known as CS-syndrome, appear within 1 hour after dosing and survivors recovered 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 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).

Our conclusions are based on the acute oral, dermal, and inhalation toxicity data obtained from studies performed with cypermethrin *cis:trans*/40:60 (oral in oil). In conclusion, cypermethrin 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 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 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 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 (combined chronic toxicity / carcinogenicity study). 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 was tested in a combined chronic toxicity / carcinogenicity study in the rat. The overall results revealed no effect of cypermethrin treatment (0.05, 0.5, 5, 50 mg/kg bw/d, orally) on the number and type of tumours.

Genotoxicity

Cypermethrin 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 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 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 2nd or 3rd confirming experiments, no data about reaching the target organ. Nevertheless, the modest or marginal increases in DNA damage reported in some studies in peripheral lymphocytes or other cells indicate, at least to a limited extent, potential genetic hazards posed by cypermethrin, and emphasize the need and the importance of protective measures and safety regulations to minimize exposure to cypermethrin.

Although the genotoxicity studies on cypermethrin did not exclude a potential for DNA damage, the global weight-of-evidence suggests that cypermethrin 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 would display aneuploidogenic or polyploidogenic properties *in vivo.*

Reproductive and developmental toxicity

The teratogenicity studies involving oral administration of cypermethrin 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 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 induced functional impairments at the neurotransmitter receptor levels in neonatal rats. However, since the multigeneration reproduction study in rats was without any indication of persistent effects in the offspring, which were also exposed to cypermethrin neonatally, it is suggested that receptor binding changes are not predicative or causally related to the behavioral 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 foetus 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 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 produced no immediate or delayed signs of poisoning, nor any histopathological lesions in the nervous system. However, the hen sciatic nerve is not be suitable for studying pyrethroid-induced nerve damage. In contrast with hens, rats treated with a single dose of cypermethrin (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 also produces epileptic activity during repeated administration. The neurotoxic effect of cypermethrin on peripheral nerves (axons, endoneurium) was highly correlated with exposure time. Cypermethrin 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. Cypermethrin also inhibits $GABA_A$ receptors.

Other: Immunotoxicity

Cypermethrin causes immunosuppression: both the humoral and cell-mediated immune response are impaired by cypermethrin.

Other: Endocrine disruption activity

The estrogenic potential of cypermethrin based on ER-mediated mechanisms remains equivocal. Contradictory results were revealed in different studies. In summary, the estrogenic and antiandrogenic

effect of cypermethrin (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 is an estrogen-like chemical that might act through signalling pathways other than direct ER binding, and as such, might function as an endocrine modulator. However, at present no definite conclusions can be drawn.

1.2.1.2 Hazard identification of the Biocidal Formulation, Cypermethrin 100 g/L EW

Dermal absorption

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

Acute toxicity

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

Irritation

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

Sensitisation

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

1.2.2 Derivation of Reference Doses

For risk characterisation, the most appropriate endpoint(s) must be identified and then compared with the exposure estimate for the relevant use situations. The risk characterisation should, at present, be performed using both the MOE and the AEL approach.

In accordance with Article 10 (2) (ii) (a) and (b) of Dir. 98/8/EC and the TNsG on Annex I Inclusion (ECB 2002), the systemic Acceptable Exposure levels (AELs) were derived from the toxicological data base for acute, medium-term, and long-term exposure.

A final guidance for setting an AEL is not yet agreed upon neither in the context of Council Directive 91/414/EEC nor in the BPD directive 98/8/EC. However, a draft guidance document: "Guidance for the setting and application of Acceptable Operator Exposure Levels (AOELs)" (EC2006 rev. 10, July 7, 2006) has been developed, and this has been used as a general guidance for this AEL proposal.

In line with the Margin of Exposure (MOE) approach (TNsG on Annex I Inclusion, ECB 2002a; TGD on Risk Assessment, final draft, ECB 2005) an occupational exposure level is derived which gives an indication for risk managers of how far occupational exposure has to be reduced.

1.2.2.1 NOAEL (No-Observed-Adverse-Effect-Level):

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), peripheral nerve damage, and a decrease in delayed type hypersensitivity, and the effect on the liver, characterised by increase in organ weight associated to 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)

1.2.2.2 Absorption by different routes:

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 [redacted] 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.

The dermal absorption of cypermethrin *cis:trans*/40:60 determined *in vivo* in the rat, resulted in an absorption of 7.6% and 12.7% of the applied dose for the concentrate (500 g/l) and spray solution (25 mg/l), respectively. Consequently, for assessment of the human internal dermal exposure, a value of **13%** is used for **dermal absorption**, as humans are exposed to a water-based biocidal formulation containing cypermethrin 100 g/l (10% a.s. concentration) or less when applied as a solution (0.1% a.s. concentration in final applied product).

Inhalative absorption has not been determined. Pyrethroids 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.

1.2.2.3 Assessment Factors (AF):

To convert the selected NOAELs into an AEL, assessment factors accounting for uncertainties in extrapolation from the results from the toxicological documentation (animals) to the exposed human population have to be applied. The hazard assessment of the effects seen in the central nervous system and liver is based on the assumption of a threshold concentration for effect and makes use of standard default Assessment Factors used in the absence of substance-specific data. The default 100-fold AF is calculated as the product of a 10-fold factor for inter-species variation and a 10-fold factor for intra-species variation.

1.2.2.4 Derivation of Systemic Acceptable Exposure Levels (AELs):

Table 1.2.2.4. Overview of Systemic AELs

Endpoint	Route	NOAEL (mg/kg bw/d)	Route-specific absorption (%)	AF	Reference doses		
					External reference dose (mg/kg bw/d)	Route-specific absorption (%)	Systemic AEL (mg/kg bw/d)
Acute	Oral	20	44	100	0. 2	44	**0.088**
Medium-term	Oral	12.5	44	100	0.125	44	**0.055**
Long-term	Oral	5	44	100	0.05	44	**0.022**

AEL setting for cypermethrin

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.

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

1.2.2.5 Derivation of the reference Margin of Exposure (MOE_{ref})

The MOE_{ref} is derived by combining default assessment factors. MOE_{ref} : 10 x 10 = 100.

All estimated exposure is given as internal total uptake. As such, the MOE is calculated on the basis of the systemic NOAEL taking into account the substance-specific oral absorption factor, because all NOAELs used for risk characterisation are taken from oral studies.

MOE values are evaluated using the corresponding MOE_{ref}.

1.3 EXPOSURE ASSESSMENT

1.3.1 General aspects

The biocidal product containing the active substance cypermethrin 40:60 cis/trans would be used by professionals in domestic and public buildings and food processing factories. Indirect exposure to the general public will be through entering areas that have been treated by the professional.

The risk characterisation will therefore focus on professional use and indirect exposure to the general public.

1.3.2 INDUSTRIAL EXPOSURE: Formulation of the biocidal product PT18.01

The biocidal use fraction of cypermethrin cis:trans/40:60 is expected to be much less than that used in agrochemicals. This section has not to be evaluated completely by the CA-BE because the production process of the active substance is outside the scope of the Biocidal Products Directive.

The active substance cypermethrin is manufactured in a closed process and supplied in 200-litre drums as a technical material (92% min) to a single main formulator. This formulator produces the product cypermethrin 100 g/L EW batch-wise in an enclosed system. 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) if this is necessary for their normal work. Engineering controls such as local exhaust ventilation and PPE are used when necessary to prevent exposure. Nevertheless, highest exposure is expected during the production of the formulation Cypermethrin 100 g/L EW, containing 10% cypermethrin cis:trans/40:60, or during interventions for leaks or equipment malfunction, and maintenance.

Table 1.3.2.1. Summary - Primary exposure during industrial formulation of the biocidal product Cypermethrin 100g/L WE containing 10% cypermethrin

Exposure scenario	a.s.* [%]	PPE (gloves)	Estimated Internal Exposure		
			Estimated inhalation uptake (mg/kg bw/d)	Estimated dermal uptake (mg/kg bw/d)	Estimated total uptake mg/kg bw/d)
Formulation: dilution step	10	-PPE	1.67×10^{-7}	0.449†	0.449
		+PPE	1.67×10^{-7}	0.045	0.045

* Concentration of active substance in the biocidal formulation

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

1.3.3 PROFESSIONAL EXPOSURE from the use of the biocidal product PT18.01

The product is used by professionals by spray for the control of insects in and around domestic and public buildings and food processing.

Table 1.3.3.1. Professional exposure from the professional biocidal use PT18.01

Exposure scenario	a.s.* [%]	PPE	Estimated Internal Exposure		
			Estimated inhalation uptake (mg/kg bw/d)	Estimated dermal uptake (mg/kg bw/d)	Estimated total uptake mg/kg bw/d)
Spraying – Acute exposure	**0.1**	*-PPE*	*0.0054*	*0.07098*[†]	*0.0764*
		+PPE (gloves)	*0.0054*	*0.02670*[†]	*0.0321*
Spraying – Chronic exposure	0.1	-PPE	0.0036	0.04667[†]	0.05024
		+PPE (gloves)	0.0036	0.01756[†]	0.0211

* Concentration of active substance in the treatment (in-use) solution

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

1.3.4 NON-PROFESSIONAL EXPOSURE from the use of the biocidal product PT18.01

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

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

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

Secondary exposure can occur immediately after application of the product as a single event (acute phase) or occurs as long term event, and may be continuous (chronic phase).

Adults may be subject to inhalation exposure only, whereas children may be exposed by inhalation and dermal contact (playing on the floor). Children, toddlers and Infants may be additionally exposed via oral ingestion (hand-to-mouth contact). These exposures were calculated using ConsExpo.

Table 1.3.5.1. Indirect exposure from the use of the biocidal product PT18.01

Exposure scenario	Phase	Estimated Internal Exposure			
		Estimated inhalation uptake (mg/kg bw/8 h)	**Estimated dermal uptake (mg/kg bw/d)**	**Estimated oral uptake (mg/kg bw/d)**	**Estimated total uptake (mg/kg bw/d)**
Adult Inhaling volatilised residues from treated floor (following crack and crevice and/or general surface spraying)	Acute	1.68×10^{-5}	-	-	1.68×10^{-5}
Child Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	Acute	4.46×10^{-5}	0.00736	-	0.0074
Toddler Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	Acute	1.02×10^{-4}	0.0176	0.0077	0.0254
Infant Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	Acute	8.48×10^{-5}	0.022	0.00963	0.0317
Adult Inhaling volatilised residues from treated floor (following crack and crevice and/or general surface spraying)	Chronic	5.8×10^{-6}	-	-	5.8×10^{-6}
Child Inhaling volatilised residues from treated floor Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	Chronic	1.54×10^{-5}	0.00254	-	0.0026

Toddler Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	Chronic	3.52×10^{-5}	0.00607	0.00265	0.0088
Infant Inhaling volatilised residues from treated floor and Post application exposure following to a **Crack and crevice** spray application of pest control products	Chronic	2.93×10^{-5}	0.00758	0.00332	0.0109
Child Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	Acute	4.46×10^{-5}	0.049	-	0.049
Toddler Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	Acute	1.02×10^{-4}	0.117	0.0513	0.168
Infant Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	Acute	8.484×10^{-5}	0.146	0.0641	0.21
Child Inhaling volatilised residues from treated floor Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	Chronic	1.54×10^{-5}	0.0169	-	0.0169

Toddler Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	Chronic	3.524×10^{-5}	0.0404	0.0177	0.0581
Infant Inhaling volatilised residues from treated floor and Post application exposure following to a **general surface** spray application of pest control products	Chronic	2.93×10^{-5}	0.0505	0.0221	0.0726

1.4 RISK CHARACTERISATION

1.4.1 Industrial Workers in production/formulation

This section (1.4.1) is not fully evaluated by the CA-BE because the production/formulation process of the active substance is outside the scope of the Biocidal Products Directive.

Table 1.4.1.1. Industrial workers in production/formulation (primary exposure) – risk characterisation

Exposure Scenario		Estimated Internal Exposure			Relevant NOAEL/LOAEL [mg/kg.bw day] - Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
		estimated inhalation uptake [mg/kg bw day]	estimated dermal uptake [mg/kg bw]	estimated total uptake [mg/kg.bw day]				
Tier 1 (-PPE)	**Formulation : dilution step**	1.67×10^{-7}	0.449†	0.449†	$NOAEL_{systemic}$: 2.2 mg/kg bw/d long-term AEL: 0.022 mg/kg bw/d	100	4.9	20
Tier 2 (+PPE)	**Formulation : dilution step**	1.67×10^{-7}	0.045	0.045	$NOAEL_{systemic}$: 2.2 mg/kg bw/d long-term AEL: 0.022 mg/kg bw/d	100	49	2

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

Production and formulation plant workers are expected to be trained and skilled in the main tasks of their occupation and should have experience and skill in the use of personal protective equipment (PPE). It is assumed that engineering controls such as local exhaust ventilation and PPE are available and used.

As such, the use of appropriate PPE including chemical resistant gloves is taken into account for this industrial scenario.

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

1.4.2 Professional Users of the biocidal product PT18.01

Table 1.4.2.1. Professional users PT18.01 (primary exposure) – risk characterisation

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

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

** An arithmetic error was identified following the ECHA/BPC review of the dossier; the estimated inhalation exposure levels have since been amended. These amendments have no material impact on the original outcome of this exposure scenario.

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

Description of the local effects:

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

Description of the exposures scenarios:

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

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

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

Conclusion

Hazard			Exposure							Risk	
Hazard category	Effects in terms of C&L	Additional relevant hazard information	PT	Who is exposed	Tasks, uses, processes	Potential exposures route	Frequency and duration of potential exposure	Potential degree of exposure	Relevant RMM & PPE	Conclusion on risk	Uncertainties attached to conclusion may increase (↑) or decrease (↓) risk or both (↑↓)
Skin sens 1B (moderate)	H317	Skin Sens 1B (moderate) based on experimental study	18 (professional Users of the biocidal products PT18.01)	PROFESSIONALSS	Mixing and Loading follows by spraying indoor, low pressure Mixing and Loading and spray application (with gloves, without RPE) according to human exposure scenario	Dermal, Inhalation	Frequency : 1 task/day Duration : 120 min/task	50 mL/m² Of surface treated	with gloves, without RPE	Acceptable: - The biocidal product used is diluted 100X - Used for short duration - Frequency varies with the period of the year. - Used by trained professional (supposed proper use of RMM and PPE)	

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

RMM and OC's:

- Containment as appropriate
- Minimize number of staff exposed
- Avoidance of contact with contaminated tools and objects
- Regular cleaning of equipment

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

- Training of staff on good practice
- Good standard of personal hygiene

PPE:

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

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

In practice, primary dermal and inhalation exposure of the professional operator will be reduced by the use of PPE (gloves) and RPE (not mandatory according the scenario). Thus, with the assumption that the obligatory PPE is used, a sufficient margin of exposure is maintained and the total internal dose is below the long-term AEL.

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

1.4.3 Non-professional users

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

1.4.4 Indirect Exposure as a Result of Use (Secondary Exposure)

Table 1.4.4.1. Indirect exposure as a result of use (secondary exposure) – risk characterisation

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

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

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

Conclusion: There is a great concern for indirect secondary exposure for infant and toddler playing on treated floor. The risk for acute and chronic exposure at the product cypermethrin 100 g/L EW is not acceptable for these categories.

For adults and children, there is no concern for indirect secondary exposure from the use of cypermethrin cis:trans/40:60 in the biocidal product, cypermethrin 100 g/L EW, as an insecticide PT18.01 in and around domestic and public buildings and food processing factories..

Following this risk evaluation, the RMS Belgium advice some risk mitigation measures in order to avoid any exposure of infant and toddler to the product cypermethrin 100 g/L EW. Please refer to the section 1.5 for the RMM.

1.4.5 Indirect Exposure as a Result of Use (Secondary Exposure)

During TM16.09.2016 , it has been accepted to that a dietary exposure assessment was not necessary due to the expected use of the substance.

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

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

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

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

1.5 CONCLUSION

The biocidal product cypermethrin 100 g/L EW, containing cypermethrin cis:trans/40:60, is produced batch-wise in an enclosed system from manufacture to drumming. The active substance and the product are only handled by industrial users with adequate training and protective equipment.

The biocidal product cypermethrin 100 g/L EW, containing cypermethrin cis:trans/40:60, is intended for the control of insects in and around domestic and public buildings and food processing factories. The biocidal product is intended to be used as insecticide (PT18.01) by professionals only.

The professional use of the product is considered safe when used in compliance with the conditions on the label.

For the secondary exposure, the use of the product is considered safe for adults and children. There is a concern for toddlers and infants (child below two years). To avoid any exposure of these populations, the BE-RMS proposed the following measure mitigation:

- Should be applied only on surface out of reach of children (below 6 years old)

Professional should decontaminate the area which could be in contact with children (below 6 years old)

Thus,

- There is concern for industrial workers in the formulation of the biocide Cypermethrin 100 g/L EW.
- The normal use of cypermethrin 100 g/L EW for the envisaged applications does not pose a health risk for professional users (PT18.01), provided appropriate PPE is worn.
- The normal use of cypermethrin 100 g/L EW as an insecticide (PT18.01) poses a health risk for indirect secondary exposure for residents/general public post-application (and infants). Measure must be taken in order to avoid any exposure of these population. For adults and children above 6 years, the normal use of cypermethrin 100g/L EW does not pose a health risk for indirect secondary exposure when applied maximally 126 times a year. Continuous exposure is not acceptable for toddlers and infants.

Keep in mind that skin sensations and other peripheral sensory phenomena should always be considered as a warning signal for overexposure, indicating that adequate preventive measures should be taken.

2 RISK CHARACTERISATION FOR THE ENVIRONMENT

2.1 Water compartment

2.1.1 Stp and aquatic compartment including sediment

The concentration of active substance in sewage treatment plant (stp) and in surface water after stp, as calculated in doc II B can be compared to the PNECstp and the PNECwater respectively. The PNECstp was set to 1.63mg/l and the PNECwater to 0.004µg/l.

Table 2.1.1.1 Risk characterisation for STP

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

Table 2.1.1.2 Risk characterisation for surface water

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

Outdoor perimeter urban	7,10E-02	1,74E-04	4,36E+01
Outdoor perimeter rural	5,75E-05	1,41E-07	3,53E-02

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

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

Based on the equilibrium partitioning method, the following formula

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

$$PNEC_{sediment} = \frac{14375.9 * PNECwater * 1000}{1.15E03} = 1.25E+04$$

Local PEC/PNEC for sediment calculated based on PECwater above and a PNECsed of 0.050mg/Kg. Since Cypermethrin strongly bind to organic matter, an extra factor of 10 should be applied on the PNECsed. Therefore, the final PNECsed is $0.0050 mg/kg_{ww}$

Table 2.1.1.3

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

Using the equilibrium partitioning method (epm) with a Koc of 575000, the highest Koc within those derived (see doc IIA), and an additional AF of 10 necessary due to the strong biding of the active to the sediment particles, a risk is identified for the sediment in all scenario's except for

the chemical barrier and the Cracks and crevices application in room where only dry cleaning occurs and for the two outdoor rural scenarios.

Conclusion for the water and sediment compartments:

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

2.1.2 Ground water assessment

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

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

Scenario	Elocal water	C_{sludge}	$Csludgesoil_0$	$Csludge_{soil\ 10}$	PEClocalsoil,porew
	kg/d	mg/kg	mg/kg		mg/l
Indoor	1,07E-02	1,36E+02	1,99E-01	1,99E-01	1,97E-05
indoor ,dry	2,85E-04	3,61E+00	5,31E-03	5,31E-03	5,23E-07
Chemical barrier	8,63E-04	1,09E+01	1,61E-02	1,61E-02	1,59E-06
Chemical barrier dry	6,74E-05	8,55E-01	1,26E-03	1,26E-03	1,24E-07
Cracks and crevices	2,82E-04	3,58E+00	5,26E-03	5,26E-03	5,19E-07
Cracks and crevices, dry	1,31E-05	1,66E-01	2,43E-04	2,43E-04	2,40E-08
Outdoor wall urban	1,10E+00	1,40E+04	2,05E+01	2,05E+01	2,02E-03
Outdoor wall rural	1,20E-05	1,52E-01	2,24E-04	2,24E-04	2,20E-08
Outdoor perimeter urban	7,10E-02	9,00E+02	1,32E+00	1,32E+00	1,30E-04
Outdoor perimeter rural	5,75E-05	7,29E-01	1,07E-03	1,07E-03	1,06E-07

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

2.2 Atmosphere

The very low vapour pressure and Henry law constant suggests that atmospheric concentrations will be negligible (2.92E-12 mg/m^3). A qualitative environmental risk assessment only can be conducted for this compartment in the absence of specific effect data. However, based on the

low PEC's, any possible adverse effects, such as ozone formation in the troposphere, is likely to be negligible.

2.3 Terrestrial compartment

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

PEC/PNEC ratios for terrestrial organisms

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

The Pec/Pnec ratio calculated for 10 year of sludge application does not show risk for indoor application in dry cleaned areas, in chemical barrier treatment

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

Outdoor perimeter rural	1,66E^{-03}	8,11E^{-03}	3.20E^{+04}	1.56E^{+05}

The PEC/PNEC ratios calculated for the outdoor use of insecticide against flying and crawling insects in rural areas triggers the need for possible Risk mitigation measures. E-CA suggested that covering the soil with plastic sheet may reduce the risk. This RMM was not deemed acceptable by all member of the WG IV 2016. Moreover, the PECS are here compared with a PNEC derived for earthworm which are most probably not the most sensitive species due to the mode of action of cypermethrin. Therefore, a high risk is identified for the soil when cypermethrin-containing products are used in rural areas which cannot be reasonably mitigated.

2.4 Risk assessment to beneficial arthropods

Cypermethrin is an insecticide. As such, bees may be impaired by the use of cypermethrin-containing products. However, a large scale outdoors exposure is not expected from the uses described in the CAR and the substance has a non-systemic mode of action. As a matter of adding security, e-CA proposes to explicitly made clear on the label that the use of cypermethrin containing product should be avoided in area close to beehive and during the scavenging hours of bees.

2.5 NON COMPARTMENT SPECIFIC EFFECTS RELEVANT TO THE FOOD CHAIN (SECONDARY POISONING)

In first instance, BE eCA did calculated secondary exposure following cypermethrin application outdoor or in stable. Applications according to outdoor and stable use patterns are not accepted due to the risks calculated. The only scenario remaining acceptable in this risk assessment is application indoor, in room where dry cleaning only is performed. As consequence, the use of cypermethrin containing products will be very limited and will be performed in area where wild life would not have an easy access. As such, a secondary exposure is no more needed.

2.6 Overall assessment of the risks to the environment from the use of the active substance in biocidal products.

The risk assessment for cypermethrin used as PT 18 has been done based on two ESD. In these documents, scenario relevant for indoor and outdoor spray application as well as use in stable and manure has been performed. As regard to the stable and animal housing scenario, difficulties in the interpretation of the scenario and how it should be properly run lead to the conclusion that this scenario will not be part of the evaluation of cypermethrin for the inclusion in the list of authorise active under the BPR.

Scenario	Surface water	STP	Sediment	soil	Ground water
Indoor	-	+	-	-	+
Indoor,dry	+	+	-	+	+
Chemical barrier	+	+	-	+	+
Chemical barrier, dry	+	+	+	+	+
Cracks and crevices	+	+	-	+	+
Cracks and crevices, dry	+	+	+	+	+
Outdoor wall urban	-	+	-	-	-
Outdoor wall rural	+	+	+	-	+
Outdoor perimeter urban	-	+	-	-	-
Outdoor perimeter rural	+	+	+	-	+

-Risk identified ; + No risk identified

Depending on which scenario is considered, surface water, soil and ground water are the compartment of concern. The result of the risk characterisation shows that no risk has been identified for STP.

A risk has been identified for soil organism when cypermethrin-containing product is applied indoor on total surface or outdoor in rural area where direct released to soil is expected. Application of sludge on soil is not of concern excepted for the outdoor perimeter scenario against crawling insects. Other used of cypermethrin containing product as PT 18 leads to no risk for soil organisms.

The estimation of ground water contamination following first tier evaluation allows to exclude risk for drinking water excepted for the two outdoor urban scenarios.

The risk for bees or other beneficial arthropod cannot be quantitively assessed. However, the use pattern of the product (indoor, dry cleaned area) combined with reasonable precautionary measure should be enough to avoid any major risk for bees.

The use of cypermethrin-containing product for PT 18 purpose also shows no risk of secondary poisoning for birds or mammal.

PBT assessment and endocrine disrupting effects has already been evaluated for cypermethrin cis:trans/40:60 for the inclusion of the active in the list of authorised substances for the PT 8. Therefore, this evaluation has not been repeated for the purpose of the PT 18 listing. The result will be included in the Assessment Report.

Overall, one safe use has been identified following indoor application of cypermethrin containing product in a cracks and crevices application with the restriction that the product is use only in dry cleaned room and no more than twice a year.

3 RISK CHARACTERISATION FOR THE PHYSICO-CHEMICAL PROPERTIES

Cypermethrin 40/60 cis:trans is thermally stable, non-flammable, non-explosive, non-oxidising and of low volatility. Therefore users are not anticipated to be at risk due to its physico-chemical properties.

4 MEASURES TO PROTECT MAN, ANIMALS AND THE ENVIRONMENT

Reference: Chimac-Agriphar s.a., 2004 (Data presented under III-A Section A8 and III-B Section B8).

4.1 ACTIVE SUBSTANCE

4.1.1 Recommended methods and precautions concerning production, handling, use, storage, transport or fire.

Production:

Appropriate engineering controls should be employed during the formulation process, including local exhaust ventilation and the use of personal protective equipment (overalls, goggles, gloves and respirator). All workers must be fully trained to handle hazardous substances on the plant.

Handling and Use:

Provide local exhaust or general room ventilation when handling the active substance.

Handle in accordance with good industrial hygiene practises. Do not eat, drink or smoke. Wash hands and exposed skin after work and particularly before meals. If splashes do occur, remove any contaminated clothing immediately and wash skin with mild soap and water. Wash splashes to eyes with copious amounts of water immediately.

Wear suitable respiratory equipment, chemical-resistant gloves, overalls and chemical goggles/face shield with safety glasses.

Storage:

Store only in the original container in a cool, well ventilated place away from all possible sources of ignition and away from food, drink and animal feedingstuffs. Keep out of the reach of children.

Transport information:

When transporting by road, ensure the driver is aware of the potential hazards of the load and is trained in the actions to be taken in case of an accident or emergency.

Transport classification

Shipping Name: UN 3352 PYRETHROID PESTICIDE, LIQUID, TOXIC (Cypermethrin), 6.1, III

Land transport:

UN No: 3352

H.I. No: 60

ADR/RID: class 6.1

ADR/RID Packing group: group III

Sea transport:

IMO-IMDG: class 6.1

IMO Packing group: group III

IMDG-Marine pollution: Marine pollutant

Air transport:

IATA: class 6.1

IATA Packing group: group III

Fire fighting measures:

Special protective equipment:	Wear full protective equipment, including breathing apparatus.
Extinguishing media not to be used:	Do not use water jet or heavy water stream.
Suitable extinguishing media:	For small fires, use carbon dioxide or dry chemical to extinguish flames. Use fluxing salts or dry sand to surround and smother the fire. For large fires use water fog or spray or alcohol foam. Cool exposed containers with water spray or fog.
Specific hazards:	When heated to decomposition, the evolution of carbon monoxide, carbon dioxide, nitrogen oxides, hydrochloric acid and hydrogen cyanide must be anticipated.
Specific protection measures:	Wear full protective equipment when dealing with fire, including breathing apparatus. Ensure area is cleared of all personnel. Do not empty fire control water into drains.

4.1.2 Emergency measures in case of an accident

First aid measures:

Inhalation	Remove victim to fresh air. If breathing is difficult administer oxygen. If breathing has stopped, apply artificial respiration. Seek medical advice.
Skin contact	Remove contaminated clothing immediately and wash exposed skin thoroughly with mild soap and water. If symptoms are severe, seek medical advice.

Eye contact Rinse immediately with copious amounts of clean water for 10-15 minutes. Obtain immediate medical advice.

Ingestion DO NOT INDUCE VOMITING! If conscious, rinse mouth with water ensuring the casualty does not swallow. If swallowed seek medical advice immediately and show the container or label.

Antidotes and treatment:

No specific antidote is known, treatment should be symptomatic.

4.1.3 Procedures to protect the environment in the case of an accident:

4.1.3.1 Accidental release in environment:

Spillages should be handled by trained cleaning personnel properly equipped with respiratory and eye protection. Ensure the area is cleared of all other persons.

Soak up spillage onto suitable inert material (e.g. clay or diatomaceous earth) as soon as possible. Collect spillage and place in an appropriate container, tightly closed and properly labelled.

Prevent spillage from entering the drainage system or watercourses. If contamination of drains or public waters occurs, notify the appropriate authorities immediately.

4.1.3.2 Cleaning, destruction or decontamination following release in

Air:

Cypermethrin is non-volatile, therefore there should be no potential hazard to the atmosphere.

Water (including drinking water**):**

Cypermethrin is a viscous liquid/semi-solid with low water solubility. Therefore it is likely that any material entering water will form an immobile mass which can be removed by mechanical means. Activated carbon can be used on any material that has dissolved and the precipitate removed by mechanical means

Soil:

Cypermethrin adsorbs strongly to soil, therefore any material accidentally released to soil should be relatively localised. Contaminated soil should be removed and placed in appropriate containers for safe disposal or incineration.

4.1.4 Procedures for waste management of the active substance

Re-use or recycling:

Empty containers should not be re-used for any purpose. Dispose of in accordance with local regulations. Destroy or puncture empty containers to prevent re-use.

Neutralisation of effects:

In the event of accidental spillage, chemical absorbents and collected spilled material should be disposed of in accordance with local regulations and by a suitable waste contractor.

The preferred method of disposal is incineration, however if this is not possible cypermethrin can be decomposed by hydrolysis at pH 12 or above. For emulsifiable material, 5% sodium hydroxide solution or saturated (7-10%) sodium carbonate can be used. For non-emuslifiable material, a 1:1 v/v mixture of either of these solutions and a water/oil soluble solvent (e.g. denatured alcohol, monoethylene glycol, hexylene glycol or isopropanol) can be used. The material should be covered with hydrolysing agent and left to stand for 7 days. The material should be analysed to ensure the active ingredient has been degraded to a safe level before being disposed of.

4.1.5 Conditions for controlled:

Discharge (including leachates)**:**

Cypermethrin is toxic to fish and other aquatic organisms and should not be discharged into surface waters under any circumstances. Disposal by controlled incineration is preferred.

Incineration:

Cypermethrin can be destroyed by controlled incineration at high temperatures, with thermal decomposition occurring at 215ºC. The halogen content of cypermethrin is below 60%, therefore no specific information about the pyrolytic behaviour is required.

4.1.6 Side-effects, on beneficial and non-target organisms

Cypermethrin is highly toxic to aquatic organisms (fish, daphnia) with the exception of green algae.

Cypermethrin is a broad spectrum insecticide and will kill beneficial insects, honeybees and other non-target arthropods. Cypermethrin has a low toxicity to earthworms.

Cypermethrin has low mammalian toxicity and should therefore not pose a risk to roosting bats. It also has a low toxicity to birds.

4.1.7 Classification under Directive 80/68/EEC

Cypermethrin is a list I substance according to Directive 80/68/EEC (organohalogen) and should not be indirectly discharged to groundwater.

4.2 CYPERMETHRIN 100 G/L EW

4.2.1 Recommended methods and precautions concerning handling, use, storage, transport or fire.

Handling:

Wear suitable respiratory equipment, protective clothing (coveralls), boots and chemical-resistant gloves. When using do not eat, drink or smoke. Keep only in the original container. Wash hands and exposed skin before meals and after work. Wash any contamination from skin or eyes immediately. Very toxic to aquatic organisms, do not release into the drainage system or watercourses

If it is foreseen that use of a biocidal product within a Member State entails significant risks to companion animals then – at the product authorisation stage – the Member State can introduce risk mitigation measures to alleviate the risk.

Storage:

Store in tightly closed containers. Keep locked up in a safe place and out of reach of children. Keep away from food, drink and animal feeding stuff.

Transport information:

Ensure that the driver is aware of the potential hazards of the load and is trained in the actions to be taken in case of an accident or emergency.

Land transport:

UN No: 3082

H.I. No: 90

ADR/RID: class 9

ADR/RID Packing group: group III

Sea transport:

IMO-IMDG: class 9

IMO Packing group: group III

IMDG-Marine pollution: Marine pollutant

Air transport:

IATA: class 9

IATA Packing group: group III

Fire fighting measures:

Product is not classified as highly flammable, oxidising or explosive.
There are no special fire or explosion hazards.

Special protective equipment:	Wear full protective equipment, including breathing apparatus.
Extinguishing media not to be used:	Do not use water jet or heavy water stream.
Suitable extinguishing media:	For small fires, use carbon dioxide or dry chemical to extinguish flames. Use fluxing salts or dry sand to surround and smother the fire. For large fires use water fog or spray or alcohol foam. Cool exposed containers with water spray or fog.
Specific hazards:	When heated to decomposition, the evolution of carbon monoxide, carbon dioxide, nitrogen oxides, hydrochloric acid and hydrogen cyanide must be anticipated.
Specific protection measures:	Wear full protective equipment when dealing with fire, including breathing apparatus. Ensure area is cleared of all personnel. Do not empty fire control water into drains.

4.2.2 Emergency measures in case of an accident

First aid measures:

Inhalation: Move to fresh air and call a doctor. If breathing has stopped administer artificial respiration.

Skin contact: Remove contaminated clothing. Wash affected area thoroughly with plenty of water. If symptoms persist consult a doctor.

Eye contact: Rinse eyes immediately with copious amounts of water for at least 15 minutes holding eyelids open. Seek medical attention immediately.

Ingestion: Wash out mouth with water. DO NOT INDUCE VOMITING! If swallowed, seek medical advice immediately and show the container or label.

Antidotes and treatment:

No specific antidote. Treat symptomatically.

Environmental precautions:

Accidental release:

Prevent entry into the drainage system or watercourses. If contamination of drains or watercourses is unavoidable, warn the local water/environmental authority immediately.

Methods for cleaning application equipment:

Application equipment should be cleaned with water and detergent. Do not allow cleaning water to enter the drainage system or watercourses.

Procedures for cleaning up a spillage:

Absorb spillage onto suitable absorbent material and transfer into secure containers for safe disposal at an official waste disposal site.

4.2.3 Disposal considerations

Recommendations: Avoid release to the environment
Contaminated packaging: Incinerate. Dispose in a safe manner in accordance with local/national regulations.

4.3 ADDITIONAL LABELLING ELEMENT

4.3.1 Measures to protect animals

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

Justification: Cats are more sensitive to pyrethroids than others animals. Generally for pets, the health risk would be comparable to these for children and infant. In the case of cats, they have a slower metabolism for pyrethroids and intoxication are very common. Since risk for secondary exposure to infants and toddler is not acceptable, the pet access of treated area should also be forbidden.

4.3.2 Additional precautionary measure for humans

Based on the toxicological properties of cypermethrin and other pyrethroids, the following sentence is highly advised on the label: “THE PRODUCT CONTAINS/ cypermethrin. May cause paraesthesia.”.

5 REFERENCES

Please refer to the single list of reference (doc RefList_DocII_PT18)